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**Fuzzy logic based solutions for the management of  
uncertainty-biased process control of fermentative systems**

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*Meinen Eltern*

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## Publications

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2. Birle, S., Hussein, M. A., & Becker, T. (2015). On-line yeast propagation process monitoring and control using an intelligent automatic control system. *Engineering in Life Sciences*, 15(1), 83-95.
3. Birle, S., Hussein, M. A., & Becker, T. (2016). Management of uncertainty by statistical process control and a genetic tuned fuzzy system. *Discrete Dynamics in Nature and Society*. doi:10.1155/2016/1548986.
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*Poster presentations*

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Birle, S., Hussein, M. A., Becker, T.: Process Analytical Technology – A paradigm change of systematic process evaluation and product release, DECHEMA-Infotag: "Von der Datenflut zum Erkenntnisgewinn - der richtige Umgang mit (Bio)-Prozessdaten". Frankfurt am Main, 2013-10-29.

## Contents

<b>Acknowledgements (Danksagung)</b> .....	<b>I</b>
<b>Publications</b> .....	<b>II</b>
<b>Conference contributions</b> .....	<b>III</b>
<b>Contents</b> .....	<b>V</b>
<b>Abstract</b> .....	<b>1</b>
<b>Zusammenfassung</b> .....	<b>2</b>
<b>1 Introduction</b> .....	<b>3</b>
1.1 About precision - A sense of uncertainty, fuzziness and expert systems .....	3
1.1.1 The importance of uncertainty .....	3
1.1.2 The role of fuzzy logic and fuzzy-based expert systems .....	5
1.2 The importance of negative experience.....	20
1.3 Getting tuned – Genetic optimization versus trial and error.....	24
1.4 A brief look on supervision and control of yeast propagation ( <i>Saccharomyces cerevisiae</i> sp.).....	30
1.5 The scope and motivation of the thesis .....	31
<b>2 Summary of results</b> .....	<b>32</b>
2.1 Paper summary .....	32
2.2 Paper copies .....	36
2.2.1 Fuzzy logic control and soft sensing applications in food and beverage processes .....	36
2.2.2 On-line yeast propagation process monitoring and control using an intelligent automatic control system.....	52
2.2.3 Management of uncertainty by statistical process control and a genetic tuned fuzzy system.....	65
2.2.4 Incorporation of negative rules and evolution of a fuzzy controller for yeast fermentation process .....	77

<b>3</b>	<b>Discussion and outlook .....</b>	<b>87</b>
<b>4</b>	<b>References .....</b>	<b>94</b>

## Abstract

The emergence and the progression of novel production concepts such as the PAT initiative in 2004 is leading to a continually increasing degree of automation in the area of life sciences, and in particular in the food industry. With respect to these concepts, the demand for increased productivity through the validation and release of process and production sections in real time while complying with GMP and HACCP concepts in terms of process safety and product quality initially appears to be difficult to meet. In order to meet both expectations, intelligent strategies for process monitoring and control as essential components of a holistic automation concept are required. A major challenge for their implementation are biological process systems such as fermentations, which are essential for the production of a variety of foods. Their high complexity and momentum in the form of non-linearity, time variance and often very sluggish system response cannot be comprehensively modeled from a scientific perspective and therefore lead to uncertainties which are very difficult to master with the traditional methods of process control. Moreover, the uncertainty can even be increased by the fact that in relation to process monitoring essential input variables and process states such as the biomass concentration can be measured online only indirectly and with a corresponding inaccuracy. From this motivation an online-enabled system for process monitoring and control on the basis of fuzzy logic was developed in the present work that makes the above-mentioned uncertainties manageable. In order to investigate and demonstrate the system's performance, the process of yeast propagation (*Saccharomyces cerevisiae* sp.) under restricted growth conditions was chosen. The linking of statistical process control, classical fuzzy control and innovative methods of genetic set optimization demonstrates the potential of this strategy. Moreover, a further improvement of the control performance could be achieved by the inclusion of negative experiential knowledge. In summary, the results comply with similar findings of other research groups and confirm that the inherent uncertainty of biological processes becomes manageable through the integration of acquired knowledge (experience) and numerical optimization into a fuzzy-logic-based digital framework for process control.

## Zusammenfassung

Das Aufkommen und der Einzug innovativer Produktionskonzepte wie der PAT-Initiative im Jahre 2004 führen zu einem nachhaltig zunehmenden Automatisierungsgrad im Life Science Bereich und insbesondere auch in der Lebensmittelindustrie. Um der aus diesen Konzepten entsprungenen zunächst scheinbar ambivalenten Forderung nach Produktivitätssteigerung durch Validierung und Freigabe von Prozess- und Produktionsabschnitten in Echtzeit einerseits, aber auch der Einhaltung bestehender GMP- und HACCP-Konzepte hinsichtlich Prozesssicherheit und Produktqualität andererseits einhalten zu können, sind intelligente Strategien der Prozesskontrolle und -regelung als wesentliche Bestandteile eines holistischen Automatisierungskonzeptes zwingend erforderlich. Als große Herausforderung für deren Umsetzung erweisen sich biologische Prozesssysteme wie Fermentationen, welche für die Herstellung einer Vielzahl an Lebensmitteln von essentieller Bedeutung sind. Ihre hohe Komplexität und Eigendynamik in Form von Nichtlinearität, Zeitvarianz und oftmals einer sehr trägen Systemantwort sind aus wissenschaftlicher Sicht nicht vollständig modellierbar und führen daher zu Unsicherheiten, welche mit den klassischen Möglichkeiten der Prozessregelung nur sehr schwer zu beherrschen sind. Darüber hinaus vergrößert sich die Unsicherheit durch den Umstand, dass seitens der Prozessüberwachung wesentliche Eingangsgrößen und Prozesszustände wie die Biomassekonzentration online nur indirekt und mit entsprechender Ungenauigkeit gemessen werden können. Aus dieser Motivation heraus wurde in der vorliegenden Arbeit auf Basis von fuzzy logic ein online-fähiges System zur Prozessüberwachung und -regelung entwickelt, welches die o.g. Unsicherheiten beherrschbar macht. Zur Untersuchung und Demonstration der Systemperformance wurde der Prozess der Propagation von *Saccharomyces cerevisiae* sp. unter limitierenden Wachstumsbedingungen gewählt. Die Verknüpfung statistischer Prozesskontrolle, klassischer Fuzzyregelung und innovativer Methoden der genetischen Setoptimierung belegt das Potential dieser Strategie. Darüber hinaus konnte durch die Einbindung von negativem Erfahrungswissen eine weitere Verbesserung der Regelgüte erreicht werden. Zusammengefasst zeigen die Ergebnisse, dass durch die Einbindung von Erfahrungswissen und numerischer Optimierung in ein digitales Framework zur Prozessregelung auf Basis von fuzzy logic, die inhärente Unsicherheit biologischer Prozesse beherrschbar wird.

# 1 Introduction

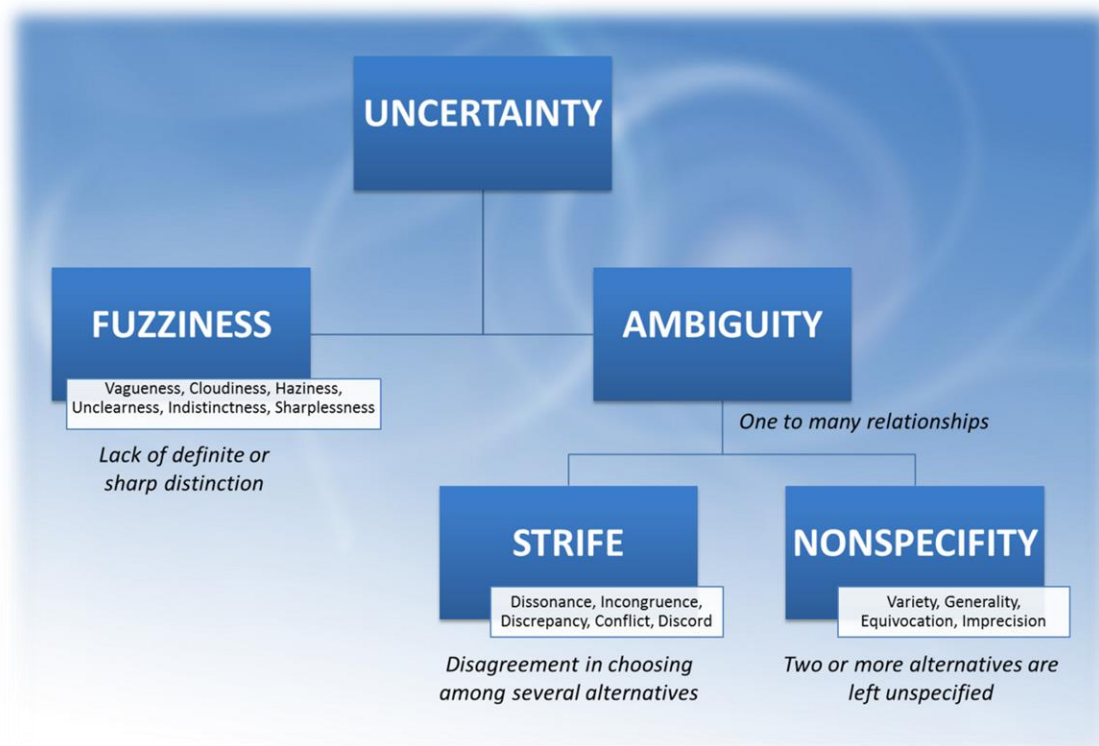
## 1.1 About precision – A sense of uncertainty, fuzziness, and expert systems

### 1.1.1 The importance of uncertainty

The phenomenon of uncertainty is present in almost every real-world problem and, in general, uncertainty is inseparable from measurement. Moreover, it comes from a combination of measurement limitations with sensors and unavoidable errors in measurement. With respect to cognitive problems, uncertainty emerges from the vagueness and ambiguity inherent in natural languages and, therefore, uncertainty is essential to human beings at all levels of their interaction with the real world (Celikyilmaz and Turksen 2009). Therefore it is not surprising that uncertainty has moved into the focus of engineers and scientists over the last decades. Following the interpretation of (Ayyub and Gupta 2012) uncertainty can be viewed as a human-related subjective notion depending on the quantity and quality of information which is available to a human being about a system or its behavior that the human being wants to describe, predict, or prescribe. The sources of uncertainty are manifold and its causes can be of diverse nature. A very comprehensive and detailed discussion about uncertainty is given by (Klir 1987; Klir and Folger 1988; Klir 1995; Klir and Wierman 1999; Klir 2005). In (Klir and Wierman 1998) they state that uncertainty is a result of information deficiency, where information may be incomplete, fragmentary, not fully reliable, vague, contradictory, or deficient in some different way. Further, uncertainty is divided into two major classes, fuzziness and ambiguity, where ambiguity contains non-specificity and strife. A conceptual illustration of this division is given in Figure 1. The appearance of uncertainty is an event which is inherently present in biologically based processes of food production (e.g. fermentations). The reasons for its occurrence are manifold. Variations in raw materials due to naturally varying harvest conditions or unpredictable changes in the physiological state and behavior of the used microorganisms are just a few examples. With respect to this work, the bioprocess of yeast propagation was investigated. The process is subjected to all classes of uncertainty, which has an immediate effect on the observability and controllability of the process. In particular, most sources of uncertainty are not directly measurable.

For example, the cause of unexpected process performance reflected in the provided sensor information can be ambiguous, as it might not be clear if it is due to the physiological state of the yeast or if there are limitations in the metabolism because of raw material variation and nutrient shortage in the substrate. The corresponding control decisions of how to react to abnormal process behavior in common practice is therefore rather made on a fuzzy basis than on concrete knowledge. Because of this and due to the fact that the process of yeast propagation is of crucial importance for the final product quality in brewing, the management of uncertainty with respect to monitoring and control was the major motivation of this work. A more detailed description of the process itself is given in section 1.4 of this thesis.

Numerous approaches and methods have been published over the last 50 years to model and analyze uncertainty (Zadeh 1965; Dempster 1967; Dempster 1967; Sugeno 1974; Shafer 1976; Negoita, Zadeh et al. 1978), ranging from the theory of fuzzy sets and fuzzy measures to evidence theory and possibility theory. In particular, fuzzy logic provides an important tool for the development of a better understanding of how to handle (process) uncertainty (Celikyilmaz and Turksen 2009).



**Figure 1: Partition of uncertainty (Klir and Wierman 1998)**



In this regard, recent approaches also try to combine fuzzy logic and methods of statistical process control that allow the visualizing and detecting of changes and the defecting or deterioration of essential quality attributes of the process through the use of control charts (Cheng 2005; Gülbay and Kahraman 2006; Gülbay and Kahraman 2007; Senturk and Erginel 2009; Huang, Chen et al. 2012; Sorooshian 2013; Wang, Li et al. 2014; Zabihinpour, Ariffin et al. 2014; Gülbay and Kahraman 2016). However, the majority of these approaches are built as a pure monitoring system and there is only little investigation that actually takes into account how to integrate the information that is delivered by statistical process control into a real feedback control system in order to keep the process within predefined statistical borders. This topic is reviewed and presented by (Lowry and Montgomery 1995; Montgomery and Woodall 1999; Woodall, Spitzner et al. 2004; Woodall and Montgomery 2014) for multivariate approaches and by (Cheng and Thaga 2006) on a univariate basis. Therefore, this shortcoming, which is also mentioned by (Montgomery, Keats et al. 1994; Montgomery and Woodall 1999; Stoumbos, Reynolds Jr et al. 2000; Woodall 2000), was addressed in this work by combining statistical process information, evolutionary optimization, and fuzzy-logic-based feedback control, as well (section 2.2.3).

### **1.1.2 The role of fuzzy logic and fuzzy-based expert systems**

A turning point in the evolution of the modern concept of uncertainty occurred with the introduction of the fuzzy logic theory by Lotfi A. Zadeh in 1965 (Zadeh 1965). In this paper he presents the theory of *fuzzy sets*, which are sets with imprecise boundaries. The individual characteristic of fuzzy sets is that membership in a fuzzy set is not a matter of acceptance or denial, but rather a matter of degree. However, despite its undoubted advantages for control applications in expert systems, which is one of the major topics of this work and which will be discussed later on, the theory of fuzzy logic has been quite controversial. However, to date there are more than 53,000 fuzzy-logic-related papers listed in the INSPEC database and over 15,000 in the Math Science Net database, showing the immense impact since its conception (Zadeh 2008). Zadeh himself describes the notable capabilities of fuzzy logic as follows (Zadeh 2008):

*“..Fuzzy logic may be viewed as an attempt at formalization/mechanization of two remarkable human capabilities. First, the capability to converse, reason and make rational decisions in an environment of imprecision, uncertainty, incompleteness of*

*information, conflicting information, partiality of truth and partiality of possibility – in short, in an environment of imperfect information. And second, the capability to perform a wide variety of physical and mental tasks without any measurements and any computations.”*

As fuzziness is present in many areas of daily life, the capabilities of fuzzy logic reveal solutions to a wide range of real-world engineering problem domains like process control (Ross 2009; Chandrasekaran, Muralidhar et al. 2010; Azadegan, Porobic et al. 2011; Nguyen, Gadhamshetty et al. 2015). The majority of real complex system control problems are still subjected to human interactions. Hence, the application of control theory with respect to complex control issues requires a formal understanding of how a human operator understands the system under consideration and how he acts when controlling it. From this perspective the principle of incompatibility between precision and maintenance of understandability when representing a system is described as follows (Zadeh 1973): *“As the complexity of a system increases, our ability to make precise and yet significant statements about its behavior diminishes until a threshold is reached beyond which precision and significance (or relevance) become almost mutually exclusive characteristics.”*

Therefore, a dedicated approach for representing human-originated information in a flexible way is needed. And with respect to the scope of this work, this is where fuzzy logic comes into focus to close the aforementioned trade-off regarding complex control issues and systems (Filev 1991). In this context, fuzzy-based expert systems have emerged. Commonly, such systems have a nontrivial inferential capability and, in particular, have the capability to infer from premises which are imprecise, incomplete, or not totally reliable (Zadeh 1983). Probably one of the most important strengths is that they allow numerical information stemming from some kind of measuring instrument to be combined with expert knowledge, which is in other words the experience of the plant operator of how to best control the system. Usually, this is accomplished using a set of control rules that are delivered by the operator or that are derived from observing his way of controlling the system. Fuzzy logic then offers a quite straightforward method to turn human control decisions into a numerical continuous control law. More precisely, for a given numerical input, an inference step takes place that results in a fuzzy output set, which is then

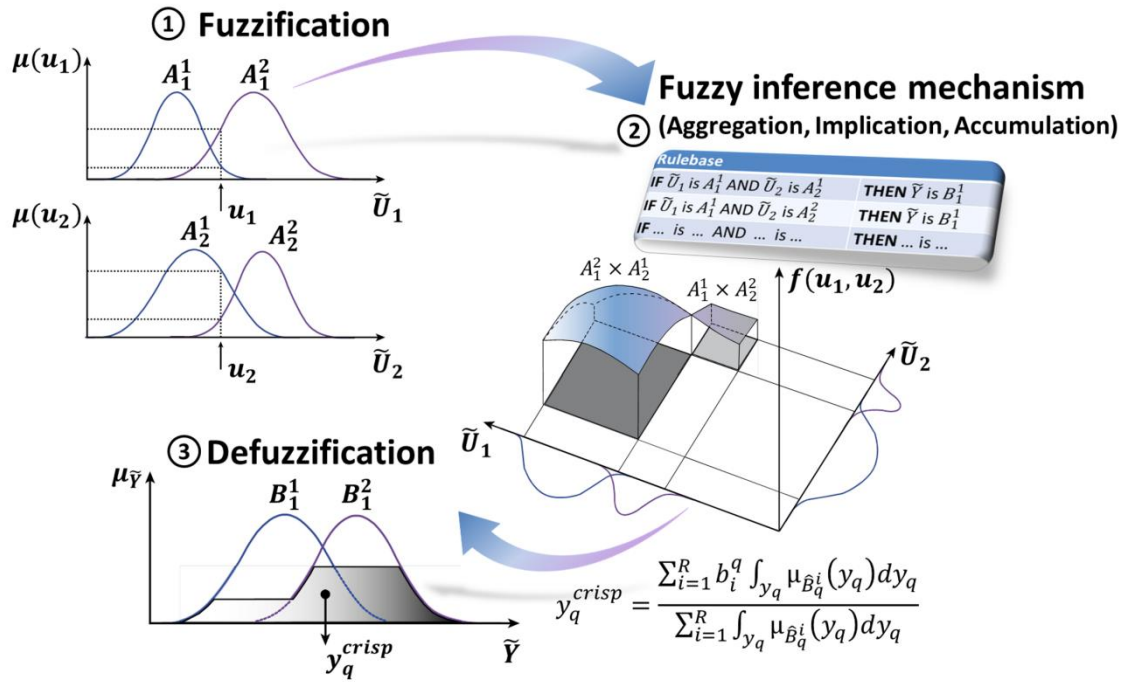


Figure 2: Schematic representation of information processing in a Mamdani-type fuzzy controller. ① Fuzzification of crisp input values  $u_1$  and  $u_2$  into the linguistic domain of the fuzzy variables  $\tilde{U}_1$  and  $\tilde{U}_2$ . By the use of Gaussian-type membership functions the crisp input values are mapped onto the distinct fuzzy sets  $A_1^1, A_1^2$  for  $\tilde{U}_1$  and  $A_2^1, A_2^2$  for  $\tilde{U}_2$ . ② shows the inference mechanism comprising the fuzzy relations and the “knowledge” of how to best control the system in the form of a rule base. The inference mechanism comprises the methods of aggregation, implication, and accumulation. The aggregation executes all the AND-conjunctions of the premise part and combines the individual membership degrees of each rule to an overall degree of fulfillment. The implication determines a fuzzy conclusion based on the aggregation result (firing degree of a rule). The accumulation denotes the OR-conjunction of all firing degrees of all rules (overall conclusion of all rules). ③ represents the defuzzification part, which is a back transformation from the linguistic conclusions drawn by the inference mechanism (overall implied fuzzy set) into a crisp output  $y_q^{crisp}$ . In this case the COG method is applied. Here,  $\mu_{\tilde{Y}}$  denotes the membership degree of the output fuzzy variable  $\tilde{Y}$ . Further,  $R$  is the number of rules,  $b_i^q$  is the center of area of the output membership function  $B_q^p$  assigned to the implied fuzzy set  $\hat{B}_q^i$  for the  $i^{th}$  rule  $(j, k, \dots, l; p, q)_i$ .  $\int_{y_q} \mu_{\hat{B}_q^i}(y_q) dy_q$  is the area under  $\mu_{\hat{B}_q^i}(y_q)$ .

retransformed into a precise control value using a distinct method of defuzzification. Figure 2 represents the inner structure of a Mamdani-type fuzzy controller (Mamdani and Assilian 1975) for use in an expert system.

In its classical structure the controller consists of four main parts, namely rule base, fuzzification, inference mechanism, and defuzzification (Passino, Yurkovich et al. 1998). The rule base contains the knowledge, in the form of a set of if-then rules, of

how best to control the system. The inference mechanism evaluates which control rules are relevant at the current point in time and then decides in dependency of the applied method of implication what the input to the plant should be by producing fuzzy conclusions (implied fuzzy sets). Therefore, the fuzzy system converts the numeric inputs  $u_i \in \mathcal{U}_i$  into fuzzy sets. If  $\mathcal{U}_i^*$  denotes all possible fuzzy sets defined on  $\mathcal{U}_i$  and given  $u_i \in \mathcal{U}_i$ , then fuzzification transforms  $u_i$  to a fuzzy set denoted as  $\hat{A}_i^{fuz}$  defined on  $\mathcal{U}_i$ . The transformation is computed by the fuzzification operator  $\mathcal{F}$ , where  $\mathcal{F}: \mathcal{U}_i \rightarrow \mathcal{U}_i^*$  and  $\mathcal{F}(u_i) = \hat{A}_i^{fuz}$ . The fuzzification interface transforms the numerical inputs into the linguistic domain so that they can be interpreted and compared to the rules in the rule base. And the defuzzification interface converts back the conclusions reached by the inference mechanism into crisp inputs to the plant. In the context of this work, classical fuzzy controllers consisting of a set of rules, fuzzification, min-max-inference mechanism, and defuzzification were developed in the first instance for controlling the process key variables temperature and aeration of the yeast propagation (see section 2.2.2). In order to perform the transformation from crisp into linguistic descriptions and vice versa the fundamental mathematical definitions and formulations that were applied for the establishment of the fuzzy controllers are presented in the following for further understanding:

#### Universes of discourse:

A fuzzy system is a static nonlinear mapping between its inputs and outputs (Passino, Yurkovich et al. 1998). Let us assume that the fuzzy system has inputs  $u_i \in \mathcal{U}_i$  where  $i = 1, 2, \dots, n$  and outputs  $y_i \in \mathcal{Y}_i$  where  $i = 1, 2, \dots, m$ , as shown in Figure 2. The inputs and outputs are crisp (real numbers), not fuzzy sets.  $\mathcal{U}_i$  and  $\mathcal{Y}_i$  are denoted as the universes of discourse (domains) for the inputs  $u_i$  and  $y_i$ , respectively.

#### Linguistic variables and linguistic values:

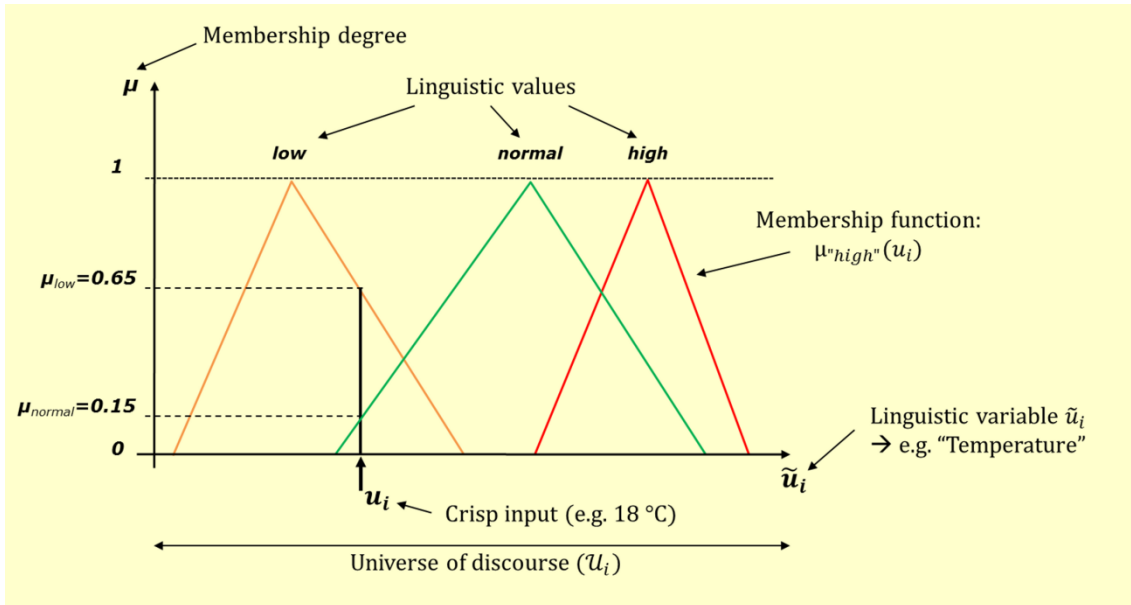
Linguistic variables  $\tilde{u}_i$  and  $\tilde{y}_i$  take on linguistic values that are used to describe characteristics of the variables (Passino, Yurkovich et al. 1998). If there exist  $N$  linguistic values defined over  $\mathcal{U}_i$ , and let  $\tilde{A}_i^j$  denote the  $j^{\text{th}}$  linguistic value of the linguistic variable  $\tilde{u}_i$  defined over  $\mathcal{U}_i$ , then  $\tilde{u}_i$  takes on the elements from the set of linguistic values denoted by

$$\tilde{A}_i = \{\tilde{A}_i^j : j = 1, 2, \dots, N_i\} \quad (1)$$

Analogue for the output, let  $\tilde{B}_i^j$  denote the  $j^{\text{th}}$  linguistic value of the linguistic variable  $\tilde{y}_i$  defined in  $\mathcal{Y}_i$ , then the linguistic variable  $\tilde{y}_i$  takes on elements from the set of linguistic values denoted by

$$\tilde{B}_i = \{\tilde{B}_i^p : p = 1, 2, \dots, M_i\} \quad (2)$$

Figure 3 illustrates the basic elements of the fuzzy logic theory schematically.



**Figure 3: Basic elements of fuzzy logic.** The figure exemplarily shows a fuzzy partition over the universe of discourse  $\mathcal{U}_i$ , which is represented by the horizontal axis.  $\tilde{u}_i$  is a linguistic variable, e.g. “Temperature”, which is defined over  $\mathcal{U}_i$ . The linguistic variable “Temperature” can be divided into several subsets (fuzzy sets), which are assigned to specific linguistic values (e.g. “low”, “normal”, high”). The triangular membership functions define the set of points for which the linguistic values are fixed on  $\mathcal{U}_i$ . Furthermore, the membership functions assign a membership degree  $\mu$  to each crisp input  $u_i$  in the range from 0 to 1.

### Fuzzy sets and membership functions:

A fuzzy set  $A_i^j$  is defined as

$$A_i^j = \left\{ \left( u_i, \mu_{A_i^j}(u_i) \right) \mid u_i \in \mathcal{U}_i \right\} \quad (3)$$

Here,  $\mu_{A_i^j}(u_i)$  is a membership function associated with fuzzy set  $A_i^j$  that maps  $\mathcal{U}_i$  to  $[0,1]$  (Passino, Yurkovich et al. 1998). The most common types that have proven their worth in practical applications are piecewise linear membership functions (triangular,

trapezoidal) and Gaussian bell-shaped membership functions. Their mathematical characterization is as follows:

$$\mu_{A_i^j}(u_i) = \begin{cases} 0: & u_i \leq l; u_i \geq r \\ 1: & u_i = m \\ \frac{u_i-l}{m-l}: & l < u_i < m \\ \frac{r-u_i}{r-m}: & m < u_i < r \end{cases} \quad (4)$$

for triangular-shaped membership functions defined by the parameters  $l$  (left),  $m$  (midth) and  $r$  (right). Figure 4 exemplarily depicts a triangular-shaped membership function for the linguistic variable “Temperature”.

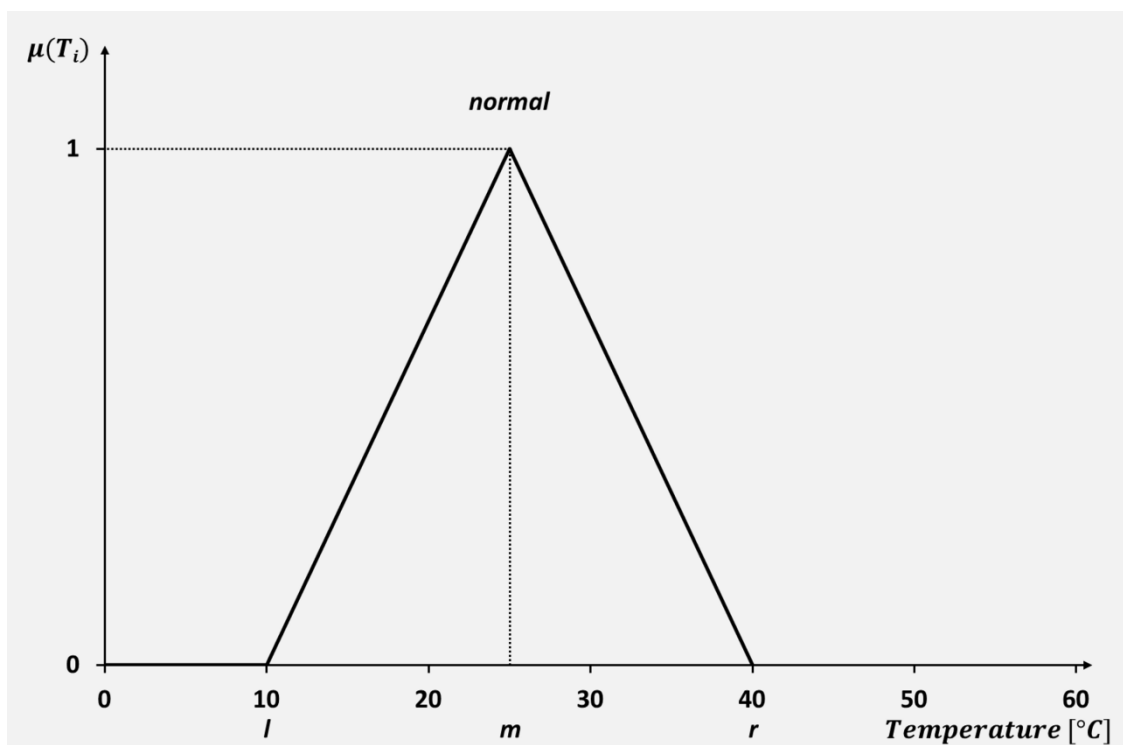


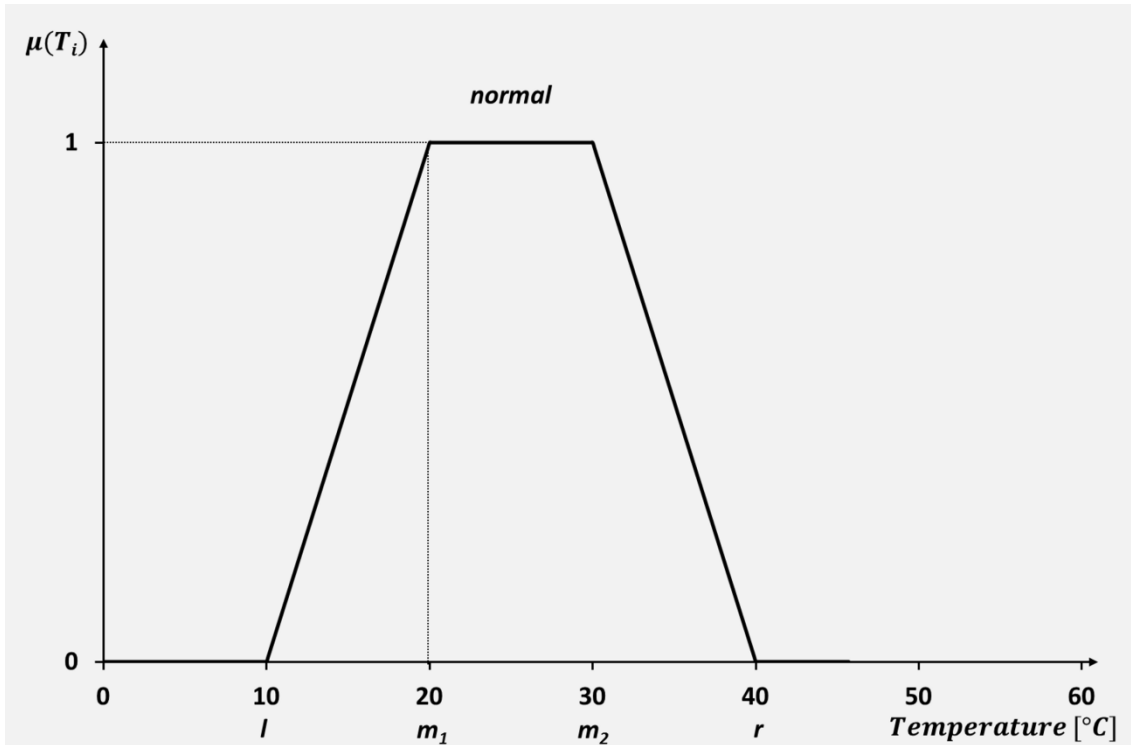
Figure 4: Triangular-shaped fuzzy set. Corresponding to eq. (4) the fuzzy set for the linguistic value “normal” could look as follows:

$$\mu_{normal}(T_i) = \begin{cases} 0: T_i \leq 10; T_i \geq 40 \\ 1: T_i = m = 25 \\ \frac{T_i-10}{15}: 10 < T_i < 25 \\ \frac{40-T_i}{15}: 25 < T_i < 40 \end{cases}$$

In the case of a trapezoidal membership functions:

$$\mu_{A_i^j}(u_i) = \begin{cases} 0: & u_i \leq l; u_i \geq r \\ 1: & m_1 \leq u_i \leq m_2 \\ \frac{u_i-l}{m_1-l}: & l < u_i < m_1 \\ \frac{r-u_i}{r-m_2}: & m_2 < u_i < r \end{cases} \quad (5)$$

Hence, the parameters are given by  $l$  (left),  $m_1$  (midpoint 1),  $m_2$  (midpoint 2) and  $r$  (right). Figure 5 exemplarily depicts a trapezoidal-shaped membership function for the linguistic variable “Temperature”.



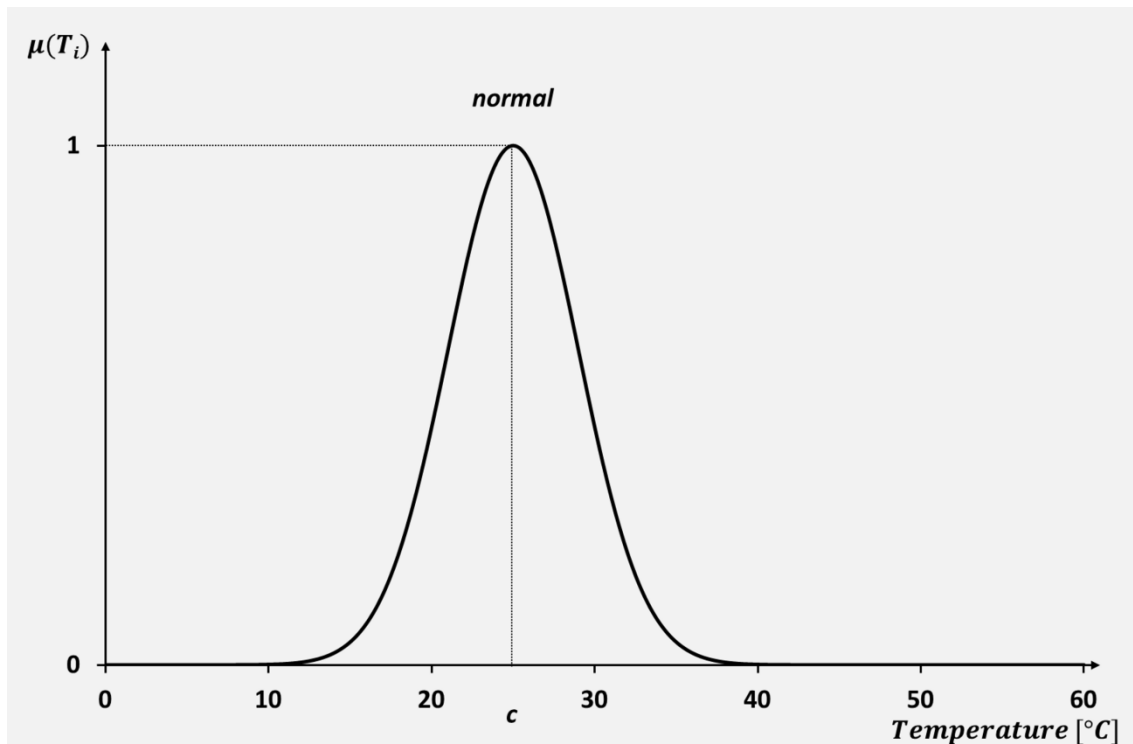
**Figure 5: Trapezoidal-shaped membership function. Corresponding to eq. (5) the fuzzy set for the linguistic value “normal” could look as follows:**

$$\mu_{normal}(T_i) = \begin{cases} 0: T_i \leq 10; T_i \geq 40 \\ 1: 20 \leq T_i \leq 30 \\ \frac{T_i-10}{10}: 10 < T_i < 20 \\ \frac{40-T_i}{10}: 30 < T_i < 40 \end{cases}$$

The mathematical expression for a Gaussian function is

$$\mu_{A_i^j}(u_i) = \exp\left(-\frac{1}{2}\left(\frac{u_i-c}{\sigma}\right)^2\right) \quad (6)$$

Here,  $c$  is the center of the function and  $\sigma > 0$  determines the spread or width of the function. Figure 6 exemplarily illustrates a Gaussian-type membership function for the linguistic variable “Temperature”.



**Figure 6: Gaussian-type membership function. Corresponding to eq. (6) the fuzzy set for the linguistic value “normal” could look as follows:  $\mu_{normal}(T_i) = \exp\left(-\frac{1}{2}\left(\frac{T_i-25}{4}\right)^2\right)$ .**

The support of a fuzzy set  $A_i^j$  is the crisp set of all points  $u_i$  in  $\mathcal{U}_i$  such that  $\mu_{A_i^j}(u_i) > 0$  and a fuzzy set whose support is a single point in  $\mathcal{U}_i$  with  $\mu_{A_i^j}(u_i) = 1.0$  is referred to as fuzzy singleton. As this work makes heavy use of set-theoretic and logical operations on fuzzy sets, the most essential concepts will be briefly explained in the following. Let  $A_i^1$  and  $A_i^2$  be two fuzzy sets in  $\mathcal{U}_i$  with membership functions  $\mu_{A_i^1}(u_i)$  and  $\mu_{A_i^2}(u_i)$ , respectively.  $A_i^1$  is also defined a fuzzy subset of  $A_i^2$  given by  $A_i^1 \subset A_i^2$ , if  $\mu_{A_i^1}(u_i) \leq \mu_{A_i^2}(u_i)$  for all  $u_i \in \mathcal{U}_i$ . The set theoretic operations of union, intersection, and complement for fuzzy sets are defined via their membership functions. More specifically, see the following (Lee 1990).

#### Fuzzy intersection:

The intersection of fuzzy sets  $A_i^1$  and  $A_i^2$ , for all  $u_i \in \mathcal{U}_i$ , is a fuzzy set denoted by  $A_i^1 \cap A_i^2$ , with a membership function defined by either of the following two methods (Passino, Yurkovich et al. 1998):



a) *Minimum*: Here, the minimum of the membership values are

$$\mu_{A_i^1} \cap \mu_{A_i^2} = \min \left\{ \mu_{A_i^1}(u_i), \mu_{A_i^2}(u_i) \mid u_i \in \mathcal{U}_i \right\} \quad (7)$$

b) *Algebraic product*: Here, the product of the membership values are

$$\mu_{A_i^1} \cap \mu_{A_i^2} = \left\{ \mu_{A_i^1}(u_i) \mu_{A_i^2}(u_i) \mid u_i \in \mathcal{U}_i \right\} \quad (8)$$

For the intersection of fuzzy sets (Zadeh 1965) the min-operator and the Algebraic product are suggested. However, there exist many other methods like the Einstein product, the Hamacher product, or the Yager operator. As their description would exceed the scope of this work, the reader is referred to (Lee 1990; Klir and Yuan 1995; Zimmermann 2001) for a comprehensive and detailed analysis. In fuzzy logic theory intersection operators like the min-operator that are used to represent the “and” operation belong to the group of triangular norms or t-norms. A general representation for the intersection of two fuzzy sets is given by  $\mu_{A_i^1}(u_i) * \mu_{A_i^2}(u_i)$ , where  $*$  is the symbol for a t-norm.

#### Fuzzy union:

The union of fuzzy sets  $A_i^1$  and  $A_i^2$ , for all  $u_i \in \mathcal{U}_i$ , is a fuzzy set denoted by  $A_i^1 \cup A_i^2$ , with a membership function defined by either of the following two methods (Passino, Yurkovich et al. 1998):

a) *Maximum*: Here, the maximum of the membership values are

$$\mu_{A_i^1} \cup \mu_{A_i^2} = \max \left\{ \mu_{A_i^1}(u_i), \mu_{A_i^2}(u_i) \mid u_i \in \mathcal{U}_i \right\} \quad (9)$$

b) *Algebraic sum*: Here, the algebraic sum of the membership values are

$$\mu_{A_i^1} \cup \mu_{A_i^2} = \left\{ \mu_{A_i^1}(u_i) + \mu_{A_i^2}(u_i) - \mu_{A_i^1}(u_i) \mu_{A_i^2}(u_i) \mid u_i \in \mathcal{U}_i \right\} \quad (10)$$

Corresponding to the class of t-norms, a general class of aggregation operators for the union of fuzzy sets called triangular conorms or t-conorms was defined (Zadeh 1965; Dubois and Prade 1989; Mizumoto 1989). The union is used to represent the “or” operation. Thus, a general representation for the union of two fuzzy sets is given by  $\mu_{A_i^1}(u_i) \oplus \mu_{A_i^2}(u_i)$ , where  $\oplus$  is the symbol for a t-conorm.

#### Fuzzy complement:

For all  $u_i \in \mathcal{U}_i$ , the complement (“not”) of a fuzzy set  $A_i^1$  with a membership function  $\mu_{A_i^1}(u_i)$  has a membership function  $\mu_{\bar{A}_i^1}(u_i)$  given by

$$\mu_{\bar{A}_i^1}(u_i) = 1 - \mu_{A_i^1}(u_i) \quad (11)$$

Figure 7 illustrates schematically the different operators for the fuzzy intersection, union, and complement.

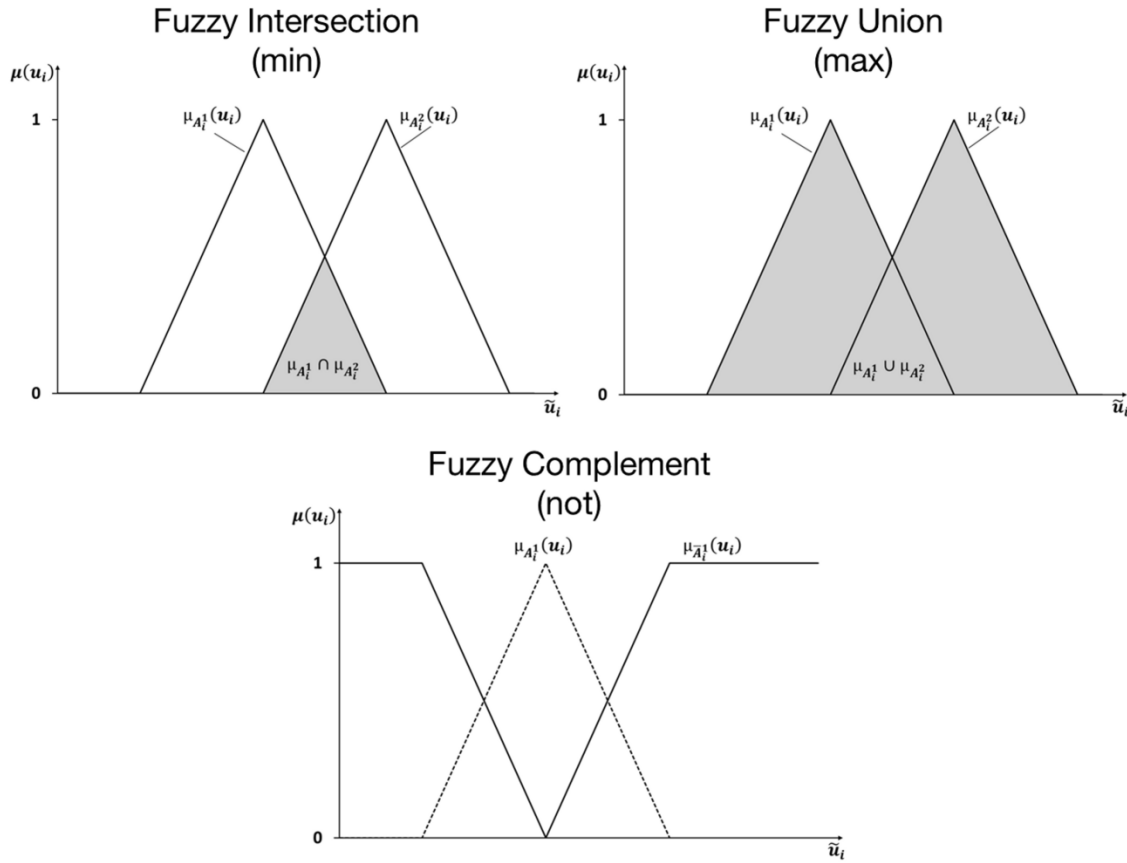


Figure 7: Fuzzy set operations using the minimum, maximum, and the not-operator.

#### Cartesian product:

If  $A_1^j, A_2^k, \dots, A_n^l$  are fuzzy sets in different universes of discourse  $\mathcal{U}_1, \mathcal{U}_2, \dots, \mathcal{U}_n$ , respectively, the Cartesian product of  $A_1^j \times A_2^k \times \dots \times A_n^l$  is a fuzzy set with the membership function

$$\mu_{A_1^j \times A_2^k \times \dots \times A_n^l}(u_1, u_2, \dots, u_n) = \mu_{A_1^j}(u_1) * \mu_{A_2^k}(u_2) * \dots * \mu_{A_n^l}(u_n) \quad (12)$$

#### Fuzzy relations:

Fuzzy relations are fuzzy subsets of  $\mathcal{U} \times \mathcal{Y}$ , which is a mapping from  $\mathcal{U} \rightarrow \mathcal{Y}$ . Let  $\mathcal{U}, \mathcal{Y} \subseteq \mathbb{R}$  be universal sets, then

$$\tilde{R} = \{((u, y), \mu_{\tilde{R}}(u, y)) | (u, y) \in \mathcal{U} \times \mathcal{Y}\} \quad (13)$$

is called a fuzzy relation on  $\mathcal{U} \times \mathcal{Y}$ . Therefore, it is straightforward to set up fuzzy relations by connecting fuzzy sets that are defined over different universes of discourse by using if-then rules. The mapping of the inputs to the outputs for a fuzzy system is characterized by a set of *condition*  $\rightarrow$  *action* rules, or in *modus ponens* (If-Then) form, which will be explained in the following section. A general form is given by

***If premise Then consequent*** (14)

Commonly, the inputs of the fuzzy system are assigned to the premise, and the outputs are associated with the consequent. Then, the standard form of a multi-input single-output (MISO) of a linguistic rule is given by

***If  $\tilde{u}_1$  is  $\tilde{A}_1^j$  and  $\tilde{u}_2$  is  $\tilde{A}_2^k$  and, ..., and  $\tilde{u}_n$  is  $\tilde{A}_n^l$  Then  $\tilde{y}_q$  is  $\tilde{B}_q^p$***  (15)

### Principles of approximate reasoning:

In fuzzy logic and approximate reasoning, there exist two important fuzzy implication inference rules which had to be considered in this work as well. The first one is the generalized modus ponens (GMP) by (Zadeh 1975). He defined a methodology known as Compositional Rule of Inference (CRI), which is used to infer fuzzy consequents utilizing GMP. Generally, GMP is defined as follows:

premise 1:  $u$  is  $A'$ ,

premise 2: if  $u$  is  $A$  then  $y$  is  $B$ ,

consequence:  $y$  is  $B'$

This principle is of fundamental importance in the fuzzy inference mechanism. The first function of the inference stage is to determine the degree of firing of each rule in the rule base (matching). Suppose that at some time we get inputs  $u_i$ ,  $i = 1, 2, \dots, n$ , and fuzzification produces  $\hat{A}_1^{fuz}, \hat{A}_2^{fuz}, \dots, \hat{A}_n^{fuz}$ , which are the fuzzy sets representing the inputs. There are then two basic steps to matching (Passino, Yurkovich et al. 1998):

1) Combine inputs with rule premises:

$$\begin{aligned} \mu_{\hat{A}_1^j}(u_1) &= \mu_{A_1^j}(u_1) * \mu_{\hat{A}_1^{fuz}}(u_1) \\ \mu_{\hat{A}_2^k}(u_2) &= \mu_{A_2^k}(u_2) * \mu_{\hat{A}_2^{fuz}}(u_2) \\ &\vdots \\ &\vdots \\ \mu_{\hat{A}_n^l}(u_n) &= \mu_{A_n^l}(u_n) * \mu_{\hat{A}_n^{fuz}}(u_n) \end{aligned}$$

2) Determine which rules are fired:

$$\mu_i(u_1, u_2, \dots, u_n) = \mu_{\hat{A}_1^j}(u_1) * \mu_{\hat{A}_2^k}(u_2) \dots * \mu_{\hat{A}_n^l}(u_n) \quad (16)$$

The second function of the inference stage is to determine the degree to which each rule's recommendation is to be weighted in arriving at the final decision and to determine an implied fuzzy set corresponding to each rule (inference step). There exist two possibilities to do the inference step:

a) Determine implied fuzzy sets:

Compute the implied fuzzy set  $\hat{B}_q^i$  for the  $i^{\text{th}}$  rule  $(j,k,\dots,l;p,q)_i$  with membership function

$$\mu_{\hat{B}_q^i}(y_q) = \mu_i(u_1, u_2, \dots, u_n) * \mu_{B_q^p}(y_q) \quad (17)$$

The implied fuzzy set  $\hat{B}_q^i$  determines the certainty level that the output should be a specific crisp output  $y_q$  within the universe of discourse  $\mathcal{Y}_q$ .

b) Determine the overall implied fuzzy set:

As an alternative, calculate the overall implied fuzzy set  $\hat{B}_q$  with membership function

$$\mu_{\hat{B}_q}(y_q) = \mu_{\hat{B}_q^1}(y_q) \oplus \mu_{\hat{B}_q^2}(y_q) \oplus \dots \oplus \mu_{\hat{B}_q^R}(y_q) \quad (18)$$

which provides the conclusion reached considering all rules in the rule base at the same time.

The fuzzy implication inference is based on the sup-star compositional rule of inference for approximate reasoning suggested by Zadeh in (Zadeh 1973) in order to compute  $\mu_{\hat{B}_q}(y_q)$ . In this terminology the “sup” corresponds to the  $\oplus$  operation, and the “star” corresponds to  $*$ . The compositional rule of inference (Zadeh 1965; Zadeh 1973; Klir and Yuan 1995) is the special case when maximum is used for  $\oplus$  and minimum is used for  $*$ . The justification for using that special convention for the inference step is that we can be no more certain about our conclusions than we are about our premises. This corresponds to the Mamdani implication (Mamdani and Assilian 1975; Mamdani 1977; Mamdani and Gaines 1981) or max-min-inference mechanism, which is well established in practical fuzzy control applications (Iancu and Popirlan 2010; Piltan, Haghghi et al. 2011; Precup and Hellendoorn 2011; Chen, Yan et al. 2014). In other words, the aggregation of the premises of all rules is done via the AND-operator (minimum) and the accumulation of the suggestions of all rules to form the overall implied fuzzy set is accomplished using the OR-operator (maximum).

The second important form of approximate reasoning is the generalized modus tollens:

premise 1:  $y$  is  $B'$ ,

premise 2: if  $u$  is  $A$  then  $y$  is  $B$ ,

consequence:  $u$  is  $A'$ .

It is closely related to the backward goal-driven inference which is commonly used in expert systems, especially when it comes to the incorporation of negative rules, which is a core topic of this work and will be introduced later.

### Defuzzification principles:

The task of the defuzzification is to convert the collection of recommendations of all rules back into a crisp output. For a rule base consisting of  $R$  rules there are  $R$  implied fuzzy sets, one from each rule, each recommending a particular output. In order to compute one crisp output  $y_q^{crisp}$  from all of these recommendations besides center average defuzzification, the center of gravity method is the most widely used one (Braae and Rutherford 1979):

$$y_q^{crisp} = \frac{\sum_{i=1}^R b_i^q \int_{y_q} \mu_{\hat{B}_q^i}(y_q) dy_q}{\sum_{i=1}^R \int_{y_q} \mu_{\hat{B}_q^i}(y_q) dy_q} \quad (19)$$

Here,  $R$  denotes the number of rules,  $b_i^q$  is the center of area of the membership function of  $B_q^p$  associated with the implied fuzzy set  $\hat{B}_q^i$  for the  $i^{\text{th}}$  rule ( $j, k, \dots, l; p, q$ ), and  $\int_{y_q} \mu_{\hat{B}_q^i}(y_q) dy_q$  is the area under  $\mu_{\hat{B}_q^i}(y_q)$ .

The disadvantage is the expensive-to-calculate integration in the determination of the centroid. If one is satisfied with an approximation, the integral can be replaced by a sum over pre-computed centroids  $b_i$  of the individual terms, weighted by the membership degrees  $\mu_i$ :

$$y_q^{crisp} = \frac{\sum_{i=1}^R b_i \mu_i}{\sum_{i=1}^R \mu_i} \quad (20)$$

Hence, in the case of the center area method the calculation is:

$$y_q^{crisp} = \frac{\sum_{i=1}^R b_i^q \sup_{y_q} \{ \mu_{\hat{B}_q^i}(y_q) \}}{\sum_{i=1}^R \sup_{y_q} \{ \mu_{\hat{B}_q^i}(y_q) \}} \quad (21)$$

Here, “sup” is the “supremum” and can be interpreted as the maximum value. In conclusion, for each fuzzy system an explicit mathematical formulation can be set up. In the case of center-average defuzzification, triangular membership functions and product operation to represent the conjunction in the premise of each rule an explicit description of the fuzzy system is

$$y = \frac{\sum_{i=1}^R b^{(j,k,\dots,l;p,q)}_i \mu_1^j \mu_2^k \dots \mu_n^l}{\sum_{i=1}^R \mu_1^j \mu_2^k \dots \mu_n^l} \quad (22)$$

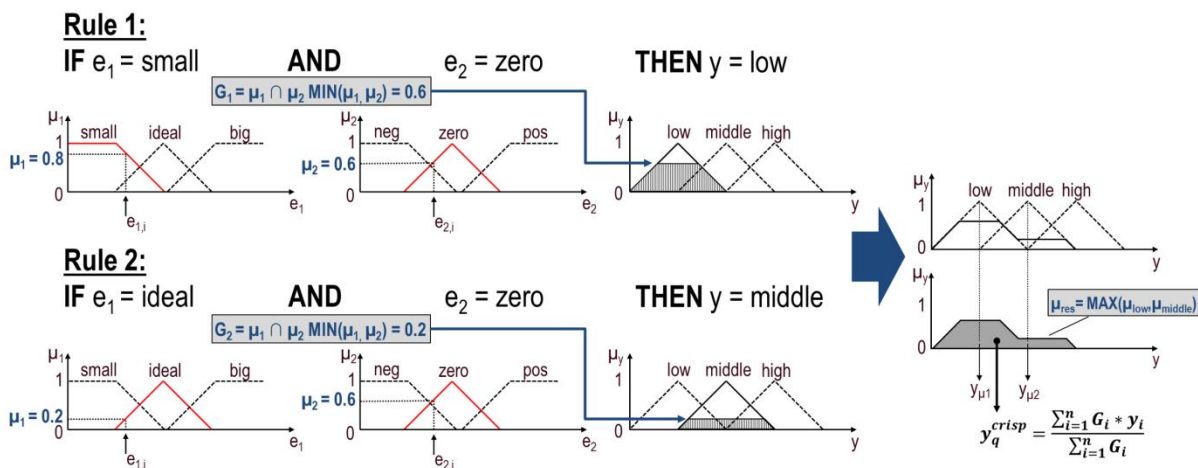
Here,  $b^{(j,k,\dots,l;p,q)}_i$  is the output membership function center for the  $i^{\text{th}}$  rule and the indices in  $(j, k, \dots, l)$  specify which linguistic value is used on each input universe of discourse and specifies the linguistic-numeric value of the input membership function used on each input universe of discourse. In the case of Gaussian membership functions eq. 19 turns into

$$y^{crisp} = \frac{\sum_{i=1}^R b_i \prod_{j=1}^n \exp\left(-\frac{1}{2}\left(\frac{u_j - c_j^i}{\sigma_j^i}\right)^2\right)}{\sum_{i=1}^R \prod_{j=1}^n \exp\left(-\frac{1}{2}\left(\frac{u_j - c_j^i}{\sigma_j^i}\right)^2\right)} \quad (23)$$

and it needs

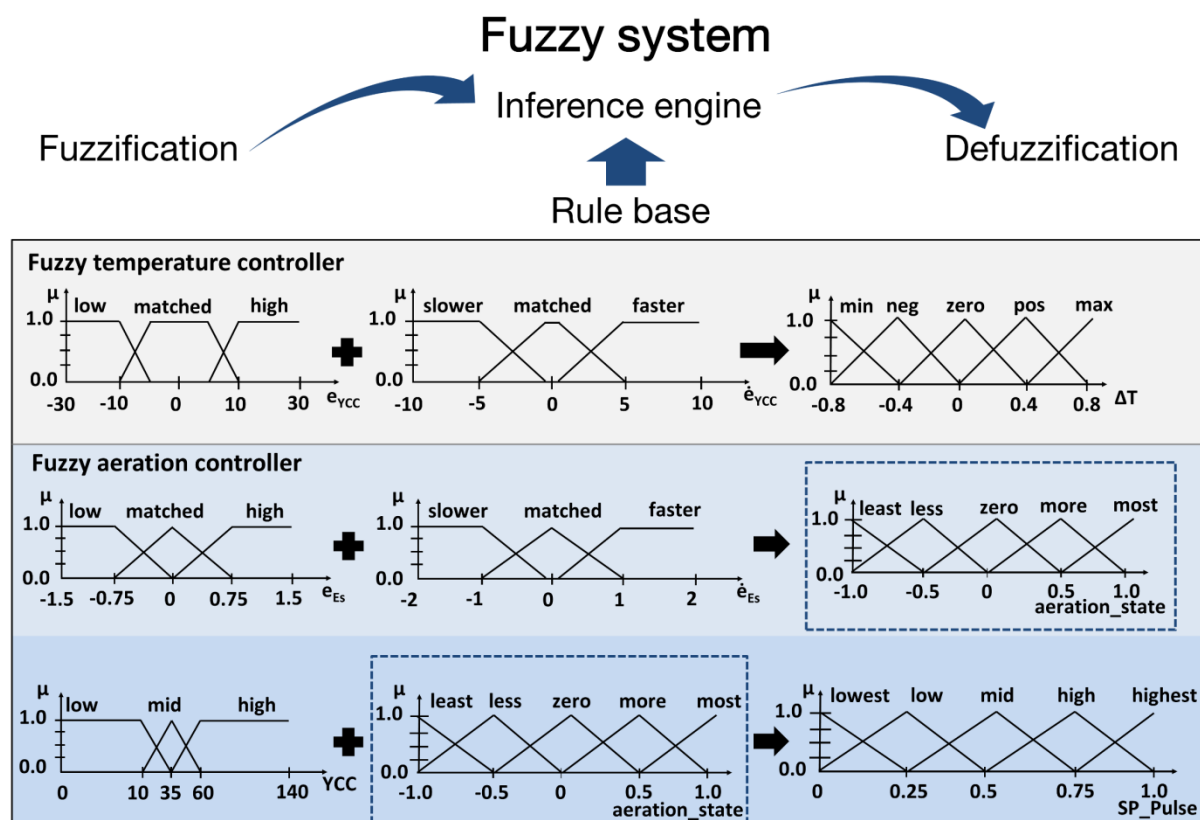
$$R(2n + 1) \quad (24)$$

parameters to describe this fuzzy system. A diagrammatic illustration of the calculations that are performed in a classical fuzzy controller is shown in Figure 8.



**Figure 8: Schematic representation of the calculations occurring in a classical fuzzy controller with two rules (modified Figure 1 in (Birle, Hussein et al. 2013)).** The controller has two inputs  $e_1$  and  $e_2$  and one output  $y_q^{crisp}$ . The inference mechanism uses the max-min method. A simplified center of gravity calculation is performed as defuzzification.

With reference to this work, a basic fuzzy inference system was established in order to control the temperature and the aeration of the brewer's yeast propagation process. The developed fuzzy controllers are diagrammatically shown in Figure 9 and were designed using the aforementioned definitions and concepts of fuzzy logic theory. A comprehensive description of the classic fuzzy system is presented in section 2.2.2 of this work.



**Figure 9: Diagrammatic representation of the classical fuzzy inference system which was designed in the scope of this work. In its basic configuration the system consists of two controllers, which are a temperature and an aeration controller. The aeration controller is a two-step controller. In the first step a state variable “aeration\_state” is created (marked by the blue dashed rectangle) and used as the output. In the second step this state variable is used as an input variable and the final output is the setpoint for the aeration interval denoted as “SP\_Pulse”.**

The main advantages of using fuzzy controllers are that they offer quite fast and problem-related tools to solve control engineering problems in a transparent, straightforward, and practical-oriented way. Furthermore, as a universal approximator a fuzzy system is able to pattern the behavior of any nonlinear system and additionally it allows the immediate incorporation of expert knowledge into control rules by means of linguistic expressions. However, there are several drawbacks of classical, static

fuzzy systems. One drawback is that the more complex a system gets, the more rules are required in order to provide a full description of the system. More clearly, there is an exponential increase in the number of rules with the number of fuzzy controller inputs or membership functions required to describe the process of interest. The consequence is that the advantage of transparency of the rule base diminishes and the system's efficiency decreases when there are rules which are not actively used. Another drawback is the lack of a learning capability with respect to fast controller implementation. In common practice manual adaptation of fuzzy controller parameters by trial and error is still the dominating method in order to reach the required performance criteria of the controller. However, this is quite cumbersome and often results in inefficient and sub-optimal control parameter configurations. Therefore, in this work two different approaches were investigated in order to optimize the control performance of classical fuzzy control within the framework of uncertainty-biased processes. One approach is the incorporation of negative experience into fuzzy inference systems. By using the principle of modus tollens rules can be formulated in order to express warnings or prohibitions for the consequents of distinct rules. This allows the transparency of the rule base to be maintained in such a way that fewer rules are required to achieve a certain control performance than would be the case if only positive rules were used. The other approach is the usage of evolutionary tuning techniques like genetic algorithms in order to add data-based learning and to achieve a fast optimization of the control performance.

## **1.2 The importance of negative experience**

In general, fuzzy control allows the incorporating of qualitative experiential knowledge in the form of rules directly into the controller. This creates a controller whose mode of operation can be interpreted and which can therefore be optimized interactively without having a process model at hand. Usually, the type of approximate reasoning and the interpretation of rules follow modus ponens, which is Latin for mode that affirms by affirming. Given this rule it is possible to incorporate positive experience that stems from different experts into a fuzzy controller. More precisely, in common fuzzy controller rules in the form of  $R_i: \text{If } p_i(e) \text{ Then } c_i(u)$  are used and interpreted as a positive rule. Here,  $R_i$  is the  $i^{\text{th}}$  rule with premise  $p_i$  and conclusion  $c_i$ . The truth value



of  $p_i(e) \wedge c_i(u)$  provides for each output value  $u$  to which degree it is recommended by the rule  $R_i$  at the current input  $e$ . By superimposition of the suggestions of all rules using the OR-operation, the overall implied output membership function results (Kiendl 1997):

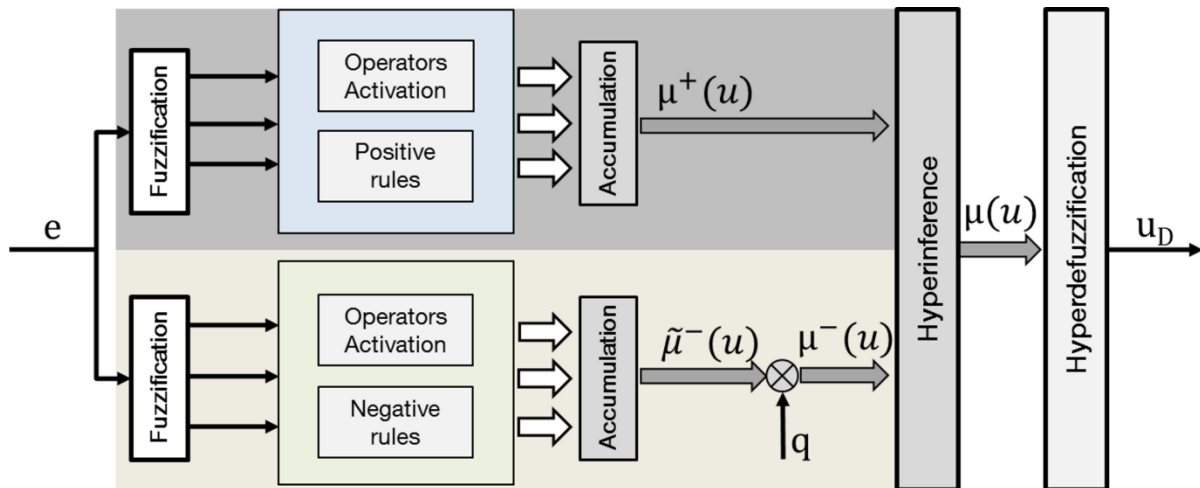
$$\mu(e, u) = \bigvee_{i=1}^R (p_i(e) \wedge c_i(u)) \quad (25)$$

It defines for each output value to which degree it is recommended by all rules at the given input. However, the above-mentioned conventional fuzzy controller structure has the deficiency that it is not possible to declare certain "forbidden manipulated variable ranges" or to ensure that the resulting real value of the manipulated variable is not under certain preconditions in these areas. Such a guarantee may be desirable in practice. For example, if the output of the fuzzy controller acts on an actuator, which consists of several units, it can be of interest that there is no frequent switching between the different units in order to protect the actuator and to achieve a more economical operation. In this case, it is therefore advisable to declare as "unfavorable" or even "forbidden" all manipulated variable values which lie in the vicinity of the switching threshold. Likewise, for example in the field of process engineering, one would like to guarantee that a valve is actually completely closed under certain preconditions. Therefore, all manipulated variable values would be prohibited at which the valve is only partly closed. Furthermore, for example in the case of position control, aside of having only positive recommendations it can be very useful to define linguistic rules of prohibition in order to avoid overshooting at the target position (e.g. "If target position is close Then high speed is prohibited"). Further, a dead band can be created in order to smooth control in the case of small control deviations (e.g. "If deviation  $e$  is small Then control output values in the range of  $0 < |y| < y_{min}$  is prohibited"). Due to that structural shortcoming, conventional fuzzy controllers are not suitable for certain control applications. However, this structural deficit can be solved by the additional incorporation of negative experience. In literature there exist two different approaches of how to incorporate negative rules into fuzzy controllers and how to handle the flow of information. The first approach is suggested by (Kiendl 1997). He introduces the concept of a two-stringed fuzzy controller structure (Kiendl 1993). A schematic outline of this approach is shown in Figure 10. For each string a positive  $\mu^+(u)$  and a negative membership function  $\mu^-(u)$  is generated. Here  $\mu^+(u)$  represents the implied fuzzy sets coming from all positive rules and  $\mu^-(u)$  denotes the implied fuzzy sets resulting from

all negative rules. Subsequently, both are combined to a membership function  $\mu(u)$  using a method denoted as hyperinference such as  $\mu(u) = \mu^+(u) \wedge \neg\mu^-(u)$ , where  $\wedge$  is a selectable fuzzy operator (AND-operator). In the case of a weak veto the hyperinference could be as follows (Kiendl 1997):

$$\mu(u) = \begin{cases} \mu^+(u), & \text{if } \mu^+(u) \geq \mu^-(u) \\ 0 & \text{otherwise} \end{cases} \quad (26)$$

A hyperdefuzzification then calculates a crisp output value  $u_D$ .



**Figure 10: Illustration of a two-stringed fuzzy controller structure for handling positive and negative rules proposed by (Kiendl 1997). The lower string processes the negative rules and creates a membership function  $\tilde{\mu}^-(u)$ . It states for each potential value of  $u$ , to which degree the negative rules advise against it. The hyperinference offsets positive and negative membership functions ( $\mu^+(u)$ ,  $\mu^-(u)$ ) against each other and creates a common membership function  $\mu(u)$ . Here,  $\mu^-(u) = q\tilde{\mu}^-(u)$ ,  $0 \leq q \leq 1$ . Successive hyperdefuzzification computes a crisp output  $u_D$ . The factor  $q$  is used for global attenuation of the warnings or prohibitions. The input is denoted  $e$  in this case.**

A second approach for incorporating negative rules into fuzzy inference systems and that was applied within the scope of this work is proposed by (Branson and Lilly 1999; Branson and Lilly 2001). Considering the principle of modus tollens, a new and practice-oriented method for the incorporation of negative rules within the framework of defuzzification denoted as dot attenuation is presented. Similar to Kiendl, an overall negative implied vector  $\mu^-$  is built as part of the inference, where the  $i^{\text{th}}$  element is the negative membership in the  $i^{\text{th}}$  fuzzy set on the universe of discourse. Each element is computed as a t-conorm of the premises of all negative rules containing the  $i^{\text{th}}$  fuzzy set on the output universe of discourse in its consequent. For any positive rules whose consequents hold the  $i^{\text{th}}$  fuzzy set on the output universe of discourse, the  $i^{\text{th}}$  element

of  $\mu^-$  is used as an attenuation factor within the applied method of defuzzification. Consequently, the same is performed to form a positive implied vector  $\mu^+$  that is analogous to  $\mu^-$ . Hence, dot product center of gravity defuzzification is given by (Branson and Lilly 2001)

$$y(x) = \frac{\sum_{i=1}^R b_i \int \mu^{imp}(i)(1-\hat{a}_i^T \mu^-)}{\sum_{i=1}^R \int \mu^{imp}(i)(1-\hat{a}_i^T \mu^-)} \quad (27)$$

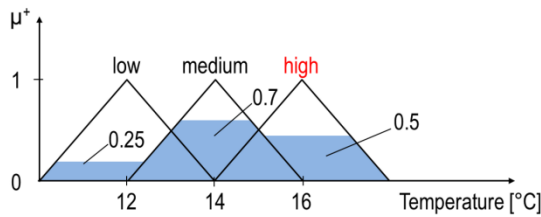
and the simplified dot product center average defuzzification is calculated by

$$y(x) = \frac{\sum_{i=1}^R b_i \mu(i)(1-\hat{a}_i^T \mu^-)}{\sum_{i=1}^R \mu(i)(1-\hat{a}_i^T \mu^-)} \quad (28)$$

Here,  $^T$  stands for transpose,  $\mu^-$  denotes the overall negative implied vector,  $\mu^{imp}(i)$  is the implied fuzzy set from rule  $i$ ,  $\hat{a}_i$  is a unit vector in the direction of the consequent of rule  $i$ ,  $R$  denotes the number of rules and  $b_i$  is the center of the membership function recommended by the consequent of rule  $i$ . Figure 11 exemplarily depicts the handling of negative experience on the fuzzy set level.

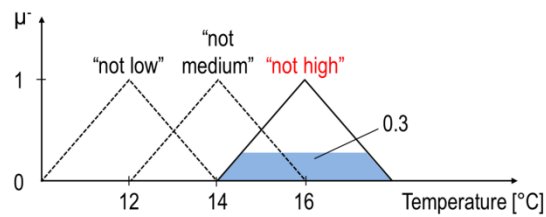
**Rulebase:**

- R1: IF Input 1 is slow AND Input 2 is low THEN Temperature is high  
 R2: IF Input 1 is slow AND Input 2 is ok THEN Temperature is high  
 R3: IF Input 1 is ok AND Input 2 is ok THEN Temperature is medium  
 R4: IF Input 1 is slow AND Input 2 is high THEN Temperature is low  
 R5: IF Input 3 is fast AND Input 1 is ok THEN Temperature is "not high"



positive implied vector:

$$\mu^+ = [\mu_{low}, \mu_{medium}, \mu_{high}] = [0.25 \quad 0.7 \quad 0.5]$$



negative implied vector:

$$\mu^- = [\mu_{not\ low}, \mu_{not\ medium}, \mu_{not\ high}] = [0 \quad 0 \quad 0.3]$$

$$Temperature = \frac{12 * 0.25(1 - 0) + 14 * 0.7(1 - 0) + 16 * 0.5(1 - 0.3)}{0.25(1 - 0) + 0.7(1 - 0) + 0.5(1 - 0.3)} = 14.15 \text{ } ^\circ\text{C}$$

**Figure 11: Incorporation of a negative rule and numerical treatment according to (Branson and Lilly 2001).** The exemplary rule base comprises four positive and one negative rule (R5). For each positive output fuzzy set, there exists a corresponding negative fuzzy set. In this case, rules that fire the output fuzzy set "high" are gradually attenuated by rule 5, which fires the corresponding implied negative set "not high". The numerical calculation of a crisp output is performed by dot product center average defuzzification (eq. 27).

Regardless of which method is used, both approaches come to the consensus that a clear advantage of the inclusion of negative rules is the possibility to alter the control surface in a very specific and targeted way, such that changes are only made where it

is necessary to improve the control performance. For this reason, the requirement to include negative experience in the form of negative rules into fuzzy systems is obvious to the controllability of uncertainty-biased processes. It provides an opportunity to further improve the performance and efficiency of the control behavior while maintaining the system's interpretability at the same time. Due to that, the concept of incorporating negative experience into the classic design of the described fuzzy-based yeast propagation system was intensively investigated.

As mentioned before, the design of a fuzzy model or a fuzzy controller, regardless of whether negative rules are taken into account or not, relies on human knowledge or is derived from data. In general both approaches are required, particularly when it comes to the control of more complex systems. Indeed if it is possible to provide a qualitatively correct description of a system behavior or a control policy by an expert, the numerical translation offered by fuzzy logic may be quite approximate. In this context, it is interesting to have methods that improve the set of fuzzy rules by tuning membership functions for instance. This requirement has led researchers to combine data-driven learning or optimization techniques with fuzzy logic, which will be introduced in the following section.

### **1.3 Getting tuned – Genetic optimization versus trial and error**

An important characteristic of fuzzy systems is that with respect to their design the number of degrees of freedom can grow rapidly depending on the number of rules, fuzzy variables, and types of fuzzy sets that are used. Hence, the tuning and adjustment of parameters that affect the performance of a fuzzy system's behavior can be quite cumbersome. Especially the practical optimization of each of these parameters usually requires a deep understanding of the underlying process. If there is uncertainty about the process behavior, the tuning of the parameters might be biased by uncertainty, as well. Due to that, parameter optimization via trial and error is not productive. As stated earlier, a fuzzy control action results from the synthesis of the overall recommendation of all active rules. This is part of matching every input value in the antecedent with the corresponding membership functions. For this reason, tuning any membership function can get quite complicated, as it usually affects more than one rule, and every rule may affect each fuzzy control action. However, in the

case of available training data, the data should contain that kind of information somehow. In consequence, a fuzzy control system should be optimized interactively and automatically using a data-driven approach, rather than tuning it separately and manually. In literature, there are several optimization methods but there are no universal methods. The standard optimization methods like gradient-based approaches might not be effective in the context of fuzzy systems given their non-linear character and the modularity of the systems (Nguyen and Sugeno 2012). This is one of the driving forces of this work to explore other optimization methods of more global optimization capabilities such as genetic algorithms. Due to the great variety of optimization strategies one could heretically ask which the best universal optimizer is. This was discussed in (Weicker 2007), who comes to the conclusion that there is no such thing as a universal optimizer. For each algorithm there exists a niche in the entire problem space for which it is particularly appropriate. Based upon these findings different optimization strategies have been analyzed (Rao and Rao 2009) and with respect to fuzzy-logic-based systems one of the most successful methodologies are genetic fuzzy systems (Cordón 2001; Cordón, Gomide et al. 2004; Herrera 2008). The use of genetic optimization with fuzzy logic allows the contradictory aims and tradeoff of high accuracy while still maintaining the system's interpretability to be overcome (Cordón 2011).

The development of genetic algorithms (GAs) goes back to (Holland 1975) and they belong to the most frequently applied evolutionary algorithms. GAs belong to the gradient-free, parallel optimization algorithms using a performance criterion for evaluation, as well as a population of potential solutions in order to detect a global optimum. In general, they are capable of handling complex and irregular solution spaces, and they can handle high-dimensional, nonlinear optimization problems. Their superiority to other optimization algorithms in terms of computational efficiency led to various engineering applications for solving complex optimization problems (Yusup, Zain et al. 2012). In its standard form the GA consists of the genetic operations selection, mutation and crossover. Solutions that are considered good are selected and manipulated to achieve new and possibly better solutions. Therefore, the manipulation is achieved by applying the *genetic operators* on the *chromosomes* in which the parameters of possible solutions are encoded. Considering the principle of elitism, in each population a part of the current generation is replaced by their offspring.

The combined effect of selection, crossover, and mutation can be expressed in the reproductive schema growth equation (Holland 1975; Goldberg 1989):

$$\zeta(S, t + 1) \geq \zeta(S, t) \cdot \frac{eval(S, t)}{\overline{F}(t)} \left[ 1 - p_c \cdot \frac{\delta(S)}{m-1} - o(S) \cdot p_m \right] \quad (29)$$

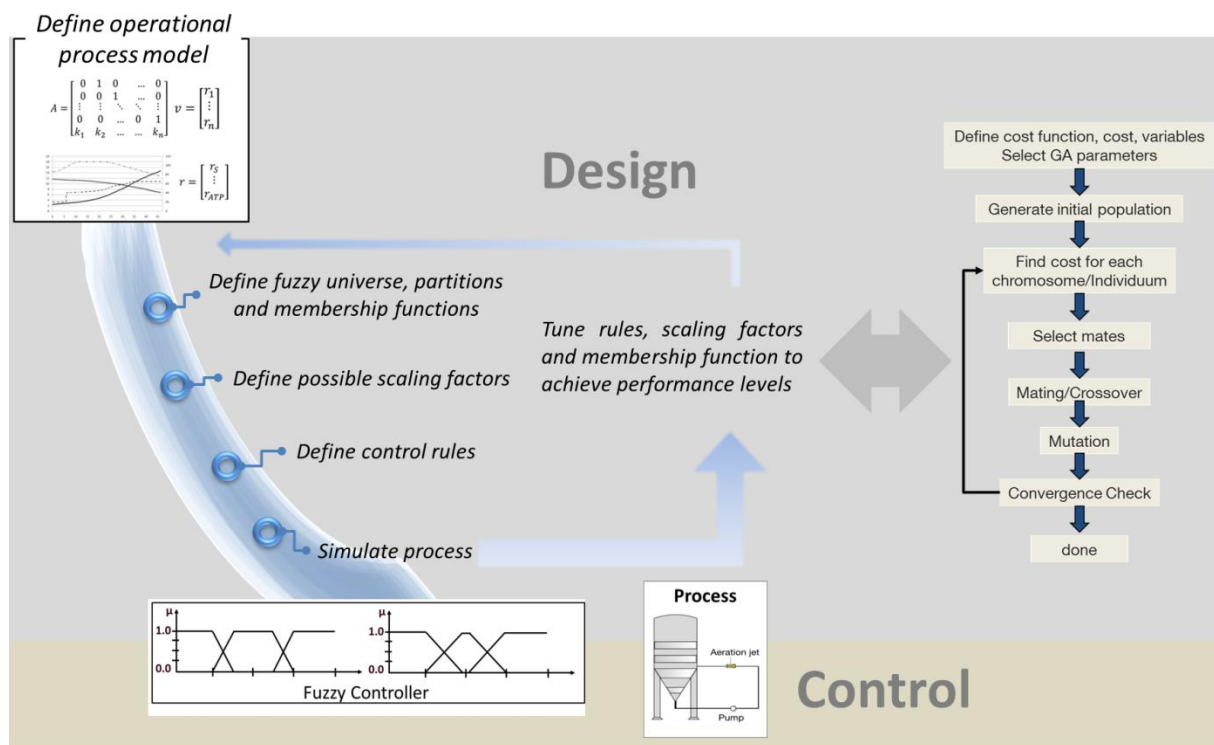
A scheme is representative of a set of chromosomes. Apart from the usual symbols 0 and 1 a schema contains additional wildcard symbols represented by the character #. Placeholders in a schema are representative of any other freely selectable symbol. In this way, a schema defines a set of chromosomes, which all correspond to its pattern. A chromosome which fits to a scheme is referred to as an instance of this schema. For example, the chromosomes 1001 and 1100 are both instances of scheme 1#0#. Conversely, the schemes ##11 and 0##1 belong to the chromosome 0011 among others.

In equation (29),  $\zeta(S, t)$  is the number of strings in a population at the time  $t$ , matched by schema  $S$ ;  $\delta(S)$  denotes the defining length of the schema  $S$  (distance between the first and the last fixed string positions);  $o(S)$  denotes the order of the schema  $S$  (number of 0 and 1 positions present in the schema);  $eval(S, t)$  represents the average fitness of all strings in the population matched by the schema  $S$ ; and  $F(t)$  is the total fitness of the whole population at time  $t$ . Parameters  $P_c$  and  $P_m$  are the probabilities of crossover and mutation, respectively. Hence, the equation computes the expected number of strings matching a schema  $S$  in the next generation as a function of the actual number of strings matching the schema, the relative fitness of the schema, and its defining length and order. The theorem states that the incidence of schemata with above-average fitness, defining length and lower order increases in the next generation. Unfortunately, the scheme theorem does not provide information about whether and in what number of steps a genetic algorithm finds an optimal or at least suboptimal solution of the optimization problem. The definition of the fitness function depends essentially on the information that will be used to assess the control behavior. The determination of the effectiveness criterion is relatively simple, if reference data of the control response are available, obtained for example by observation of an expert. In the control technology many problems can be treated very well by means of a setpoint control. The observed output  $y$  of the current process is assumed to reach a desired target value  $r$  in the shortest possible time. After the target value was reached the first time, there should only be a slight overshoot of the output. The third requirement for the setpoint control is to keep the oscillations as low as possible around the setpoint.

In this context, the fitness function judges a controller by observing its response to a changed target value. Occurring as a result of the new target value, error  $e$  and its derivative  $\dot{e}$  are both minimized. For this reason, the fitness function evaluates for example the square deviations of the error and the error change to zero (Hoffmann 1997)

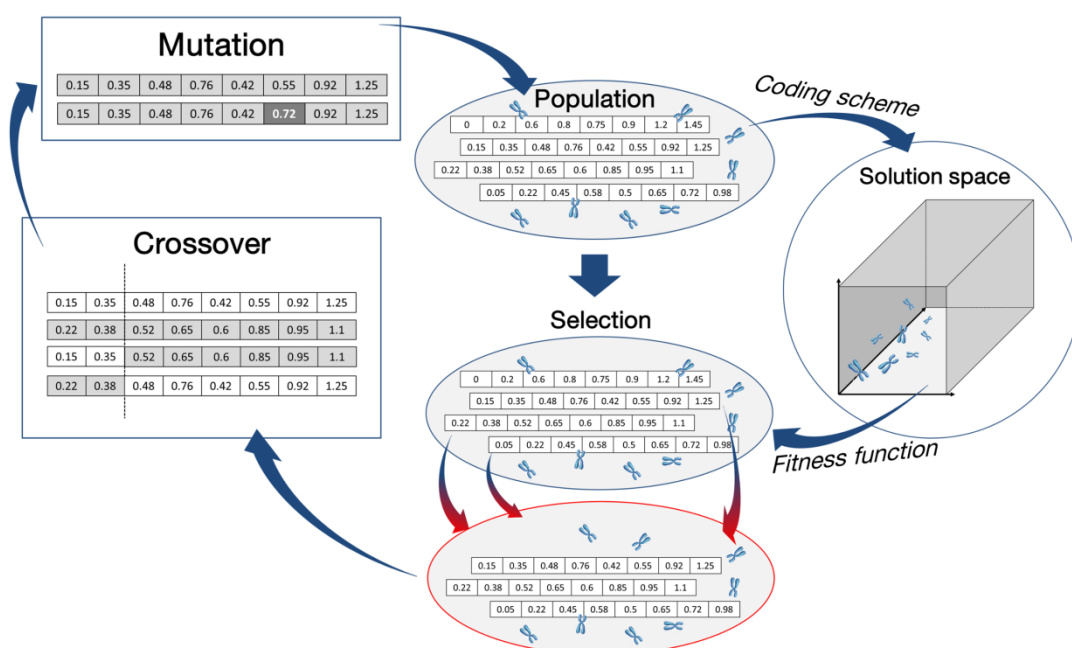
$$F(e(t), \dot{e}(t)) = \left( \int_{t=0}^T C_e e(t)^2 + C_{\dot{e}} \dot{e}(t)^2 dt \right)^{-1} \quad (30)$$

The two coefficients,  $C_e$  and  $C_{\dot{e}}$ , allow a different weighting of the two contributions to the fitness. A mathematical model of the process can be required if the optimization is carried out in a simulation rather than on the process itself. Such a simulation may be necessary for reasons of safety or with processes that are very slow in real time. An illustration of the flow chart of a GA used for tuning a fuzzy logic control system is presented in Figure 12.



**Figure 12: Diagrammatical representation of a fuzzy controller design methodology using genetic tuning. In the first instance a representative model of the process that is supposed to be controlled is required. After defining the basic structure of the fuzzy controller, as well as the boundary conditions (e.g. universes of discourse of input and output variables), the process is simulated using the process model. Then, a genetic algorithm is used (flow chart on the right-hand side of the figure) that tunes the parameters and/or rules of the fuzzy controller in order to achieve a certain control performance specified by an appropriate cost function.**

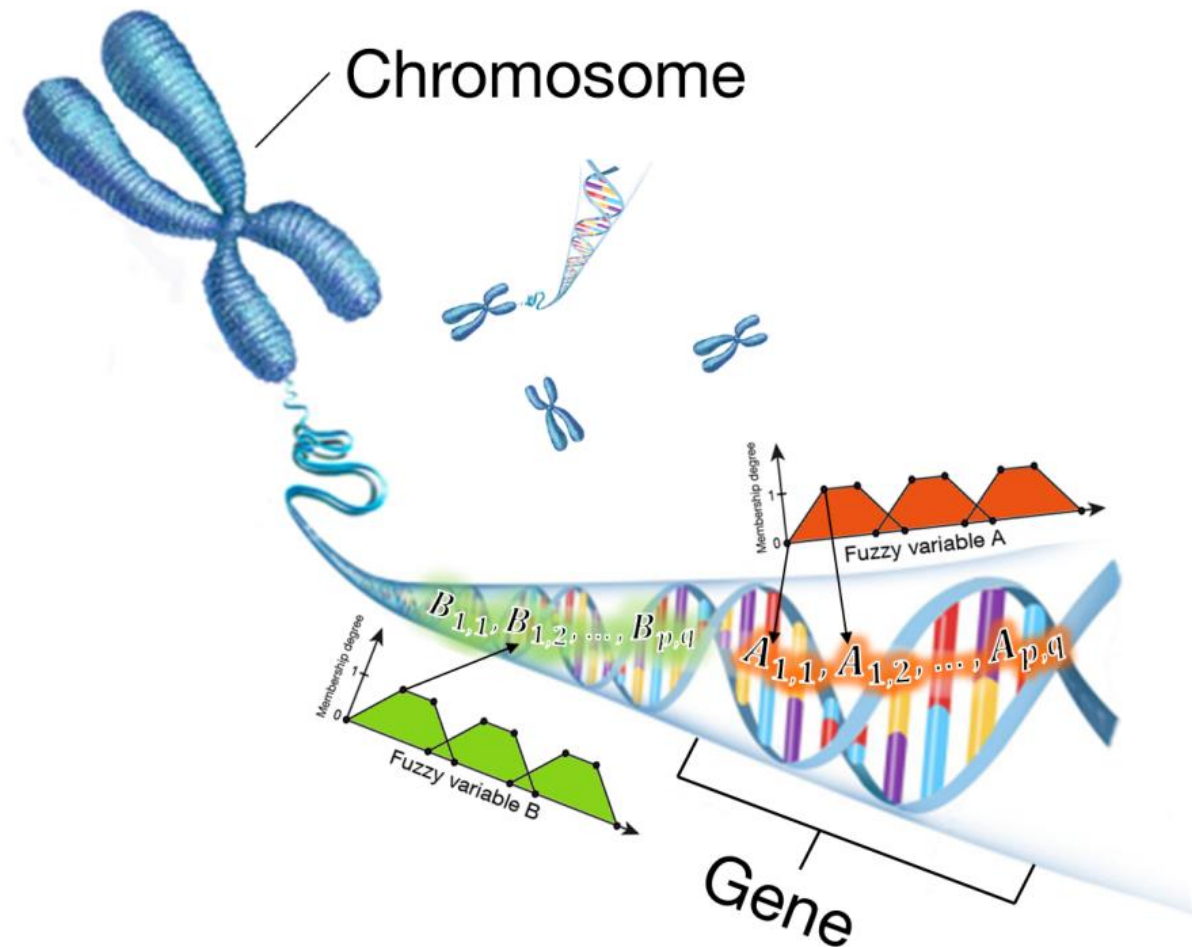
With respect to this work the focus is put on real-coded or continuous GAs (Davis, De Jong et al. 2012; Michalewicz 2013), as binary-coded GAs are considered less efficient (Goldberg 1989). The disadvantage of binary-coded GAs is that the binary strings can become very long and the search explodes. Besides requiring less storage, continuous GAs are faster than binary GAs from the perspective of computational efficiency which is lost by the conversion between the binary and real valued representation (Herrera, Lozano et al. 1998; Haupt and Haupt 2004). A diagrammatic illustration of the structure of a GA is shown in Figure 13 and a possible coding scheme for genetic fuzzy set tuning is schematically shown in Figure 14.



**Figure 13: Basic structure of a GA.** A population of chromosomes, represented by vectors of parameters, evolves from one generation to the next. Each vector corresponds to a possible solution of the optimization problem. The encoding scheme assigns each genetic vector to a potential solution to the optimization problem. From a biological point of view this transformation produces the phenotype from the associated genotype. The importance of a gene is determined by its location within the chromosome. The fitness function assesses the quality of solutions, as measured by the optimization problem. The selection decides which parents contribute by propagation to the descendants of the next generation. It is a stochastic process, where well-adjusted individuals are more likely to contribute offspring. Genetic operators such as crossover and mutation produce from the existing genetic material new genotypes and therefore new candidates for solutions. When crossing over the vectors of two parents are cut at a randomly selected position and the resulting partial vectors are interchanged crosswise. From time to time, the mutation alters single, randomly selected genes. Mutation mainly has the



task of preserving the diversity in the population in order to avoid premature convergence of the algorithm.



**Figure 14: Diagrammatic illustration of the genetic coding scheme of fuzzy membership function parameters on a chromosome. Here, the fuzzy variables are coded via their fuzzy set parameters as genes on the chromosomes.**

The presented principle was also applied in the context of this work, in order to add the capability of data-driven learning and tune the parameter configuration of the fuzzy system used for the control of the brewer's yeast propagation process.

## **1.4 A brief look at supervision and control of yeast propagation (*Saccharomyces cerevisiae* sp.)**

In the previous sections the phenomena of uncertainty as well as the concept of fuzzy logic as an appropriate tool for encountering uncertainty with respect to issues of process control were introduced. In this section, a brief outline of the brewer's yeast propagation process as a typical and representative process biased by various sources of uncertainty is given. Furthermore, the transfer of the aforementioned aspects of uncertainty management with respect to the supervision and control of bioprocess yeast propagation is one of the main objectives of this work. Considering the final product quality, yeast propagation itself is a crucial step in beer production and is of great economic and technological importance in brewing practice. Particularly the vitality and quality of the produced yeast has relevant influence on the subsequent production steps of fermentation and the resulting beer quality (Heyse 1989; Narziß and Back 1995; Lehmann 1997; Lehmann 1997; Maemura, Morimura et al. 1998; Kunze, Manger et al. 2011). Due to that, one of the most important necessities for the step of primary fermentation is that the yeast inoculum must be available at pitching time in the required amount and with the right quality. In order to guarantee this prerequisite the development and provision of monitoring and control tools is a main part of this work. Up to now current management tools at the supervisory control level in breweries do not allow for the compensation for disturbances in the production plan (which can be up to 2–3 days) with respect to yeast propagation performance. Generally, in common practice the process control is based upon experience and empiric, purely time-driven recipes for the setpoints of manipulated variables. In consequence, human interventions and corrective control actions in the case of disturbance will occur with delay and no adequate inoculum will be delivered for the subsequent fermentation.

In general, yeast propagation is performed as a batch process, whereby the yeast passes through the different growth phases of a static culture (lag phase, exponential phase, transition or deceleration phase, stationary phase, degeneration). The duration of the individual phases and the transition time from one phase to another is dependent on manifold factors. For example, the lag phase, which is the time from inoculation until the maximum growth rate occurs, depends on the physiological state of the inoculum and the specific growth medium (Eitinger, Schlegel et al. 2007). The physiological state

in turn depends on its conditions of storage and its upstream treatment (Annemüller 2008). Furthermore, the whole growth behavior is highly influenced by the fed substrate beer wort. Its composition and ingredient concentrations are dependent on natural variations of the raw materials used. In consequence, the effects of substrate limitations on the metabolic behavior due to unavoidable variations in available carbohydrates, nitrogen, zinc, or vitamins are subjected to uncertainty. Moreover, metabolic regulation effects occurring under brewing-related conditions have to be taken into account in the case of *Saccharomyces cerevisiae* cultivation. In this regard, the two most important regulation mechanisms that affect the catabolic rates of the different metabolic pathways are the Pasteur effect (Eitinger, Schlegel et al. 2007) and the Crabtree effect (Crabtree 1929). Pasteur found that glucose uptake rate and glycolysis rate is higher under the absence of oxygen. If oxygen is provided to an anaerobic culture, glucose uptake decelerates (Hartmeier 1972). The Crabtree effect, which is also known as overflow metabolism, catabolite repression, aerobic fermentation, or oxido-reductive metabolism, leads to the formation of ethanol upon exceeding a critical glucose concentration in the substrate, although aerobic condition is present (Gschwend-Petrik 1983; Sonnleitner and Kaeppli 1986; Pham, Larsson et al. 1998). In summary, the process of yeast propagation is affected by various factors of uncertainty that in consequence influence the observability and controllability of the process. Hence, in order to obtain vital and active yeast from the physiological point of view an adaptive online monitoring and process control system is required.

## **1.5 The scope and motivation of the thesis**

In summary, the motivation for this work lies in the provision of a practical framework for the online monitoring and control of uncertainty-biased systems with a special focus on brewing yeast propagation as a predestinated test case to demonstrate the developed tools. However, there is still no integrative approach combining data-driven and expert knowledge in order to dynamically achieve the main objective of producing the right amount of yeast of the right quality at the right time by means of fuzzy logic. All in all, the following tasks and topics were addressed in order to meet the requirements:

- Critical review of the state of the art with respect to intelligent control and soft computing applications in the food and beverage sector.
- Development, design, and implementation of a fuzzy-based monitoring and control framework for a pilot yeast propagation plant.
- Analysis and implementation of evolutionary optimization of the fuzzy system combined with statistical process control.
- Incorporation of negative experience in the form of negative rules in order to enhance the system performance.

## **2 Summary of results**

### **2.1 Paper summary**

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#### **Part 1 – A Review**

##### **Fuzzy logic control and soft sensing applications in food and beverage processes**

Extensive parts of the production processes in the food and beverage industry are characteristically dominated by biologically based processes, particularly fermentations. The supervision and control of such complex, nonlinear, and time-variant systems require novel sophisticated systems that are capable of managing the underlying uncertainty-biased process behavior. As an essential prerequisite in order to develop a holistic system approach, the review provides a comprehensive and critical outline of the scientific state of the art of soft computing approaches and applications in the relevant processes. The findings show that intelligent combinations of hard and soft sensing devices can provide powerful tools and sources of information generation with respect to process monitoring and control. Furthermore, the description of the system's behavior can be achieved and realized faster by means of fuzzy logic than using methods of complex mathematics. Despite of the advantages of fuzzy logic based controllers their major drawbacks (e.g. missing inclusion of negative experience) are addressed and their potential solutions are reviewed. In this context the merging of fuzzy logic, optimization methods like evolutionary computation, but

also the inclusion of chemometric evaluation to hybrid systems offers new scientifically suitable methods. The intelligent combination of these technologies into an integrated system reveals a promising direction to the creation of reliable, efficient, and accurate process monitoring and control.

---

## **Part 2 – A fuzzy-based framework**

### **Online yeast propagation process monitoring and control using an intelligent automatic control system**

Following the findings from the review, a basic framework of online monitoring and control for brewing yeast propagation was built. For this, a pilot bioreactor for yeast propagation was constructed. Information about the process state is provided by an array of sensors (optical density, temperature, pressure, density, dissolved oxygen, and pH value) that was implemented into the propagation plant. However, as the cell concentration cannot be detected directly, a software sensor was developed. The soft sensor consists of a neural network that uses online sensor data of OD, pH value, and density in order to compute the yeast cell concentration. The virtual operating system, or fuzzy based expert system, then uses the sensor information as input data for two fuzzy logic controllers. The first controller is a temperature controller. It uses the deviation of the predicted cell count from that of a reference trajectory and its temporal derivative as inputs and adjusts the process temperature based upon a collection of if-then control rules. In this context, the reference yeast cell count trajectory is derived from a metabolic growth model. The second fuzzy controller triggers the aeration intervals of the system. Similarly to the temperature controller, it uses the deviation of measured extract concentration from that of the reference trajectory, the predicted cell count, and the dissolved oxygen concentration in order to construct a fuzzy rule base and to control the aeration. With respect to the main objectives of yeast propagation, a dynamic control of the process is possible, and it could be shown that the system is able to provide the desired yeast cell concentration of  $100\text{--}120 \times 10^6$  cells/ml at a minimum residual extract limit of 6.0 g/100g at the required point of time and of the required quality.

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## **Part 3 – Optimizing the system and setting up statistical corridors for the control errors**

### **Management of uncertainty by statistical process control and a genetically tuned fuzzy system**

Fuzzy logic is generally a powerful tool when dealing with uncertain process conditions. It allows process and expert knowledge to be made use of by incorporating it into linguistic expressions and applying it to control routines. However, one drawback of classical fuzzy control systems is their cognitive fixedness of the used linguistic expressions, that is, that words have different meanings to different people. Furthermore, it can be very inefficient and time-consuming to adjust the parameters by trial and error. To overcome the first challenge, a data-driven approach using statistical process control was applied in order to define statistical corridors for the linguistic input variables of control error and its temporal derivative. As mentioned, manual adjustment of the control behavior of a fuzzy controller can be very tedious. Evolutionary computation, more specifically a genetic algorithm, was then applied in order to tune the fuzzy sets of the input and output domains of the fuzzy temperature controller. The resulting controller parameterization was then compared with the non-adjusted controller by experimental validation. The presented experimental results show that the genetically tuned fuzzy controller is able to keep the process within its allowed limits. The average absolute average error to the reference growth trajectory is  $5.2 \cdot 10^6$  cells/ml. The controller proves its robustness to keep the process on the desired growth profile.

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## **Part 4 – The incorporation of negative experience**

### **Incorporation of negative rules and evolution of a fuzzy controller for yeast fermentation process**

Fuzzy control aims to transfer qualitative empirical knowledge in the form of rules directly into the functionality of the controller. Following this, controllers are created whose mode of operation is kept interpretable and can therefore be optimized interactively without necessarily having an appropriate process model at hand. The range of applications where fuzzy controllers compared to conventional controllers actually provide benefits depends crucially on the type of the available experience and knowledge. In this regard, conventional fuzzy controllers have a structural defect because they only make use of empirical rules which are solely capable of providing proposals of positive action. Therefore, common fuzzy controllers are unsuitable for certain applications, such as when prohibitions are observed. This shortcoming can be solved by the incorporation of negative rules into the inference structure of the fuzzy controller. The suggested method implements the negative experience on the fuzzy set level. As part of the inference mechanism, the negative and positive implied sets are offset against each other in the defuzzification part. The incorporation of negative rules leads to a much more stable and accurate control of the process as the root mean squared error of reference trajectory and system response could be reduced by an average of 62.8 % compared to the controller using only positive rules.

## 2.2 Paper copies

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### 2.2.1 Fuzzy logic control and soft sensing applications in food and beverage processes

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Review

#### Fuzzy logic control and soft sensing applications in food and beverage processes

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#### ABSTRACT

Biotechnological processes – particularly fermentation processes – play a very important technological and an economical role for the production steps in the food and beverage sector. In order to ensure constantly high product quality combined with efficient manufacturing, intelligent control systems and strategies are required. However, biosystems contain living organisms and therefore underlie particular process dynamics such as nonlinear and time-varying behavior. Furthermore, initial process conditions cannot be kept constant and therefore precise process reproducibility hardly can be achieved. On that account these multivariate systems put high requirements to the practical on-line observation, control, monitoring and prediction of significant process key parameters whose acquisition is of crucial importance for a comprehensive understanding and control of the process. During the last decades great efforts have been undertaken to cope with those challenges by means of intelligent soft computing and reveal great opportunities to integrate human expertise and learning procedures for improved process control strategies of biological systems. Particularly fuzzy logic based control systems show high potential to manage the complex production processes and to deal with fragmental process information. This review critically presents the chances as well as the limitations of fuzzy and hybrid expert system approaches in food and beverage process control from a theoretical and application based point of view.

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#### Contents

1. Introduction .....	254
2. Theory of fuzzy logic and fuzzy-based expert systems .....	255
3. Fuzzy reasoning, sensing and control .....	257
3.1. Quality evaluation .....	257
3.1.1. Fuzzy symbolic approach .....	257
3.2. Sensing and control .....	259
3.2.1. Fuzzy based soft-sensing of process parameters and phase recognition .....	259
4. Hybrid fuzzy systems .....	260
4.1. Introduction to neural network techniques .....	260
4.2. Soft sensing via artificial neural networks .....	261
4.3. Hybrid systems .....	263
5. Conclusion and outlook .....	266
References .....	267

#### 1. Introduction

Due to their inherent complexity and abundance of uncertainty factors biotechnological systems, especially fermentation processes, are very difficult to describe. The quality of the product is decisively determined by its taste which is extremely difficult to

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model or sense as it is highly influenced by cultural and personal perceptions. Additionally, there is a big difference in the process objective itself, comparing manufacturing of foods to other biotechnological production steps. In proceedings like the penicillin production the focus is on the exploitation of a single component of the final product and the main concern is a yield as high and efficient as possible. The residual composition of the product is mostly of lower interest. In contrary to this, instead of subcomponents, the food as a whole is in the focus of the (fermentation) process. Regarding fermentations, the most important process sequences are directly or indirectly related to living organisms by what the realized biochemical turnovers are based on complex biological and biochemical processes whose comprehensive description would need a high number of state variables. However, due to the fact of intra- and extracellular metabolic side products, flavor substances and various cell states there exist hundreds of state variables. For setting up an appropriate process model at reasonable cost from the abundance of available state variables those have to be selected that significantly describe the process behavior. On the basis of the previously mentioned biological and biochemical processes the dynamic performance of those systems can be characterized as nonlinear and time-variant. Whilst continuous or fed-batch processes are commonly run at a fixed operating point, this is not possible for a batch operation (Chmiel, 2006). Hereby the process undergoes a wide range of nonlinear behavior (Trelea, Trystram, & Courtois, 1997). An example would be the oxygen concentration of wort which decreases from saturation to zero during the fermentation and maturation of beer and forces the yeast to shift from the aerobic to the anaerobic metabolism. Therefore, the process model cannot be linearized or limited to a fixed operating point, but rather to a combined biochemical trend to follow. Thus, the classical methods of control engineering and system theory that assume linearity and time-invariance can be applied only in a very limited way or under permanent personal control and continuous manual interventions.

The implementation of new strategic directions in the field of process control like the PAT (Process Analytical Technologies) initiative opens new gates for better process understanding (Administration, 2004; Dünneber & Tups, 2007; Junker & Wang, 2006). By launching the PAT initiative in 2004, the FDA (Food and Drug Administration) developed a system for the design, analysis and control of production processes via defined and timed measurements of critical quality and performance parameters of raw and process parameters as well as of the contemplated methods with the objective of ensured product quality and therefore presents an innovative tool for an optimal design of process control. In contradiction to the practical established product release and validation by costly laboratory analysis that is inevitably connected to time-delayed reactions on process changes, a shift to a process-oriented validation and release of process sequences in real-time in respect to the aspect of "Quality by Design" (QbD) is intended. This indicates the demand for a quality assessment which has to take place simultaneously to the manufacturing process and requires a comprehensive understanding of the process. However, the prompt on-line detection of crucial key parameters such as biomass or substrate concentrations is still difficult to achieve and often lacks the required accuracy. For this reason, in the field of biotechnological process control, numerous approaches have been undertaken to develop corresponding indirect measuring methods that are capable to cope with the complex behavior bioprocesses. An overview of these software sensors is given in (de Assis & Filho, 2000; Becker & Krause, 2010; Shioya, Shimizu, & Yoshida, 1999). The strategy of

soft-sensing hereby offers various attractive properties (Fortuna, Graziani, Rizzo, & Xibilia, 2007):

- they can represent a low-cost alternative to expensive hardware devices, allowing the realization of more comprehensive monitoring networks
- they can work in parallel with hardware sensors, supplying useful information for fault detection tasks and thus allowing the realization of more reliable processes
- they can easily be implemented on existing hardware and retuned if system parameters change
- they allow real-time estimation of data, overcoming the time delays of slow hardware sensors (e.g. gas chromatographs) and therefore improve the performance of the control strategies

In order to obtain the needed process information as a premise for process control the basic demand is to combine innovative sensor arrays (soft and hard sensing) with intelligent control operations based on comprehensive process and product knowledge. Therefore, the second part of this paper gives a short introduction to the theory of fuzzy logic as a powerful tool to implement a priori knowledge into process control actions and to handle uncertainty or vagueness by linguistic system formulation. The third section treats various food and beverage applications of fuzzy based reasoning, sensing and control approaches. The last part presents the opportunities offered through hybrid systems outlined by a comprehensive study of applications.

## 2. Theory of fuzzy logic and fuzzy-based expert systems

The control of food and beverage manufacturing processes in common practice is predominantly carried out discontinuously and receipt based. This way of process control is accompanied by permanent manual interactions and demands perpetual sample taking, lab analysis and process surveillance by the operator what is directly connected to higher economical efforts, incomplete process information and uncertainties. On that account sophisticated methods of soft computing could offer an alternative way to overcome the discrepancy of cost efficient process control and perpetuating claimed quality objectives. Knowledge-based expert systems are programs able to deal with uncertain and vague process information and mimic human expert-like reasoning and decision-making within a certain domain of expertise (Patterson, 1990, p. 496). The historical development of fuzzy reasoning and expert systems in food industry is given by Linko (1998). Since the implementation of fuzzy logic by Zadeh (1965), this technique has established as a fixed part for the control of biotechnological and food processes (Besli, Türker, & Gul, 1995; Davidson & Smith, 1995; Filev, 1991; Filev, Kishimoto, & Sengupta, 1985; Herrera, 2007; Nyttle & Chidambaram, 1993; Venkateswarlu & Naidu, 2000). The theory of fuzzy logic is an extension to the classical crisp set theory and allows the transition from the classical, bivalent notion of truth to a gradual, multivalued concept of truth. Characteristic for fuzzy systems is that they enable to present a complex system behavior by simple linguistic formulations. In contradiction to a quantitative, mathematical description of the systems transfer behavior, the system behavior is expressed by linguistic variables and algorithms that can be written as follows (Jantzen, 2007):

- Rule 1: { IF  $x_{1,1}$  is  $\tilde{A}_{1,1}$  AND  $x_{1,2}$  is  $\tilde{A}_{1,2}$  AND  $x_{1,n}$  is  $\tilde{A}_{1,n}$  THEN  $y_1$  is  $\tilde{B}_1$  } OR  
 Rule 2: { IF  $x_{2,1}$  is  $\tilde{A}_{2,1}$  AND  $x_{2,2}$  is  $\tilde{A}_{2,2}$  AND  $x_{2,n}$  is  $\tilde{A}_{2,n}$  THEN  $y_2$  is  $\tilde{B}_2$  } OR  
 .....  
 Rule m: { IF  $x_{m,1}$  is  $\tilde{A}_{m,1}$  AND  $x_{m,2}$  is  $\tilde{A}_{m,2}$  AND  $x_{m,n}$  is  $\tilde{A}_{m,n}$  THEN  $y_m$  is  $\tilde{B}_m$  }

Here  $x_{m,n}$  are the crisp input values,  $\tilde{A}_{m,n}$  designate the fuzzified input sets, respectively linguistic input variables and  $\tilde{B}_m$  the fuzzified output sets of the viewed system.

By means of those "IF-THEN"-rules, consisting of a premise and conclusion part, the discrete, physical values (input variables received e.g., from the sensor device) get fuzzified and connected to linguistic variables. The entity of all rules reflects the expert knowledge implemented in the control system. Fig. 1 shows schematically the max-min-inference method with fuzzification and defuzzification by calculating the centroid of the resulting membership function.

The fuzzification is accomplished by transferring the crisp input values into fuzzy variables. For this, the discrete input values get mapped on a membership function and the degree of membership to the corresponding fuzzy set, respectively linguistic variable is calculated. Hence, the membership functions which are usually expressed as triangular, linear line or phi membership functions indicate the degree to which extent a particular element is a member of the fuzzy set. Let  $X$  being the universe of discourse and  $\tilde{A}$  is a fuzzy subset of  $X$ , then a fuzzy set  $\tilde{A}$  can be defined as a set of ordered pairs (Jantzen, 2007):

$$\tilde{A} = \{ (x, \mu_{\tilde{A}}(x)) | x \in X \} \quad (1)$$

Here,  $\mu_{\tilde{A}}$  denoting a membership function and  $x$  a crisp value. Using the max-min-inference method, first the membership degree of the premise parts of the rules is determined via minimum-operator. Afterward, following the center of area (COA) method, all conclusion parts are interpreted as areas and the resulting fuzzy set  $\mu_{res}$  is determined via maximum operation. Calculation of the centroid is accomplished by the following equation and delivers a crisp value  $y_{akt}$  (Jantzen, 2007):

$$y_{akt} = \frac{\sum_{i=1}^n G_i * y_i}{\sum_{i=1}^n G_i} \quad (2)$$

The above mentioned fuzzy inference system shows exemplary a fuzzy controller configuration according to Mamdani (King & Mamdani, 1977; Mamdani, 1976; Mamdani, 1977). However, for the integration of fuzzy-based expert systems there exist further controller models like the Takagi-Sugeno model as well as a great

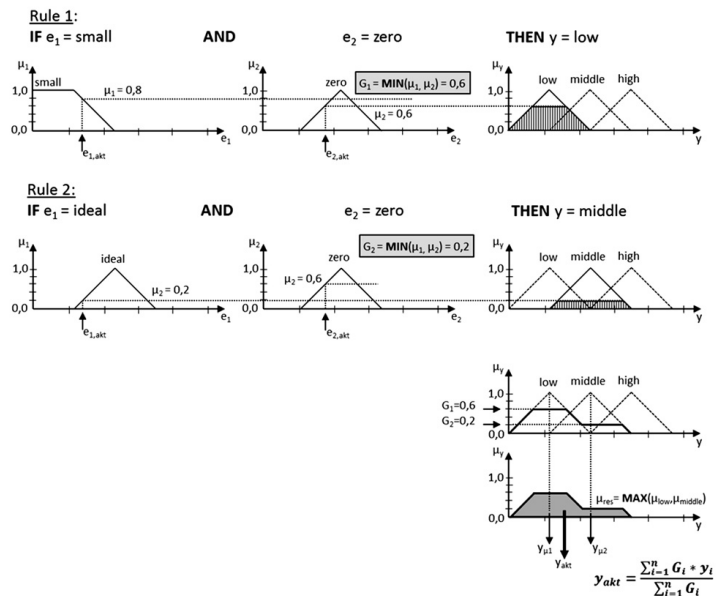


Fig. 1. Fuzzy inference scheme according to Mamdani.

variety of inference engines and defuzzification methods whose practicability has to be verified specifically for the corresponding application or system. A detailed description of fuzzy logic controller design and its applications is presented by Cao, Rees, and Feng (1997a, 1997b), Chen, Chen, and Chen (1993), Lee (1990), von Altrock (1995).

**3. Fuzzy reasoning, sensing and control**

Control strategies using fuzzy logic for control operations and decision making have encountered great interest to improve food and beverage manufacturing operations during the last years. Statistically research shows that especially in the field of quality assessment and analysis fuzzy reasoning for decision support of experts plays an important role (Miguel, 2002; Perrot et al., 2006).

**3.1. Quality evaluation**

Focusing on the field of quality assessment supported by expert systems (ES) and fuzzy reasoning techniques there can be distinguished between two main directions. The first one treats the chemical analysis of foods concentrating preliminary on providing artificial intelligence for analytical instrumentation and lab analysis. Thus, it opens interesting possibilities to ease on-line monitoring of key chemical parameters in the laboratory. Applications of expert systems in food analysis are quite numerous and can be found in chemical analysis like automated ammonia monitoring systems in fish farming, metal detection or to define olive oil origin and have been reviewed by Miguel (2002) taking into consideration a comparison of centralized and structural distributed approaches of ES systems. The second main direction covers the topic of quality evaluation not from a lab based analytical point of view but a generic, process-oriented, linguistic evaluation of product quality through human expertise.

In this context particularly the fuzzy symbolic approach has gained the interest of the food industry and is discussed in the next section.

**3.1.1. Fuzzy symbolic approach**

The representation and inference of linguistic rules coming from expert knowledge has developed to a wide topic of research and food applications during the last 10 years and has developed to a new concept under the name fuzzy symbolic approach based on the concept of a fuzzy symbolic sensor (Mauris, Benoit, & Foulloy, 1994). The principle of this approach is to apply fuzzy inference techniques to set up a common linguistic platform that links a set of

words (symbols used by an expert to assess a process or product quality) and numerical set. The strength of the relation between the symbols and the numeric scale is expressed by a membership function. In other words numerical and symbolic data is handled at the same level to make it understandable both by the operators and by a control system.

Following this approach, a detailed description of how human knowledge can be implemented into the control strategy of food batch processes if there is no sensing device and reliable process model available is given by Curt, Trystram, and Hossenlopp (2001), Curt, Hossenlopp, Perrot, and Trystram (2002), Curt, Hossenlopp, and Trystram (2007), Curt, Trystram, Nogueira-Terrones, and Hossenlopp (2004). The knowledge of an expert is modeled using the theory of fuzzy logic and applied to control the chopping operation for manufacturing the meat emulsion and the ripening operation to obtain the dry sausage. For control two strategies are applied. The first one is a batch-to-batch principle where the quality assessment of the product is delayed until the end of the run and was applied to the chopping operation. The other case is that the product is evaluated several times during the production process and the control is carried out using a batch-to-batch approach combined with feedback control. This strategy was used for the dry sausage ripening process. Fig. 2 shows a schematically structure of the symbolic approach and its implementation in sausage ripening control. The necessary measurements to characterize the product quality are sensory evaluations performed at-line by scheduled and experienced operators. To give a linguistic characterization of the chopping process, five sensory indicators, fat particle size, size homogeneity, cohesiveness, firmness and adhesiveness were taken from an expert as fuzzy input variables to calculate a global state variable of the product named chopping degree (CD) using COA as defuzzification. The objective is to obtain a meat batter with a CD from 4.5 to 5. In dependency of the resulting CD the output values rotation speed and mixing duration are changed. The rule base comprises 19 rules, each of them associated to a parameter of the two outputs. Similar to the chopping operation, the ripening progress was divided into six stages and evaluated through human sensory measurements. To characterize the ripening progress the expert used four sensory indicators (surface humidity, color, surface flora development, sticky defect) as input variables and evaluates if the product changes accurately according to the different ripening stages. If not, corrective actions are necessary and the operator modifies the set values of the process parameters. The rule base comprises 42 "IF-THEN" rules and proposes the necessary control actions by adjusting the output parameters hygrometry set

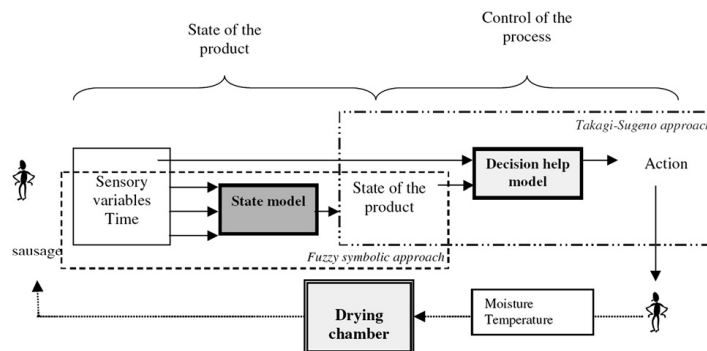


Fig. 2. Integration of a fuzzy symbolic approach for sausage drying (Allais, Edoura-Gaena, et al., 2007; Allais, Perrot, et al., 2007).

value, ventilation time, duration and temperature set value. The presented approach delivers a quite easy solution to integrate quality assessment into a control system if there is no process model or hard sensing device available. However, the stability of the control system if sampling intervals change, are delayed or even are omitted is not stated.

The idea of using fuzzy logic to represent the semantics of human assessment is a quite recent field of research and meanwhile there exist quite a lot of similar approaches compared to the aforementioned. (Davidson, Brown, & Landman, 1999) present a multiple input-single output fuzzy control system for a continuous, cross-flow peanut roasting process based on a process model and a combination of process sensors and human assessment for a feedforward and feedback control mechanism. In this context inputs to the fuzzy control system comprise crisp values for air temperature and roasted product color which is measured by an at-line colorimeter. Additionally, linguistic assessment of operator is performed evaluating peanut size and mass flow ratio as the quotient of peanut mass loading and air mass flow. A total of 60 rules and a simple max-min fuzzy inference system were applied to compute a single output of the controller being a numerical value for residence time to adjust the motor speed of the conveyor. The control model is a combination of fuzzy rules to estimate the heating time and a data-based mathematical zero-order kinetic model to describe the browning kinetics. Actually, the browning model is the major weakness at the same time. It is very data-specific and thus likely to fail if initial conditions of raw material change or setup modifications are done. However, to capture process disturbances a feedback correction of browning estimation via fuzzy error calculation is applied.

Further recent applications picking up on the symbolic approach are presented by Ioannou, Perrot, Curt, Mauris, and Trystram (2004), Ioannou, Perrot, Mauris, and Trystram (2004) and Perrot et al. (2004). Both works do not implement any hardware sensor as system inputs and rely exclusively on human assessment. The first one presents the development of a control system based on a fuzzy supported diagnosis and decision model to evaluate and control product browning in a continuous browning oven. The latter one (Perrot et al., 2004) introduces a decision support system to control the process of cheese ripening and informing the operator on-line about the global state change of the cheese toward the standard ripening trajectory at each sampling point.

The aforementioned applications show that using a symbolic approach offers an uncomplicated method to implement human reasoning semantics at each stage of the process where the operator is involved in measurement, diagnosis or control of a process. The data is processed on a symbolic level which can be simply accessed and used by the operator. In this respect (Allais, Edoura-Gaena, Gros, & Trystram, 2007) present four approaches to associate human expertise at a process level from laboratory results focusing on at-line sensory measurements combined with lab scale measurements, the use of lab expertise or experimental results for extracting qualitative rules, a reverse engineering approach to define the operator conditions for a new product and the comparison of operators expertise with bibliographic data to extract a kernel of knowledge.

Besides the advantage of presenting a simple way of accessing human expertise for food control actions the symbolic approach presents a method of standardizing quality assessment by unifying different operators evaluations to one consistent evaluation tool. A methodological guideline to handle expert-operator knowledge for sensory quality assessment of food products is illustrated by Allais, Perrot, Curt, and Trystram (2007).

However, the presented systems are to a high extent still dependent on expert decisions and therefore do not fit to the

automation aspect of process control. In respect to an automated process control system the systems input should not merely rely on operator's assessment. Fast developing techniques in computer vision and improved sensor technology open various options for reliable quality assessment in food production. For instance, (Iliev, Lindquist, Robertsson, & Wide, 2006) present a fuzzy based quality assessment system for food- and water quality evaluation with an electronic tongue. Here, fuzzy clustering is used instead of an operator's estimation to obtain quality parameters. Comprehensive studies of computer vision techniques and applications (Brosnan & Sun, 2004; Du & Sun, 2004, 2005, 2006; Gunasekaran, 1996) show high potential for reliable quality evaluation as presented by Ioannou, Perrot, Hossenlopp, Mauris, and Trystram (2002) using a camera and image processing techniques for representing human evaluation of sausage crusting based on fuzzy set theory. Another critical point is the underlying modeling of the assessment process being very specific concerning the production setup and the operators, respectively experts' estimation. Thus, it cannot reflect a generic solution that can be transferred to a different operating plant without greater modifications. Besides this a further bottleneck is the difficulty to capture system dynamics just by implementing expert knowledge. Accurate process modeling is a key issue for appropriate control actions. This is stated in recent publications pointing out the great scientific importance of food process and bioprocess modeling (Gernaey, Lantzi, Tufvesson, Woodley, & Sin, 2010; Perrot, Trelea, Baudrit, Trystram, & Bourguine, 2011; Trystram, 2010). Following this, dynamic models combining knowledge integration via means of computational intelligence, data and mechanistic based approaches together with multivariate process information from on-line measurements of multi-sensing concepts should be able to cope with the complexity and uncertainty of food production and establish a platform for accurate control actions.

Besides fuzzy logic, the field of chemometrics offers certainly various alternative approaches and opportunities for quality evaluation in food industry. However, existing chemometric tools, which are already extensively discussed in (Abdi & Williams, 2010; Lopes, 2005; Wold, Esbensen, & Geladi, 1987) cannot provide an integrated process control strategy or direct control actions. Their main scope addresses the purpose as an evaluation or analysis tool (data mining, pattern recognition, clustering and multi-linear regression). Thus, they can be used to generate process information for process monitoring reasons (e.g. soft-sensing) that can be used for control actions, but in a separate control system. On the contrary, fuzzy logic allows using a-priori process knowledge for immediate integration into process control. The multidimensional, non-linear mapping rules of fuzzy logic based systems allow approximating every technically causal system. Chemometric tools like Partial Least Squares, Principal Component Regression or Support Vector Machines belong to the group of data-based, mathematical approaches that do not contain a-priori process knowledge. The process knowledge is stored indirectly in independent parameters that do not necessarily represent the underlying biophysical and biochemical principles. Moreover, those methods are limited by the linearity of the included measured variables, as well as the boundaries of the data sets used for calibration. Crossing those borders leads to misinterpretations, as the underlying model is not valid any longer. Nevertheless, these approaches are of increasing interest and provide powerful tools for applications throughout the PAT environment (Lopes, Costa, Alves, & Menezes, 2004; Pomerantsev & Rodionova, 2012). Therefore, they provide highly sophisticated instruments for optimizing a system's control part and in consequence, play an important role in quality evaluation of food as stated by Escuder-Gilbert, and Peris (2010), Sádecká (2007).

### 3.2. Sensing and control

Combining heuristic expert knowledge, mathematical or mechanistic modeling techniques as well as the information retrieved from direct or indirect measurements, prediction of process parameters or trajectories can be carried out and used for process control strategies. In this section different feedback control applications are discussed using direct fuzzy control determining immediately the outputs from the knowledge base and on-line measurements or indirect fuzzy control of process variables as a kind of soft-sensing via phase recognition mainly based on multivariate sensing approach of state variables.

Applications of direct fuzzy control approaches can particularly be found in the field of fermentation. Here, a very interesting area of applied fuzzy control strategies is the production of baker's yeast which is commonly operated as fed-batch. During the fed-batch cultivation the necessary nutrients are supplied to the fermenter while the cell culture and products remain in the bioreactor until the end of the process. In contrary to batch operations the fed-batch method allows to adjust the specific substrate uptake, respectively the specific growth rate to a physiological optimal value. Therefore, it is of crucial importance to set up an accurate feeding control in order to avoid over- or underfeeding since both result in lower growth rates and thus a worse productivity of the plant. An industrial branch where this circumstance is of great importance is the production of baker's yeast. Here, a direct fuzzy control mechanism is presented by Kasperski and Miśkiewicz (2002), Miśkiewicz and Kasperski (2000) using a Mamdani type fuzzy controller to adjust nutrient dosage in a fed-batch baker's yeast process. The controller has five input variables (variation in the amount of glucose dosed, variations in glucose uptake rate, difference of glucose added and difference of glucose uptake rate between the last two dosing cycles, maximum respiratory quotient, quantity of each portion added and dissolved oxygen concentration). The knowledge base consists of 64 linguistic rules and a MAX-MIN inference engine was applied. Center-of-area method was applied to calculate the numeric value of the consecutive glucose portion which is the single output of the system. Sensors were used to measure CO<sub>2</sub> and O<sub>2</sub> content in the off-gas and the dissolved oxygen concentration in the culture. The system is merely based on linguistic expert knowledge and lacks a mathematical or mechanistic process model reflecting the relationship of respirator quotient, dissolved oxygen concentration and residual glucose concentration in the broth. The proposed system is able to prevent the occurrence of the Crabtree effect and thus giving a yield of 55% and a maximum specific growth rate of 0.16 h<sup>-1</sup>. However, results for specific growth rate cannot be satisfying compared to similar approaches (Besli et al., 1995; Mahjoub, Mosrati, Lamotte, Fonteix, & Marc, 1994). (Wang, Cooney, & Wang, 1979) report a constant specific growth rate of 0.25 h<sup>-1</sup> and an overall cell yield of 0.51 g/g. This might be due to the lack of a process model or direct measurement of substrate concentration. In an approach given by Besli et al. (1995), the fuzzy controller uses a mathematical process model according to (Sonnleitner & Käppeli, 1986) and the respiratory quotient to adjust the glucose feeding rate in a fed-batch fermenter. The results show that the controller is able to obtain the maximum yeast production only limited by the oxygen transfer capacity of the fermenter. As proposed by Mahjoub et al. (1994) direct measurement of substrate concentrations as well allow a more precise control of feeding rates resulting in higher specific growth rates.

An insight of implementing fuzzy logic into the fermentation process of a brewery is given by O'Connor et al. (2002). The applied fuzzy system includes three parts. The first one uses fuzzy logic as a control system that consists of two input variables: temperature

and present gravity. A rule-base of six rules in the "IF-THEN" format delivers the decisions for temperature control and to lead the process so that a distinct present gravity endpoint is achieved. An additional developed failure detection system tries to cover the safety aspect of process control by modeling and taking into consideration several opportunities of leakage flows. The latter part is a predictive decision model for process optimization. In this context the approach is undertaken to predict output values for alcohol content, bitters concentration, colors, present gravity, pH value and yeast cell count by focusing on the influence of temperature as the sole input parameter. However, reliability of the predicted parameters is merely promising for wort present gravity and pH values. Therefore, the fuzzy predictor needs improvement in accuracy. Regrettably, the accuracy or prediction error is not stated. The controlling parts of the system are able to compete with conventional controllers.

A practical approach for a brewers' yeast propagation control system based on a fuzzy expert system is presented by Birle et al. (2010). The fuzzy system receives on-line all relevant process data from a sensor array measuring turbidity (yeast cell count), extract concentrations, dissolved oxygen concentration, temperature and pressure. Via predefined model functions for extract decline and cell propagation which use the propagation time as an adjustable variable the plant operator sets the desired point of yeast harvest. Based on the entered propagation time the fuzzy expert system computes and controls the process temperature and aeration settings to achieve an aspired biomass concentration of 80–100\*10<sup>6</sup> cells/ml within the desired time space. The presented method shows good results for propagation intervals from 24 up to 72 h. However, the above mentioned control strategies do not take into consideration the physiological condition of the culture that has great influence on the substrate consumption rate or product formation rate. Due to that, the control behavior should be adapted to the different physiological stages of the microorganism which can be identified through the determination of distinct key state variables. Hence, latest published research by Krause, Birle, Hussein, and Becker (2011) point out the relevance of on-line detection of crucial process variables via ultrasonic measurement, principles of soft sensing and fuzzy logic control including mechanistic growth modeling.

#### 3.2.1. Fuzzy based soft-sensing of process parameters and phase recognition

As a tool of soft sensing, fuzzy inference is stated to be a meaningful device for monitoring the physiological phase of biological cultures (Horiuchi, Kamasawa, Miyakawa, & Kishimoto, 1993; Horiuchi, Kamasawa, Miyakawa, Kishimoto, & Momose, 1993; Konstantinov & Yoshida, 1989). The process is divided into culture states like lag phase, growth phase, production phase and declining phase. Splitting up the fermentation process into its distinct phases allows to diskew its complexity into relatively simple sub models for the different phases and thus permits a more precise control. An approach for on-line physiological state detection using fuzzy inference based on error vectors is given by Hiroshi, Keigo, Suteaki, and Ken-ichi (1995). They present a combined system of fuzzy procedures and molar flux calculations founding on a metabolism reaction model for yeast fed-batch cultures that is able to successfully characterize the physiological phases of cell growth and ethanol formation. However, an integration of the state estimator into an appropriate control system is missing.

In this context another very detailed description of applying fuzzy logic to fermentation and maturation shows the work of Hege (1997). Based on the leading process parameters extract concentration, pH value, diacetyl and ethanol concentration a fuzzy-



decision module divides the process into 4 phases. A second fuzzy controller calculates the deviations of the leading parameters from their idealistic progression and then takes influence on the process by adjusting the fermentation temperature.

Whitnell et al. (1993) present a fuzzy logic based expert system used as a software sensor to estimate the endurance of fermentation time based on the parameters pitching rate, pitched volume and viability. For this, a three stage fuzzy system for parameter estimation was developed at the first instance giving an initial prediction of fermentation time at the point of yeast pitching. Then, an estimate of the vicinal diketone level (VDK) during the fermentation process is proposed and finally, a revised estimation of fermentation time based on VDK decline in the end state of fermentation is suggested. The accuracy of the initially predicted fermentation times was in between 24 h of the actual fermentation times for 9 of 13 fermentations of the validation data set. However, the VDK estimation needs further investigation in respect to reliability and accuracy (only 4 of 7 usable validation sets were predicted within 24 h of the actual time) as the number of validations is too less. Furthermore, the prediction is only based on evaluation of history data sets and expert assessment. An evaluation tool for the current process behavior and information is missing. In this respect, assuming sufficient training data, the application or combination with a neural network could deliver more reliable results. Another point is that the system still needs feeding with off-line measured data. Thus, a fully automated system is not given.

Another approach to ally process control and soft sensing is presented by Kashihara, Mawatari, Inoue, Prior, and Cooney (1993) who use a knowledge-based system as a software sensor in combination with temperature control. Thereby, the application of an expert system based on "IF-THEN" rules to control the beer fermentation process by temperature manipulation based on the pH-value of the suspension is presented. The employed knowledge base comprises 6 major sets of rules in the matter of "IF-THEN". In this context a knowledge-based software sensor for process parameter estimation and filtering out erroneous parameters due to sensor noise was developed. Control parameters (pH, amino acid, sugar concentration) are estimated by the knowledge based system by evaluating the reliability of the input data. This is done by comparing the process data which consist of on-line (pH, dissolved oxygen, temperature, time, exhaust gas data) and off-line analysis data (amino acid, optical density, sugar) to standard profiles data that was obtained from experiments at different fixed temperatures. If the allowed constraints (based on an operator's expertise) are exhibited, an error signal and a possible proposal for action are communicated to the operator. The second element of the system provides recognition of the fermentation process phases and their separation into 3 stages (lag, growth, stationary phase). Parameters oxygen uptake rate, CO<sub>2</sub> evolution rate and fermentation time are taken for phase recognition and compared to standard profiles that were obtained for distinct temperatures. From the deviation the expert system then changes the actual temperature in order to guide the process into the right direction. Although the rules were kept very simple the process could be controlled and kept within tolerable constraints. This fact indicates that the pH value is a meaningful parameter for a prosperous and economic control of fermentation processes. However, the parameter estimation is done by comparison with a standard profile and thus is not transferable to other systems without greater modifications. The proposed system also is in need of off-line data analysis.

The several approaches described before show that fuzzy logic is a powerful tool to control multivariate and non-linear process behavior such as fermentation processes using its advantage of approximate reasoning. By applying fuzzy sets one is able to give a description of complex biological circumstances that can easily be

handled and represented by modern data processing systems. The rules containing the expert knowledge of the process can be set up without any complex mathematic modeling and are easy to understand. Summarizing, fuzzy systems can be interpreted as a special case of local modeling techniques, where the input domain is partitioned into a number of fuzzy regions represented by multivariate membership functions (Azar, 2010). For each region, a rule is set up that defines the system's output in that region. The class of functions that can be properly replicated by the resulting model is identified by nonlinear mapping through using the multivariate membership functions. However, not to neglect are some disadvantages referring particularly to fuzzy logic's application by means of soft sensing and parameter or state estimations. The simplicity of fuzzy logic systems is paid by their inaccuracy in case of parameter prediction, for instance. The imprecision is not immediately due to the fuzziness itself the system is working with, but more to a fine tuning of the rules. In most cases there exist just a few rules with the consequence that a single rule may have big impact on the process although the rule is rather inconvenient. Actually, the major drawback of the described approaches above is that control systems based on fuzzy logic are not capable of learning and therefore do not adapt to changing process states or subtle variations of raw materials that might affect the process behavior as well. For this reason, a continuous and independent optimization of the process by means of expert knowledge is not possible. Those systems are more suitable for maintaining distinct process boundaries and quality corridors. Furthermore, only fragmental or no expert knowledge of the process is available. Then, a manual tuning process of the fuzzy parameters by modifying membership function and/or the rule base of the fuzzy system has to be performed. To overcome the drawbacks of mere fuzzy-based control systems, hybrid systems including neural network or kalman filtering techniques for have been developed and will be discussed in the following sequences.

#### 4. Hybrid fuzzy systems

##### 4.1. Introduction to neural network techniques

Artificial Neural networks (ANNs) are an approach to virtually mimic the actions of neurons in the human brain (Kramer, 2009). Basically, they consist of artificial functional neurons that are connected to each other. Neurons or units that are ordered on top of each other are usually comprised to layers. The strength of the connection between two neurons is expressed by a weight (Beale & Jackson, 1990; Lippmann, 1987). The bigger the absolute value of the weight, the bigger is the impact of the unit to the other unit. Hence, the knowledge of a neural network is stored in its weighting parameters. A widely chosen structuring is the so called multilayer perceptron which is shown exemplary in Fig. 3. In artificial neural networks a consistent approximation to a threshold function is applied to accomplish non-linearity. The most common function used in this context of constructing an artificial neural networks activation level is a sigmoid function. Mathematically, the threshold value or bias represents the point with the highest gradient of a monotonically increasing activation function. In the biological sense it denotes the threshold that has to be reached to make the neuron able to "fire". To adjust the threshold value, a node can be equipped with an additional weighted input, called bias weight  $w_j^b$  (Dreyfus, 2005; Simon, 1994). The obtained value due to non-linearity is then handed to all subsequent connections at which a multiplication with the corresponding weights is done as well. This procedure continues throughout all layers until the output values  $y_n$  are obtained.

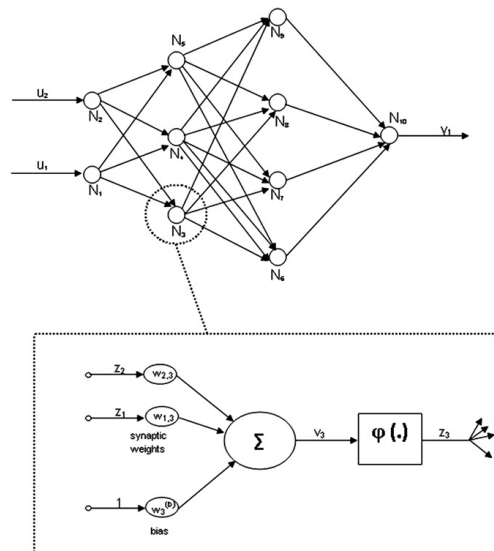


Fig. 3. Structure of a multilayer-perceptron.

Besides the topology, the training and learning algorithms are another crucial aspect in implementing a neural network. Using means of feedback control mechanisms allows adjustments in the structure and parameterization of the network via self-modification. Depending on the applied training and learning algorithms connections are cleared, added or strengthened. A widely used training method is the backpropagation algorithm commonly applied to multilayer feed-forward-networks consisting of an input layer, an output layer and at least one hidden layer (Lippe, 2006). The main idea of this method is to run the neural network backwards in order to compute the gradient by setting up the partial derivative of an error function with respect to all weights. The single elements of the gradient quote in which direction and to which extend the error function is changed if a corresponding weight is modified.

#### 4.2. Soft sensing via artificial neural networks

In this section the practicability of ANNs for soft sensing applications with special focus on beer fermentation and maturation is described. Besides the economical factor fermentation time, the most important parameters of primary beer fermentation are the concentrations of ethanol and sugar. The successful control of this process via temperature and pressure adaptation is highly dependent on the knowledge these trajectories. In addition to that information about threshold concentrations of aroma components like diacetyl, esters or phenols is of crucial importance for final product quality. The lack of appropriate hardware sensors that allow an accurate on-line determination of those key process parameters has led to the development of soft sensing approaches. An example using a backpropagation neural network for estimation of ethanol concentrations is given by Syu and Tsao (1994). A three layer (3–3–7) neural net using initial free amino nitrogen concentration, initial oxygen concentration and initial viable cell count to predict produced ethanol concentrations at timely intervals of 24 h

over seven days of brewing fermentation is presented. A back-propagation learning routine using delta learning rule was applied as algorithm demonstrating good simulation results. However, an on-line capability is not possible as input values are determined off-line.

An approach of combining fuzzy logic and an extended kalman filter is presented by Simutis, Havlik, and Lübbert (1992). A system is presented to reduce the uncertainty of the applied fermentation model and hence to improve on-line state estimation and time prediction in case of productional scale beer fermentation. The whole process is piecewise modeled corresponding to process phases. Founding on that, break down of a comprehensive process model into several single state models and parameter estimation is carried out with a fuzzy-extended kalman filter (FEKF). The model assignment to a given situation is accomplished by means of fuzzy reasoning. For modeling of the fermentation process an adapted version of the model of Engasser et al. (1981), including temperature effects and eliminating the biomass concentration was used. On-line measuring comprises temperature, gas flow rate at the fermenter output and volume of the liquid phase. Based on this the total  $\text{CO}_2$  evolved is permanently computed. Total sugar concentration was analyzed off-line every 24 h. Process operationalization consists of 5 process phases described by six further models. The fuzzy expert system consists of 5 input variables that are process time, sugar concentration process temperature sum of evolved  $\text{CO}_2$  and  $\text{CO}_2$  evolution rate. The only output variable is the detected output phase, chosen from the 5 predefined classifications. Results of the realized experiments show that the FEKF is able to achieve sufficient predictions with an average prediction error of sugar concentration of 2.72 g/l after two off-line sampling points. The presented system is adopted by Beil et al. (1992) for state estimation of sugar and ethanol concentrations to predict fermentation trajectory for a certain temperature profile. In this context a comparison to a fuzzy-neural network trained with a back-propagation algorithm is made. According to the premier approach for each identified process phase a separate ANN is set up instead of an extended kalman filter. Both systems are strictly correlated and reflect the off-line analytics quite well, whereas the fuzzy-ANN has a slight advantage (average prediction error of sugar concentration 2.1 g/l) in respect to the predicting performance compared to the FEKF (average prediction error of sugar concentration 2.8 g/l). For both approaches it could be shown that the separation of the process into several process phases led to significant improvements. Moreover, the implementation of fuzzy logic allows a smooth transition from one process phase to another.

Two dynamic models were developed by Corrieu (2000) and compared to estimate density and ethanol concentration as well as end time during primary beer fermentation for two types of beer. One model is based on a neural network approach and the other one takes into consideration empirical developed temperature dependent fermentation kinetics. First, the development of a software sensor for wort density and ethanol concentration based on an artificial neural network is described. In this respect the other aim was to give a prediction of the fermentation process. The dynamic prediction model in form of an ANN has two inputs, the relative progress factor and the temperature at the current time, two hidden neurons and one output which being the predicted relative fermentation process one step (one step corresponding 2 h) ahead. The progress factor is a dimensionless variable and related to time dependent differential equations of wort density, released  $\text{CO}_2$ , ethanol concentration and residual sugar concentration. The temperature follows a fixed temperature profile. Network training comprised 22 fermentation experiments using a quasi-Newton algorithm for optimization of the network coefficients by minimizing the sum-squared prediction errors.  $\text{CO}_2$  release rate was

obtained from a differential pressure measurement and correlated linear with density variation and ethanol concentration. For density estimation the average error is 0.27 °P and 0.12 mL/100 mL for ethanol which is a quite acceptable and sufficient error under practical conditions. After half of the CO<sub>2</sub> is released fermentation end time is predicted with a mean error of 4.75 h. However, a weakness of the kinetic model is the fact of a not negligible offset of the differential pressure sensor due to noise and the requirement of a highly accurate detection device for wort density and volume for the calculation of CO<sub>2</sub> to be released. Despite this, final wort density must be known in advance, as well as total CO<sub>2</sub> to be released. In addition to that and as indicated from the author, the underlying models need more investigations in order to improve the reliability of time prediction. Nevertheless, the system points into the right direction: to replace costly measuring devices by means of soft sensing. The presented satisfying results for density prediction emphasize this progress.

The work of Enders (1999) presents a software sensor for diacetyl estimation using a dynamic neural network with the aim to replace time-consuming and costly off-line analysis. The basic idea of the software sensor for diacetyl is to determine the concentration of diacetyl during beer fermentation from easily measurable physical factors like temperature, pressure, extract concentration, turbidity and pH value so that a laborious off-line detection of diacetyl is not necessary. The software sensor consists of a dynamic neural network based on an adapted resilient backpropagation training algorithm. The neural network receives the input values as on-line measured values from the process and delivers as output an estimated value of the current diacetyl concentration. Bygone input values are taken into consideration as well. For training the applied algorithm compares the estimated value with the actually measured value and uses the deviation to compute in several cycles the stepwise adaption of the neural networks' weights. Although there is some discrepancy and wider limits of variance in predicting the trend of the commanding variables and diacetyl concentrations the presented approach actually is able to decrease off-line sampling to a great extent and thus, reveals the high potential of software sensors and what can be achieved in respect to their field of application in the brewing industry. Riverol and Cooney (2007) describe estimation of the ester formation during beer fermentation using neural networks. The influences of fermentation temperature and dissolved oxygen content in the production of ethyl acetate and isoamyl acetate are studied. Therefore a comparative study between analytical determined kinetic parameters and their estimation via an ANN is done showing a prediction accuracy of around 1.0%. A mathematic method is established to control the production of esters in quantitative respect. Functions containing rate constants of ester formation for the stationary and logarithmic phase were set up. The experiments were carried out with variation of temperature and dissolved oxygen within fixed ranges. Influence to esters and ethyl acetate and their formation rate respectively was analyzed and studied. The developed equations were used for comparing the performance of the neural network in the prediction of the ester formation and thus its fitness for soft sensing. The results obtained confirm the results of previous studies (Nakatani, Fukui & Nishigaki, 1991).

Another approach of an ANN-based software sensor is presented by Mileva (2008) describing an artificial neural network-based approach for prediction of antioxidant characterizations during the brewery fermentation. Three variables are predicted: Total antioxidative capacity, amount of glutathione and total phenols. Input variables are the biomass content, limiting substrate concentration and alpha-amine nitrogen. For experimental surgery three yeast strains have been investigated. The applied neural network structure includes one hidden layer consisting of five neurons and output layer containing three output neurons. The

transfer functions selected for each layer are tan-sigmoid transfer functions in the hidden layer and linear transfer functions in the output layer respectively. For training process a Levenberg–Marquardt algorithm is used. The simulation and validation tests show a high accuracy of the designed software sensors.

Having a look on large scale production of baker's yeast Karakuzu, Tuerker and Oeztuerk (2006) present two soft sensors based on a three layered feedforward neural net to estimate biomass concentration and specific growth rate. The inputs of the ANN are fermentation time, respiratory quotient as the ratio of CO<sub>2</sub> production rate to O<sub>2</sub> uptake rate and molasses feeding rate. The soft sensors are embedded in a Mamdani type fuzzy controller that determines substrate and air feeding rates in order to maintain set points for specific growth rate and dissolved oxygen concentration. Controller inputs are the errors of specific growth rate and dissolved oxygen concentration as well as elapsed time, ethanol concentration and changing amount of dissolved oxygen concentration. Estimation results of the soft sensors are quite satisfying for fixed initial process conditions. However, it is shown that the soft sensors are very sensitive to unintentional variations of initial conditions like inoculum size. Actually, this is also one of the major drawbacks of the aforementioned approaches. Sensitivity analyses and robustness studies in respect to error-prone, incomplete or missing input data is generally neglected. Despite their advantages of learning abilities, optimization abilities and connectionist structure, ANNs some disadvantages like slow convergence speed, the need of sufficient training data and the syndrome of a "black box" behavior (Jack, 1996).

To overcome the weaknesses of ordinary static neural networks Becker et al. present a dynamic approach of a neural network for on-line fermentation optimization and prediction of trajectories of gravity, pH value and diacetyl (Becker & Delgado, 2002). In contradiction to static neural networks, modified dynamic neural networks, like self-recurrent neural networks, are capable to consider the process history of a current running process and therefore are able to handle time dependencies of state variables and the dynamic attitude of the fermentation process in a more accurate way. Based on the works of Peters (1999) and Enders (1999) the presented system uses separate neural networks for each state variable to predict and each output variable is conjoined and fed back to the input layer of each neural network. The innovation is the implementation of "finite-impulse response" neurons (FIR) that substitute the weights of a standard feed-forward network at the connection between two neurons. The neurons comprise three time-delay elements that shift the current activation  $y_i(t)$  of the neuron  $i$  in three future time steps to the subsequent storage position. The application of those time-delay neurons is that the activity of each neuron can be delayed for a certain number of time steps and thus, can be taken into consideration for the output calculation of the neural network. By minimizing a cost functional  $J$  the trajectory of the control variable temperature  $T$  is optimized:

$$J = \varphi(x(N)) + \sum_{t=0}^{N-1} \lambda^T(t+1) \{f[x(t), u(t), t] - x(t+1)\} \quad (3)$$

Here the applied system equation  $f[x(t), u(t), t] = x(t+1)$  is added a multiplier term  $\lambda(t)$  resulting from the scalar Hamilton sequence (Bryson, 1975, 1999; Srinivasan, Palanki, & Bonvin, 2003). The control vector  $u(t)$  depends on temperature  $T$  and time  $t$ . The vector  $x(t)$  defines the state variables gravity, pH value and diacetyl.

The obtained results for prediction are quite convincing for gravity. Compared to a reference course the fermentation time could be reduced by about 20% which leads to a better and more



efficient utilization capacity as well as a reduction of variable resource costs. However, the major drawbacks are the lack of reliable and precise software sensor for diacetyl estimation. Moreover, the applied training data for the neural network was very specific and came from one brewery. For this reason the system is not conveyable to another brewery without additional modifications and training steps.

Fellner et al. (2003) present another hybrid and innovational approach to combine and integrate a-priori knowledge in a feed-forward neural network using functional nodes. The described methods are for the use in a software sensor applied to diacetyl formation during yeast fermentation. For this a set of differential equations describing the progress of diacetyl formation is embedded into arbitrarily located functional nodes of the neural network. For training a gradient descent method is applied, where the error gradient is calculated by a backpropagation algorithm. The hybrid approach increased the efficiency of training and improved the generalization and robustness. The amount of training data sets could be reduced by 50%, giving the same accuracy compared to a conventional approach. For evaluation a set of practical relevant constraints and criteria was defined and the obtained results from the hybrid approach were compared to a pure ANN without any functional nodes showing a better efficiency and accuracy of prediction for the hybrid model.

It is obvious that artificial neural networks play an essential role in various life science applications. Due to this importance some very relevant aspects concerning the engineering part of neural networks should be discussed. The engineering part and particularly the choice of pre-processing the data and feature extraction are one of the most important parts in establishing an artificial neural network and assessing the final system's performance (Bishop, 1995). In this context, the complexity of pre-processing can vary from simple linear transformations of input or output data to complex operations reducing the dimensionality of input data in order to condense available information into representative features. Beyond that, the incorporation of prior knowledge into the networks structure or its pre-/post-processing sections can be used for modifications of the training process. As the training procedure may contain an iterative algorithm, the pre-processed data set should be used to train the ANN. For applications using on-line learning each new data point has to be pre-processed prior to its delivery to the network. One of the most common tools of pre-processing is a simple rescaling of the input variables (Bishop, 1995; Bishop, 2007). This is very advantageous if different variables differ by several orders of magnitude according to their units of measurement. Applying linear transformations allows to having similar values for all inputs. Thus, each variable is treated independently and for each variable its mean and variance with respect to the training set is calculated. Normalization ensures that all input and target (in case of regression issues it might be suitable to apply linear rescaling to target values) variables are then of order unity and the weights can be assigned an appropriate random initialization before training. If there exist interdependencies among input variables there can be applied a more complex rescaling, known as whitening, allowing for correlations amongst the variables (Fukunaga, 1990). Those transformation techniques count for continuous variables. In case of discrete data an appropriate approach is to distinguish between ordinal variables having natural ordering and categorical variables. A detailed description of transforming discrete variables into continuous variables is given by Bishop (1995).

Multilayer networks are known for their capabilities as universal approximators. Here, the contrariness of overfitting the network on the one hand and choosing the right number of neurons and layers to achieve a sufficient accurate approximation

of a distinct problem on the other hand, has to be considered. There exist various possibilities to improve the generalization (inter- and extrapolation) of a neural network. One method is regularization, where the performance index is modified by applying a term that penalizes the networks complexity. One of the most common penalty terms is the sum of squares of the network weights. The basic idea is to having small values for the weights by using the performance index. The difficulty is to select a proper regularization parameter for obtaining a smooth network response but not having the network overfitted. One of the most successful methods for choosing the accurate regularization parameter is Bayesian regularization described by Dan Foresee and Hagan (1997), MacKay (1992). A detailed and comprehensive study of generalization and overfitting is given by Hagan and Demuth (1999), Hagan, Demuth, and Beale (1996), Hagan, Demuth, and Jesús (2002), Haykin (1994).

Another very serious point in processing the data is to handle missing data, e.g. due to sensor failure. A possible solution could be to fill the missing data via a regression function over other variables using available data. However, this might be error-prone as this approach underestimates the covariance in the data due to the noise-free regression function. Managing missing data can be treated by expectation-maximization (EM) algorithm as stated by Ghahramani and Jordan (1994). Ahmad and Tresp (1993) suggest managing missing data by integration over the corresponding variables, weighted by the appropriate distribution. Missing data points then are filled with values randomly (e.g. by a simple Monte Carlo approximation) drawn from the distribution as stated by Lowe and Webb (1990). However, this approach needs the distribution to be modeled.

The way of identifying unknown parameters or feature selection is based on two components. The first one is to determine a criterion to assess which subset of features is best (selection criteria). The second is to find a procedure to search through potential subsets of features (search procedure). Numerous search procedure methods are proposed in the literature. One of the most known methods are the stepwise (Kittler, 1978) or Sequential Forward Selection (SFS)/Sequential Backward Selection (SBS), branch-and-bound (Narendra & Fukunaga, 1977) and genetic algorithms (Il-Seok, Jin-Seon, & Byung-Ro, 2004). The stepwise search is one of the simplest algorithms, adding or removing single feature to or from a given subset. However, this approach is considered to be sub-optimal as it suffers from the "nesting-effect" (features that were once selected/deleted cannot be removed/reselected afterward). The branch-and-bound approach uses monotonic evaluation function for discarding subsets not meeting a specific bound. However, this method gets inefficient for feature selection problems treating a large number of features, particularly because it may need to search the entire possible region to find the optimal solution. Genetic algorithms propose a combinatorial search technique based on both random and probabilistic measures. A fitness function is applied for evaluating subsets of features. Combinations via cross-over and mutation operators produce the next generation of subsets. In summary the GA employs a population of competing solutions, evolved over time, to converge to an optimal solution. The solution space is searched in parallel. This targets to avoiding local optima. Latest published studies propose the use of Swarm optimization like Ant Colony Optimization for feature subset selection (Al-Ani, 2005). A general review of feature selection techniques in bioinformatics is given by Saeyns, Inza, and Larranaga (2007).

#### 4.3. Hybrid systems

To close the gap between fuzzy logic and neural networks hybrid systems denoted as fuzzy-neural or neural-fuzzy networks

have emerged in the field of biological process engineering, covering the advantages of both computational philosophies (Gupta & Rao, 1994). Once, the parts of a fuzzy system have been arranged in a parametric form, the inference engine turns into a parametric model that can be automatically tuned by the learning procedure of an ANN. The merging of fuzzy logic and neural networks leads to an integrated system combining the advantages of both technologies (Fullér, 2000).

However, only little applications can be found for process control in industrial food production. A fuzzy neural network (FNN) system is presented for temperature control of a sake mashing process by Honda, Hanai, Katayama, Tohyama, and Kobayashi (1998). The structure of the FNN is shown in Fig. 4. The inference system is simplified using singletons in the consequence part. The tuning of membership functions in the premise part and the identification of fuzzy rules is performed by adjusting connection weights via backpropagation learning algorithm. Subsequent to learning, the determined connection weights can be described linguistically.

A hybrid control strategy for industrial scale temperature control of a 300 m<sup>3</sup> cylindroconical fermenter based on quality parameter estimation of diacetyl is described by Gvazdaitis (1994). Therefore, an extended version of the neural network described by Simutis, Havlik, and Lübbert (1993) is used. The control part is realized with a fuzzy-based expert system and by implementing a cost function, cooling costs could be reduced by 20% maintaining the quality claims at the same time. Kurz (2000) uses a cognitive approach for observation and control of beer fermentations. A multisensor system (pH, gravity, turbidity, temperature) for better observability of beer fermentation and maturation is presented. Particularly the on-line determination of diacetyl by using an artificial neural network was aspired. In this context, a fuzzy logic system for fermentation state detection based on on-line information was used. The prediction of diacetyl was accomplished by a cognitive estimator for diacetyl based on a multilayer feedforward neural network. To adapt the ANN, a supervised training of the network was done with the sum of squared errors as error measure. There are 5 input neurons for the ANN consisting of temperature, time, gravity, turbidity and pH value, 9 hidden neurons and 1 output neuron. Classification of the states into 4 phases is

performed by a fuzzy based detection system. The information therefore used is gravity, estimated diacetyl, turbidity, pH value and process-time. A set of 10 rules is used to characterize the different phases in a reliable manner. The presented method provides a practicable and promising approach stating a potential to reduce fermentation time by 25%. However, the applied ANN needs more training data so that it is sufficient for diacetyl determination in other breweries and other yeast types. To ease the training process, a central training center is suggested for data pre-processing and training of the neural net. The systems strength is its robustness. The displayed rule base delivers a declined, but still reliable detection of the several fermentation states although measurement failures occur.

As a very recent approach (Ghoush, Samhouri, Al-Holy, & Herald, 2008) applies an adaptive neuro-fuzzy inference system (ANFIS) to formulation and modeling of emulsion stability and viscosity of a gum-protein emulsifier in a model mayonnaise system. In this case, ANFIS was used to model and determine the properties of the resulting mayonnaise with temperature and rations. The system takes two techniques for parameter updating as shown in Fig. 5. For the membership function parameters in the premise part a gradient descent backpropagation neural network is applied, while for the consequence part least squares method is used for identification. In the forward pass of this hybrid learning method functional signals are passed until the fourth layer and consequent parameters are detected by least squares prediction. In the backward pass, error rates are processed in the other direction updating the premise parameters via gradient descent. The system is able to produce a sufficient average prediction error of output properties of 4%.

Following this way, it is possible to combine the low level learning capabilities and computational strength of neural network techniques with sophisticated humanlike IF-THEN thinking and reasoning of fuzzy systems. ANFIS structures offer quite attractive features for transparent implementation in food applications like uncomplicated implementation, fast and accurate learning capabilities, good generalization abilities, easy traceability due to linguistic fuzzy rules and simple incorporation of linguistic and numeric knowledge for problem solving (Jang & Chuen-Tsai, 1995; Jang, Sun, & Mizutani, 1997). However, it should be noted that with growing system complexity and amount of variables the degrees of

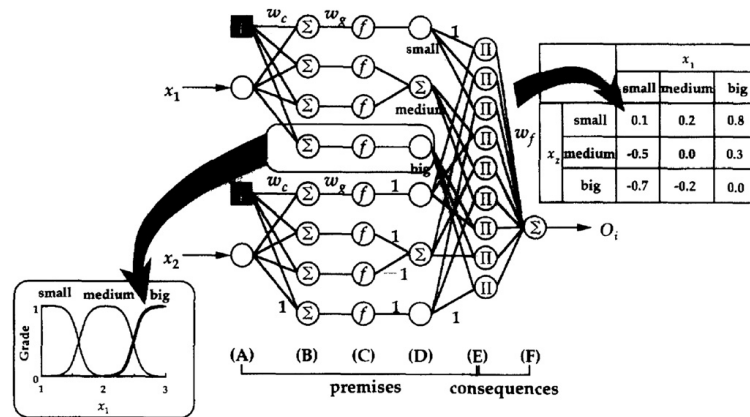


Fig. 4. Structure of a fuzzy neural network. Circles and squares reflect units of the neural net and  $w_c$ ,  $w_g$ ,  $w_f$ , 1 and  $-1$  are the connection weights. Membership functions in the premise part are tuned and fuzzy rules are identified by adapting the connection weights  $w_c$ ,  $w_g$  and  $w_f$  by backpropagation algorithm. After the learning procedure, determined weights  $w_i$  can be described linguistically, e.g. IF  $x_1$  is big AND  $x_2$  is small, THEN output is 0.5 (Honda & Kobayashi, 2000).

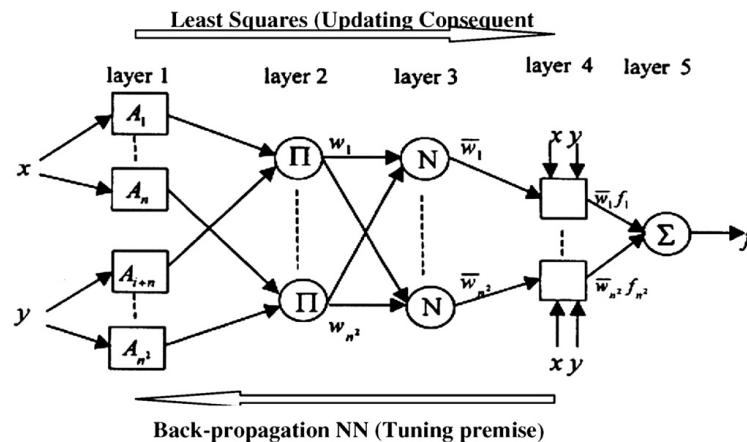


Fig. 5. General ANFIS architecture. Nodes in layer 1 are adaptive nodes with node functions (membership functions) and parameters are referred to premise or consequent parameters. In layer 2 all nodes are fixed nodes multiplying incoming signals and sending product output (firing strength of fuzzy rule). Fixed nodes in layer 3 calculate the ratio of the one firing strength to the sum of all rules' firing strength (normalized firing strength). Adaptive nodes of layer 4 contain node functions (i.e. linear combination of input variables) and parameters are referred to consequent parameters. The fixed single node of layer 5 computes overall output as the sum of all incoming signals (Ghoush et al., 2008).

freedom for parameter calculation increase tremendously, leading to high computational effort especially when least-squares estimation is applied. Using gradient descent has the limitation that all membership functions and inference functions have to be differentiable, hence, making this technique more employable to Takagi-Sugeno fuzzy systems compared to Mamdani type ones (Azar, 2010). Another point is that they tend to get stuck in finding local optima instead of global optima (Beyer & Schwefel, 2002; Schwefel, 1993). Thus, evolutionary optimization strategies like genetic algorithms or particle swarm optimization that perform random search in the parameter space are applied to various control operations (Andrés-Toro, 1997; Andrés-Toro, Girón-Sierra, Fernández-Blanco, López-Orozco, & Besada-Portas, 2004; Benjamin, Emmanuel, David, & Benjamin, 2008; Mohebbi et al., 2008; Perrot, Mé, Trystram, Trichard, & Decloux, 1998; Xiao, Zhou, & Zhang, 2004). The merging of knowledge based fuzzy systems, neural networks and evolutionary optimization strategies have moved into the recent focus in process optimization and control as it combines their individual strengths. This trend has been reviewed by Shapiro (2002) and is reflected in current applications (Oliveira & Schirru, 2009; Zhen, 2011). However, applications in the food and beverage sector are very scarce and offer a wide range of scientific research.

Taking a look on the engineering part the choice of appropriate sampling times is a serious issue in every control application, however, little attention is given to this topic in most of the proposed approaches. Derived from the Shannon's theorem the Nyquist frequency is twice the bandwidth of the signal and states that the *minimum sampling frequency* must be at least twice that of the highest frequency component present in the original signal in order to avoid aliasing (Leis, 2011). However, a too high sampling rate wastes computational capacity and is likely to produce additional noise in the signal.

This issue gets very important in terms of time series predictions with neural networks (Frank, Davey, & Hunt, 2001) to find the appropriate sample rate and to identify a correctly sized input window. In case of on-line sensing, a variable is measured or sampled on-line to create a series of discrete data points that are

equally spaced in time. The rate at which the samples are taken determines the maximum resolution of the underlying model. However, this does not state that the model with the highest data density has the best predicting performance. Due to this, the right choice of sampling rate is of great importance for the control strategy. Current studies of controller design use a variable-period sampling approach for networked control systems with random time delays (Liu, Liu, Zhang, & Li, 2007; Rahmani & Markazi, 2012; Sadeghzadeh, Afshar, & Menhaj, 2008; Xinlan, 2009). The main problem of networked control systems are the network-induced delays randomly occurring at data exchange between sensors, actuators and controllers across the network. This has great influence on the system's stability as a whole. The stability of the networked control systems with variable sampling period was already studied by Jianqiang, Qian, Dongbin, Wen, and John (2007). The induced time delay can be predicted on-line using a back-propagation feedforward neural network. The predicted time delay is then chosen as the sampling period leading to an improved performance.

Another problem rises, if measurements of distinct key variables cannot be performed on-line due to e.g. the lack of accurate on-line sensors and additional off-line measurements have to be performed. Taking into consideration fermentation processes, i.e., only a part of fermentation variables is measured on-line. Most variables are merely available through off-line laboratory analysis resulting in delayed and infrequent measurements reducing the system's observability. To overcome these challenges various adaptive control strategies have been developed allowing estimation of important not directly measurable variables like substrate or biomass concentrations. In this context remarkable work was done by Bastin and Dochain (1990) in the field of bioprocess control. This work presents a detailed and comprehensive study on the on-line estimation of state variables and parameters. Special focus is put on extended state observer techniques of Luenberger and Kalman type, as well as adaptive control of bioreactors. The on-line estimation of unknown variables and their implementation into the control law reveals significant advantages of compensating model and process uncertainties. The predicted state variable information

allows complementing hard sensor data or delayed measurement information and provides frequent feedback signals to the controller leading to an enhanced control performance. For this reason bioprocess state estimation is an essential tool in advanced process control. A comprehensive review of different estimation methods is presented by Venkateswarlu (2005). In relation to food process control, a summary of relevant applications using (non-) linear adaptive and predictive control design strategies is given by Perez-Correa and Zaror (1993). An interesting approach for on-line prediction in fermentation using adaptive neural models is presented by van Breusegem, Thibault, and Chéry (1991). The proposed approach applies a modified sliding window learning procedure that allows handling delayed and/or infrequent measurements. A different method of adaptive estimation and control is presented by. This approach applies an extended multirate adaptive estimation algorithm to predict nutrient levels in a fed-batch fermentation using frequent on-line measurements of CO<sub>2</sub> evolution rate and infrequent, delayed off-line measurements of biomass and substrate concentration. However, infrequent off-line sampling still burdens the observability of a system. In case of non-uniformly sampled multirate systems studies propose to recover the continuous-time system from its non-uniformly sampled discrete-time model (Ding, Qiu, & Chen, 2009). Systems with two or more operating frequencies are called multirate systems, where the control updating period is not equal to the output sampling period and the whole pattern is repeated every period  $T$ . Such systems exist numerously throughout the field of PAT (Gudi, Shah, & Gray, 1994; Gudi, Shah, & Gray, 1995). In this context different approaches can be found, e.g. for parameter estimation using an auxiliary model based on recursive least-squares algorithm (Liu, Xie, & Ding, 2009) or an extended stochastic gradient algorithm (Xie, Liu, Yang, & Ding, 2010).

## 5. Conclusion and outlook

The presented methods of process control and soft sensing reveal great opportunities to overcome the dilemma of economic interests on the one hand and accurate process control to ensure product quality on the other hand. The overall aim should be to ensure a constant quality within predefined corridors simultaneously keeping an eye on cost efficiency of the process with respect to the necessary technical equipment. Hence, the underlying demand is to provide comprehensive process intelligence via innovative sensor concepts to improve process continuity, process safety and process efficiency. In consequence a major task is to combine innovative sensor principles with modern methods of data analysis and modeling using process- and product knowledge (Krause et al., 2011). Thus, software sensors provide very useful tools in monitoring and controlling food and beverage processes, particularly fermentations.

The first part of this review presents approaches which have been achieved by now in respect to means of fuzzy reasoning and the implementation of expert knowledge with deeper focus on the fuzzy symbolic approach and quality evaluation. The main advantages of fuzzy controllers are that they present quite fast, problem-related and meaningful tools for a smart control of complex system showing a non-linear behavior. In this connection, the description of the system's behavior can be achieved by means of linguistic expressions and integration of expert knowledge what is way simpler than using methods of complex mathematics. Likewise positive is the traceability of the obtained results. Furthermore, fuzzy controllers are designed for the whole working range and therefore a distinct point of operation does not need to be the center on which the developed algorithm has to be exactly designed for. By choosing appropriate definitions of fuzzy sets and

fuzzy rule bases the controller behavior can be forced with the necessary sensitivity for the whole operating range. Therefore, fuzzy controllers are suitable even to formulate firmly nonlinear control rules and distinguish themselves by their robustness.

As mentioned in the beginning the major drawback of fuzzy logic is the lack of learning ability. Hence, an automated adaption to a steadily changing environment is not possible. Errors implanted in the initial phase can hardly be repaired at a later point of time. Applying the convenient method of defuzzification can be of crucial importance. A trade-off between computation performance and quality of the result has to be dealt with. Therefore, the great potential of fuzzy logic lies mainly in the field of securing definite stakes of quality with a smooth process control. The suitability of fuzzy logic in the sense of software sensors is rather limited. For optimization requirements further systems like evolutionary algorithms have been developed. Those strategies of optimization are acknowledged to be very efficient and fast finding the optimal solution for a distinct problem. The property of their robustness lies therein established that no assumptions of the actual problem have to be made and that there exist several possibilities of suitable solutions. Thus, different ways are tested simultaneously to reach the optimum providing several potential solutions. As they are able to cope with ill-behaved problem domains, exhibiting attributes such as multimodality, discontinuity, time-variance, randomness and noise they seem to be particularly suitable for parameter optimization of fermentation processes. Regrettably, there exist only sparse applications and experience in the field of food and beverage production. This might be mainly due to the fact that EAs are very computationally intensive and frequently require massive parallel implementations in order to deliver usable results within an acceptable timeframe. Hence, their on-line application to real-time control is mostly infeasible up to now. However, this circumstance opens space for further scientific research.

A major part of this paper deals with applications for soft sensing by artificial neural networks and hybrid systems additionally offering means of process control. On account to their ability to treat noisy, incomplete and contradictory data, neural networks are still highly popular for distinct prediction operations. However, their practical application is weakened by several disadvantages. For instance they need long periods of training and the choice of suitable sets of training data can be very tedious. Learning success as well as generalization ability (overfitting) cannot be guaranteed. The most weighing obstacle for industrial implementation is their negative attribute of a "black box" behavior which does not allow comprehension of why a particular decision is made. In order to manage this disadvantage most of the presented approaches use many small neural nets instead of displaying the whole process with one big net. Another step to overcome those weaknesses is accomplished by the use of hybrid systems such as neural fuzzy systems. Those systems have the advantage that the inputs and outputs can be linguistic expressions, while optimization and inference is accomplished by the flexibility of a neural structure. The intelligent combination of these two technologies into an integrated system seems to be a promising direction to optimized process control reducing development time, as well as costs and improving accuracy of the underlying fuzzy model.

However, the up to now presented soft sensing approaches need more investigation with particular respect to robustness and sensitivity analysis to error-prone input data in order to compete with the steadily changing process conditions and satisfy the high quality demands in the case of large scale production. Especially in the event of predicting and determination of the crucial quality parameter for fermentation and maturation of beer, the diacetyl concentration, is yet not possible in a reliable and practice-relevant extent. Furthermore, most of the described approaches for process



control mechanisms try to guide the process along empirical found concentration or temperature profiles. Particularly parameter estimations are made on the basis of fixed temperature profiles. This is not close to practical application where the main process influencing variables have to be adjusted from batch to batch due to permanently changing raw materials. These circumstances have great impact on the kinetic parameters of the ongoing process reactions and therefore make the underlying process models fail with respect to precise prediction. Another point is the lack of implementing mechanistic models or chemometric evaluation methods for quality parameters like yeast vitality, sedimentation behavior, fluid dynamics in cylindrical tanks or yeast flocculation properties and for this reason the lack of software sensors detecting those essential quality parameters, respectively. This opens a great potential of research particularly in the field of brewers' yeast propagation where still only little applications can be found in this direction. In conclusion, the merging of intelligent computation techniques together with innovative sensor concept and generic process modeling provides promising opportunities for a more reliable, efficient and accurate sensing and prediction of crucial process parameters as well as robust control strategies.

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## 2.2.2 On-line yeast propagation process monitoring and control using an intelligent automatic control system

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Research Article

### On-line yeast propagation process monitoring and control using an intelligent automatic control system

The monitoring and control of bioprocesses is a challenging task. This applies particularly if the actions to the process have to be carried out in real-time. This work presents a system for on-line monitoring and control of batch yeast propagation under limiting conditions based on a virtual plant operator, which uses the concept of intelligent control algorithms by means of fuzzy logic theory. Process information is provided on-line using a sensor array comprising the measurement of OD, operating temperature, pressure, density, dissolved oxygen, and pH value. In this context practical problems arising through on-line sensing and signal processing are addressed. The preprocessed sensor data are fed to a neural network for on-line biomass estimation. The root mean squared error of prediction is  $4 \times 10^6$  cells/mL. The proposed system then triggers temperature and aeration by usage of a temperature dependent metabolic growth model and sensor data. The deviation of the predicted biomass from that of the reference trajectory as modeled by the metabolic growth model and its temporal derivative are used as inputs for the fuzzy temperature controller. The inputs used by the fuzzy aeration controller are the deviation of measured extract from that of the reference trajectory, the predicted cell count, and the dissolved oxygen concentration. The fuzzy-based expert system allows to provide the desired yeast cell concentration of  $100\text{--}120 \times 10^6$  cells/mL at a minimum residual extract limit of 6.0 g/100 g at the required point of time. Thus, a dynamic adjustment of the propagation process to the overall production schedule is possible in order to produce the required amount of biomass at the right time.

**Keywords:** Expert system / Fuzzy logic control / Intelligent control / On-line monitoring / Yeast propagation

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### 1 Introduction

In the food and beverage industry fermentation processes play an essential role for the uniqueness of the final product. However, these kinds of processes contain living organisms that have their individual intrinsic behavior. Thus, they can be characterized as multivariate; nonlinear, and time-variant which is a challenging task with respect to process monitoring and control.

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**Abbreviations:** PID, proportional-integral-derivative; PLC, programmable logic controller; RMSE, root mean squared error; YCC, yeast cell concentration

Additional complexity is added, as initial process conditions cannot be kept constant due to quality variations in raw materials or pretreatment of the biological culture. In most cases, accurate process models are not available with respect to the underlying biochemical reactions and dynamic change of model parameters [1]. There is also a lack of reliable sensors for measuring critical process parameters in real-time and the data provided by those sensors is biased by noise and uncertainty.

In the field of bioprocess engineering monitoring, modeling and control has made significant progress during the last two decades and tackles the above mentioned challenges [2–5]. Recently, several critical reviews focused on the importance of sophisticated monitoring and control strategies have appeared [6–8]. In this context, particular attention is paid to the importance of the recently launched process analytical technology initiative [9–14]. One of the most important key messages of this initiative is real-time measurement and determination of



essential process variables and critical quality parameters. Consequently, the aim is to achieve product release or approval of process sections in real-time by evaluating the product quality simultaneously to production. In the context of cell cultivation processes, the state variable biomass concentration is certainly one of the most important values. However, up to now it cannot be measured directly in an on-line process. Therefore, indirect measurements based upon soft sensing techniques such as artificial neural networks are applied [15–21].

With respect to process control, the application of expert systems plays an increasing role, particularly in the food and beverage sector [6, 22–24]. The ability to simultaneously provide a mathematically precise but manageable system definition is rather limited. In this regard, many expert systems make use of the concept of fuzzy logic, introduced by Zadeh [25]. It uses the principle of linguistic description by means of IF-THEN algorithms in order to mimic human reasoning and process assessment. Due to the capability to handle complex nonlinear processes and uncertainty in data, the concept of fuzzy logic meanwhile has become a powerful tool in intelligent control of biological based systems [26–29]. However, despite the great variety of sophisticated monitoring and control approaches, most systems have never been transferred and tested under real-world conditions. Also, the problems arising with on-line sensing of key variables and preprocessing of the obtained data before feeding to the actual control system are rarely addressed.

In this work an on-line monitoring and control system for yeast propagation under brewing conditions is presented. The term “brewing conditions” will be explained below. The fuzzy-based expert system influences the process behavior within pre-defined boundaries such that the process is pushed to a desired final state. Therefore, the system triggers operating temperature and aeration intervals in order to keep the process on track. The reference input trajectories of substrate and biomass concentration are calculated using a metabolic growth model. Temperature dependency of the specific growth rate and substrate uptake is included using an adapted square root model proposed by Kurz et al. [30, 31]. The necessary process information to calculate the current states is provided by a comprehensive sensor array comprising on-line measurement of OD, operating temperature, pressure, density, dissolved oxygen, and pH value. Due to signal noise and systematic signal disturbances, methods of data pretreatment and signal processing using frequency domain filtering are discussed in this context. The next section will give a brief characterization of the yeast propagation process subjected to brewing conditions.

The yeast propagation process is a crucial step in the production sequence of beer and plays a central role in the entire yeast management process of the brewery. Here, the required quantity and quality of yeast biomass is produced for the subsequent step of primary beer fermentation. Therefore, it has immediate influence on the sensory and physical quality of the final product. Furthermore, the propagation of yeast is right in between the two main production sequences of wort production and primary fermentation, making it a temporal bottleneck of production.

Usually, the propagation process is done batch wise, causing the yeast to pass the different growth phases of a static culture (lag, exponential, limitation/inhibition, stationary, decline). In coordination with the production schedule the propagation

plant is filled in bypass mode with beer wort, which is used as substrate. In contrast to other technologies like baker's yeast production, the growth medium cannot be composed in a definite way. The composition of beer wort and the amount of limiting nutrients strongly depends on the quality of used raw materials and the way they are processed. Typically, common lager beer wort is characterized by high concentrations of sugar ( $> 100$  g/L). This leads to regulation effects such as the Crabtree effect and causes distortions in the respiratory chain. That phenomena is expressed by oxido-reductive growth of *Saccharomyces sp.* [32]. As a consequence, a limited respiratory capacity can be observed and ethanol is produced [32, 33]. Besides this, there exist several other constraints of biomass growth such as lack of nitrogen ( $< 40$  mmol/L  $\text{NH}_3$ -equivalent) [34] and trace elements, e.g. Zinc ( $< 0.2$  mg/L) [35, 36]. Beyond this, the provision of oxygen is a critical point and ethanol production during the growth process causes additional inhibition effects, as well [32, 37–39].

Furthermore, at the end of the process the biomass is not separated from the liquid phase. Instead, the whole yeast suspension is used to pitch the successive fermentation. This circumstance prohibits the addition of adjuncts, e.g. to adjust the pH value.

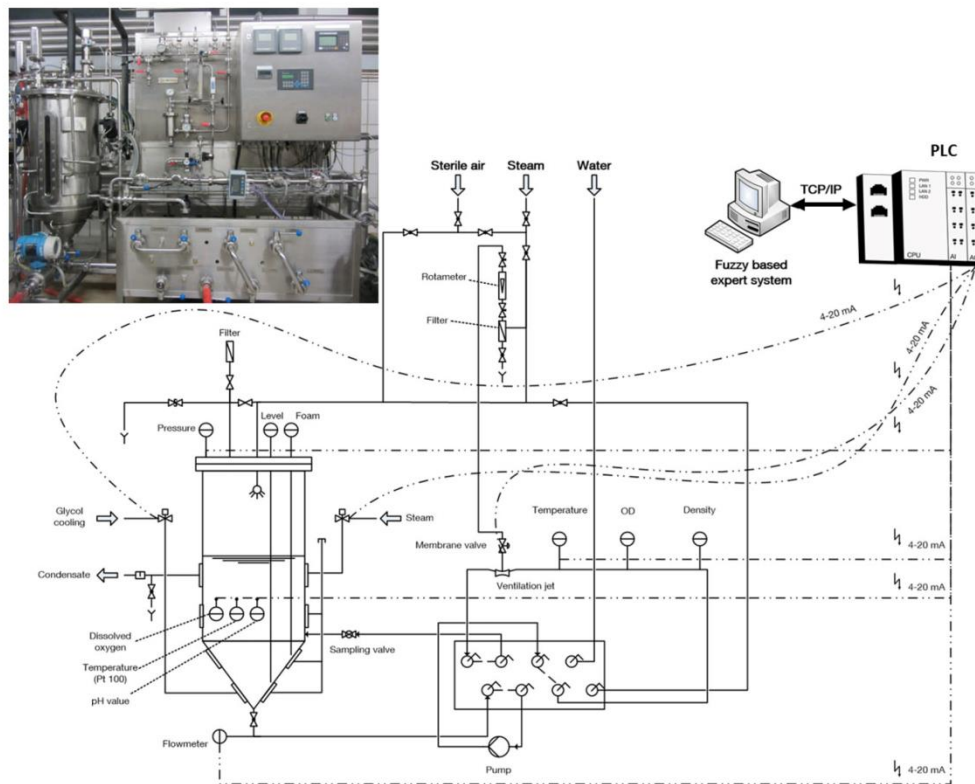
On account of the special conditions mentioned, monitoring and control strategies that are suggested in literature, cannot be applied without comprehensive adjustments, e.g. the feed control of baker's yeast production [26, 40–43].

## 2 Materials and methods

### 2.1 Plant setup and experimental

#### 2.1.1 Technical plant configuration

The plant setup where the experimental runs were performed is schematically shown in Fig. 1. It consists of a pressure tank with a total volume of 120 L. The working volume is 70 L and the residual part is left for foam generation. Homogenization is performed using a circulation pipe and an impeller pump. During the circulation the suspension is aerated with sterile air. The aeration is performed in intervals using a ventilation jet by Esau & Hueber. The volume flow was fixed to 40 Nl/h by a rotameter. To adjust the temperature, the volume flow of glycol running through the cooling jackets is regulated by opening or closing of a valve. In order to avoid a high mortality rate of yeast cells, no direct heating with steam is performed. Temperature increase is merely achieved by the metabolic activity of the yeast and application of energy by aeration and the pump. The most important sensors in the tank are temperature (Pt 100, accuracy  $< \pm 0.1^\circ\text{C}$ ), pressure (Negele, NSK-358/0750/01, accuracy  $\pm 0.5\%$ ), dissolved oxygen (Mettler-Toledo, InPro<sup>®</sup> 6800, accuracy  $\pm 0.5\%$ ), and the pH value (Mettler-Toledo, InPro<sup>®</sup> 3250, accuracy  $< \pm 0.1$  pH units). In the circulation line temperature (Pt 100, accuracy  $< \pm 0.1^\circ\text{C}$ ), OD (Optek-danulat, AF 16, accuracy  $< \pm 0.005\%$ ), and the density (Centec, Rhotec<sup>®</sup>, accuracy  $\pm 0.0001$  g/cm<sup>3</sup>) are detected. Density is measured by vibrating U-tube in a bypass. The density and temperature are used as inputs to a linear regression model developed by the authors in order to predict the apparent extract concentration in g/100 g, which has in comparison to the pure density value, a higher significance to the user in terms of process



**Figure 1.** The setup consists of a cylindro-conical tank with a working volume of 70 L. For homogenization and aeration the fermentation broth is pumped through a circulation pipe. The on-line measured values comprise temperature, pressure, dissolved oxygen, pH value, optical density, density, volume flow, liquid and foam levels. Implemented actuators are valves for aeration, cooling, heating, and a circulation pump. All signals are analogue (4–20 mA) and the basic control and processing of signals is performed on a PLC system. Curved lines show connections to actuators and straight lines connect sensors. Nominal values for aeration and temperature control are provided by the fuzzy-based expert system.

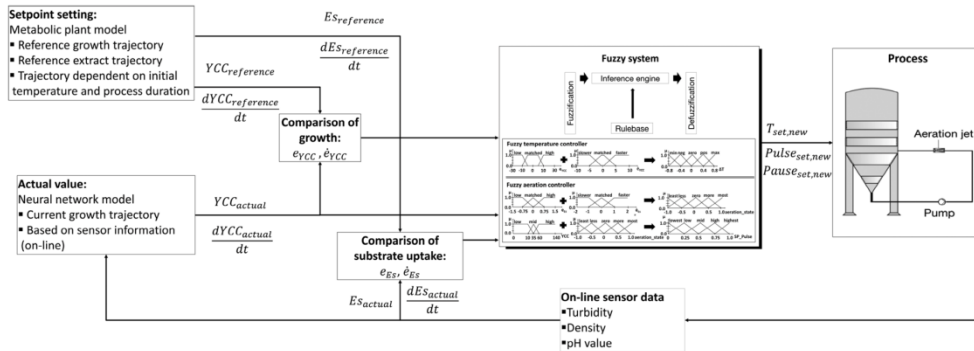
assessment. All sensor signals are analogue (4–20 mA) and fed to a programmable logic controller (PLC). On the PLC, a pulse-pause-modulation for adjusting the aeration intervals and a PID controller for temperature control was programmed. The pulse-pause-modulation opens and closes the membrane valve corresponding to the outputted aeration times of the fuzzy expert system. The PID controller adjusts the temperature in the tank by regulating the volume flow of glycol through a pneumatic valve. The desired temperature value for the PID controller is provided by the fuzzy system.

### 2.1.2 Experimental procedure and analytics

For all experiments, beer wort produced from standard malt extract (Weyermann®, “Bavarian Pilsner”) was used. Therefore, the malt extract was mixed with water and boiled for 15 min.

During boiling hop pellets were added (25 IBU) in order to stay close to the industrial production process. After boiling coagulated proteins were removed and the wort was cooled down. The obtained wort resulted in an extract content of ca. 12 g/100 g.

In order to have approximately equal yeast quality for starting the propagation process, a preculture was raised. For this, *Saccharomyces cerevisiae* sp. of strain W34/70 was added to 4 L of the above mentioned wort. An initial concentration of about  $5 \times 10^6$  cells/mL was obtained. The culture was shaken at 90 rpm at 25°C and propagated for 24 h. At the end a yeast cell concentration in a range of 100–120  $\times 10^6$  cells/mL had to be reached. Thereby, the decline in sugar concentration, which is also denoted as extract concentration, should not exceed a difference of 4 g/100 g. Otherwise, this is an indication that the culture starts shifting to the anaerobic metabolism [44]. Additionally, at the end of the process, the extract concentration should not go



**Figure 2.** Interaction of the single components of the system. The metabolic plant model provides reference trajectories, respectively, set points for yeast cell count ( $YCC_{reference}$ ), extract concentration ( $ES_{reference}$ ), and their derivatives. Those values are compared with on-line predicted yeast cell count ( $YCC_{actual}$ ) and on-line sensor data. The resulting errors are used as inputs for the corresponding fuzzy temperature controller and fuzzy aeration controller. Here,  $e_{YCC}$  is the difference between actual YCC and nominal YCC.  $e_{YCC}$  is the derivative over time. The same applies to the extract calculations ( $e_{ES}$ ,  $e_{ES}$ ). Based on that information the fuzzy system provides new setpoints for temperature ( $T_{set,new}$ ) and aeration ( $Pulse_{set,new}$ ,  $Pause_{set,new}$ ).

below 6 g/100 g, as the culture slowly begins to flocculate, which leads to inhomogeneity of the suspension. The preculture then was used as inoculum for the main propagation process. Prior to pitching, the propagation tank was filled with 70 L of beer wort. The wort was kept circulating for 30 min and the turbidity (OD) was determined in order to correct the measured value after pitching. For pitching, yeast from the preculture is added and the process is started with an initial yeast cell concentration of  $5 \times 10^6$  cells/mL. In the beginning of the process the desired duration in hours is entered by the operator. The fuzzy expert system then triggers process temperature and aeration intervals based on sensor information, expert knowledge, and a process model which is described in the next section. Figure 2 shows the interaction of the different system components. All experimental runs were performed at atmospheric pressure. The desired final process states and process corridors are stated as follows:

- Min. yeast cell concentration to be attained:  $> 100 \times 10^6$  cells/mL
- Drop in sugar concentration (extract):  $\Delta E \leq 4$  g/100 g
- Final extract concentration:  $E_{final} \leq 6$  g/100 g
- Range of temperature: 8–20°C
- Flexible run times: 24–96 h

The ranges are based upon empiric knowledge and fit to common industrial standards [44,45].

Off-line lab analytics were performed as reference measurement for yeast cell count, extract concentration, ethanol concentration, and density. The yeast cell concentration (YCC) was determined by plate count using a Thoma counting chamber [46]:

$$YCC \left[ \frac{10^6 \text{ cells}}{\text{mL}} \right] = \text{Counted cells} \times \frac{4}{256} \times \text{dilution rate} \times 10^6 \quad (1)$$

The error of this method is stated to be  $\leq 1\%$ . However, the method is highly dependent on the human factor.

Extract concentrations, ethanol concentration, and density were measured by Anton Paar, Alcolyzer Beer Analyzing System. The measurement errors are as follows:

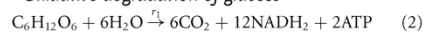
- Extract:  $\pm 0.01\%$  w/w
- Ethanol:  $\pm 0.01\%$  v/v
- Density:  $\pm 0.00001$  g/cm<sup>3</sup>

All off-line measurements were performed threefold.

## 2.2 Plant model

An adapted metabolic model following the approach of [30,31] is introduced. The model is used as a reference biomass trajectory and serves the expert system to evaluate if the process is still on track and meets the required performance. The model includes respiratory metabolism on sugar and ethanol and fermentative metabolism on sugars, as well. Furthermore, it takes into account limitation effects occurring due to lack of specific nutrients, such as sugar, nitrogen, ethanol, and oxygen. Additionally, a mathematical square root model is included modeling the temperature dependency of the specific substrate uptake rate by introducing a factor  $f_{temp}$  and the maximum specific oxygen uptake rate  $q_{O_2,max}$ . The considered substances and rates are summarized in table (A) of Fig. 3. Dependent on the surrounding medium, the model characterizes the states of metabolism following the approaches of [47–49]. The metabolic pathways are expressed in eight reactions [30]:

### 2.2.1 Oxidative degradation of glucose



A			B			
Substance	Formula	Rate	Parameter	Value	Unit	Reference
Glucose	C <sub>6</sub> H <sub>12</sub> O <sub>6</sub>	r <sub>g</sub>	Y <sub>X/Sox</sub>	3.527	mol/mol	[32]
Biomass	CH <sub>1.79</sub> O <sub>0.57</sub> N <sub>0.15</sub>	r <sub>x</sub>	Y <sub>X/SF</sub>	0.72	mol/mol	[47]
Nitrogen source	NH <sub>3</sub>	r <sub>n</sub>	Y <sub>X/E</sub>	1.12	mol/mol	[47]
Dissolved oxygen	O <sub>2</sub>	r <sub>o</sub>	HX	1.79	mol/mol	[32]
Carbon dioxide	CO <sub>2</sub>	r <sub>c</sub>	OX	0.57	mol/mol	[32]
Water	H <sub>2</sub> O	r <sub>w</sub>	NX	0.15	mol/mol	[32]
Ethanol	C <sub>2</sub> H <sub>5</sub> OH	r <sub>e</sub>	c	0.095	mol/mol	[47, 49]
Glycerol	C <sub>3</sub> H <sub>8</sub> O <sub>3</sub>	r <sub>gly</sub>	c <sub>e</sub>	0.266	mol/mol	[47]
NADH/H <sup>+</sup>	NADH <sub>2</sub>	r <sub>NADH2</sub>	δ	1.5	mol ATP/mol NADH/H <sup>+</sup>	[31]
ATP	ATP	r <sub>ATP</sub>	K	2.2	mol ATP/C-mol biomass	[31]
			K <sub>e</sub>	5.1	mol ATP/C-mol biomass	[31]
			g	0.1825	mol/mol	
			n	0.09	mol/mol	
			w	0.335	mol/mol	
			w <sub>e</sub>	0.469	mol/mol	
			n <sub>e</sub>	1.698	mol/mol	
			e	0.633	mol/mol	

D			
Parameter	Value	Unit	Reference
q <sub>S,max</sub>	0.486	mol/mol/h	[32]
q <sub>O2,e,max</sub>	0.25	mol/mol/h	[30]
m <sub>ATP</sub>	0.013	mol/mol/h	[47]
K <sub>S</sub>	2.8	mmol/l	[32]
K <sub>O</sub>	0.00121	mmol/l	[58]
K <sub>e</sub>	2.2	mmol/l	[32]
K <sub>n</sub>	2	mmol/l	[59]
K <sub>1,eth</sub>	500	mmol/l	[60]
K <sub>1,eth,o</sub>	217.39	mmol/l	[61]
K <sub>1,e</sub>	0.55	mmol/l	[32]
t <sub>lag</sub>	8	h	
t <sub>lag,eth</sub>	0	h	

E		
Parameters	f <sub>temp</sub>	q <sub>O2,max</sub>
b	0.02782	0.0209
T <sub>min</sub>	270.7616	276.3958
c	11.98	0.2823
T <sub>max</sub>	308.1539	305.8223

Figure 3. (A) Considered substances and rates. (B) Applied stoichiometric parameters of the plant model. (C) Kinetic equations and known rates for the distinct metabolic rates: divided into oxidative, oxidoreductive, fermentative growth and in rare cases oxidative growth on ethanol [30]. (D) Applied kinetic parameters of the plant model. (E) Square root parameters for modeling temperature dependency.

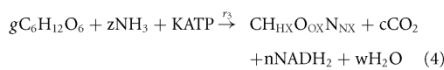
2.2.2 Respiratory chain



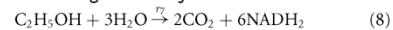
2.2.6 Maintenance



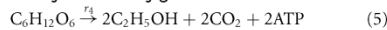
2.2.3 Biomass formation of glucose



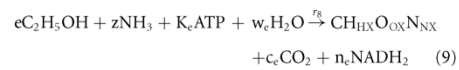
2.2.7 Oxidative degradation of ethanol



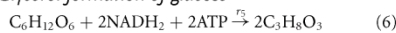
2.2.4 Ethanol formation of glucose



2.2.8 Biomass formation of ethanol



2.2.5 Glycerol formation of glucose



The metabolic turnover rate of a specific substance can be expressed as the sum of the turnover occurring in the corresponding single reactions. Therefore, the relation of the turnover of all substances and the reaction rates can be written as a linear



equations system. Here, the vector  $r$  denotes the vector of the turnover of the single substances,  $A$  is the matrix of stoichiometry and  $v$  represents the vector of the reaction rates [30]:

$$r = \begin{bmatrix} r_s \\ r_x \\ r_n \\ r_o \\ r_c \\ r_w \\ r_e \\ r_{gly} \\ r_{NADH2} \\ r_{ATP} \end{bmatrix} \quad A = \begin{bmatrix} -1 & 0 & -g & -1 & -1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & -z & 0 & 0 & 0 & 0 & -z \\ 0 & -0.5 & 0 & 0 & 0 & 0 & 0 & 0 \\ 6 & 0 & c & 2 & 0 & 0 & 2 & c_e \\ -6 & 1 & w & 0 & 0 & 0 & -3 & -w_e \\ 0 & 0 & 0 & 2 & 0 & 0 & -1 & -e \\ 0 & 0 & 0 & 0 & 2 & 0 & 0 & 0 \\ 12 & -1 & n & 0 & -2 & 0 & 6 & n_e \\ 2 & \delta & -K & 2 & -2 & -1 & 0 & -K_e \end{bmatrix} \quad v = \begin{bmatrix} r_1 \\ r_2 \\ r_3 \\ r_4 \\ r_5 \\ r_6 \\ r_7 \\ r_8 \end{bmatrix} \quad (10)$$

$$r = A \times v \quad (11)$$

Consequently, in this system 10 equations and 16 rates have to be calculated. It is assumed, that NADH/H+ and ATP are neither accumulated nor excreted in the cell ( $r_{NADH2} = 0, r_{ATP} = 0$ ). The table in Fig. 3B shows the final applied stoichiometric coefficients. The parameters  $g, w, n, w_e, n_e,$  and  $e$  are calculated from the balance of the single elements. In order to completely solve the equation system, kinetic equations have to be calculated for the different metabolic states of oxidative growth (OG), oxidoreductive growth (ORG), fermentative growth (FG), and oxidative growth on ethanol (OGE) [30]. A summary of the applied kinetics and rates for the different metabolic states is presented in the table of Fig. 3C. The final applied kinetic parameters are listed in Fig. 3D.

Rates for OG ( $r_c = r_{gly} = r_7 = r_8 = 0$ ), ORG ( $r_{gly} = r_7 = r_8 = 0$ ), FG ( $r_o = r_1 = r_7 = r_8 = 0$ ) and OGE ( $r_1 = r_3 = r_4 = r_5 = 0$ ) are assumed to be known. To shift between the different metabolic states, switching points are calculated by comparing the generic kinetic equation for substrate uptake  $r_s$  with critical rates dependent on substrate and oxygen concentration. A detailed description of the switching process is given in [30, 31].

The parameters  $L_t$  (initial lag-phase) and  $L_{t,eth}$  (diauxic lag phase) are calculated using sigmoid functions [30]:

$$L_t = \frac{1}{1 + e^{-(t-t_{lag})}} \quad (12)$$

$$L_{t,eth} = \frac{1}{1 + e^{-(t-t_{lag,eth})}} \quad (13)$$

The temperature dependency of substrate uptake is expressed introducing a factor  $f_{temp}$ , which is calculated using a square root model originally developed by [50, 51]. The model was adopted and further developed by [30]:

$$f_{temp} = \{b \times (T - T_{min}) \times \{1 - \exp[c \times (T - T_{max})]\}\}^2 \quad (14)$$

The temperature dependency of oxygen uptake expressed by  $q_{O2,max}$  is calculated analogous with different parameter values for  $b, T_{min}, c,$  and  $T_{max}$ . The used parameters are shown in Fig. 3E.

The model was tested using experimental data. It was observed that the values for the temperature dependent parameter  $q_{O2,max}$  had to be adapted in order to fit the experimental results. A comprehensive listing of all applied model parameters is given in [30]. For this work, some parameters had to be adjusted for a better fitted model. The consumption rate for nitrogen  $z$  was found to be  $-0.105$  mol/mol instead of  $-0.15$  mol/mol. Diauxic lag-time parameter  $t_{lag,eth}$  was set to 0 h. There is no diauxic shift to ethanol consumption expected. The initial lag-time  $t_{lag}$  was fixed to 8 h. Figure 4 shows off-line measured yeast cell concentration by plate count and the simulated trajectory using the metabolic modeling approach. It shows that the model is capable to catch the process dynamics and follow the process trajectory. The root mean squared error (RMSE) to the off-line sampling is  $RMSE = 10.1$  mmol/L.

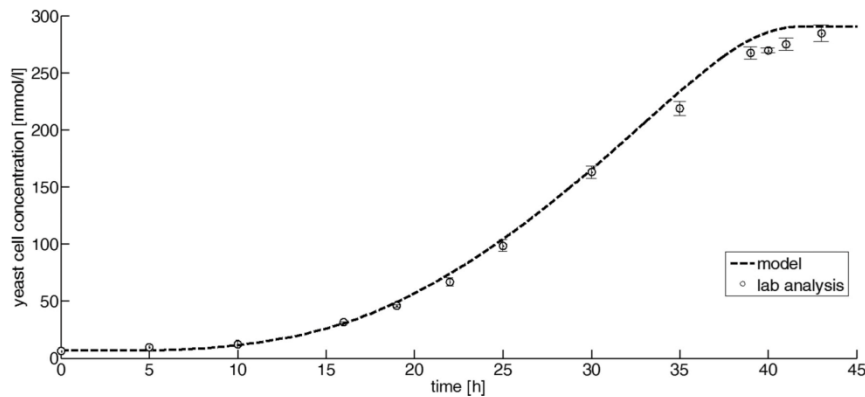
### 2.3 Signal processing of relevant data and parameter adjustment of basic PID controller

#### 2.3.1 Signal filtering

In general, fermentation processes are exposed to a wide range of external and internal disturbances, which reflect on the monitoring system. Within the investigations of this study, heavy influence on the measured turbidity and dissolved oxygen due to the pulsed aeration was observed. The duration of pulsing (aeration on) and pausing (aeration off) cycles is controlled by the fuzzy system and will be described later on. In order to make the signals usable for a control action, they had to be filtered. Therefore, a signal analysis in the frequency domain was done in order to determine the impact on the signal by switching the ventilation on and off. In order to smooth the dissolved oxygen signal a low pass filter was applied (stop band 0.06 Hz, end of pass band 0.009 Hz, sampling frequency 10 Hz). Because the turbidity signal is also influenced by the aeration cycles, a corresponding low pass filter (stop band 0.06 Hz, end of pass band 0.01 Hz, sampling frequency 10 Hz) was applied.

#### 2.3.2 PID controller tuning

In order to adequately follow the provided nominal temperature by the fuzzy system, the PID controller of the PLC system had to be adjusted and tuned. As most of the physical system parameters such as heat capacity of cooling liquid or flow conditions were unknown or uncertain, a pure mathematical modeling of thermal dynamics was not possible. Thus, the thermal transfer function was determined experimentally by analyzing the process reaction curve which was obtained by applying a unit step to the cooling system of the plant. To simulate the disturbances to the system, the pump was set to 30% and a continuous air flow of 40 NI/h was applied. In its simplified physical representation, the system can be considered as a thermal system with at least two different energy storages. The behavior of such a system corresponds to a proportional element with second order delay



**Figure 4.** Experimental validation of model. The dashed line shows a simulation of the model. The circles are the reference measurements by plate count. The error bars represent the SD of a triple determination. In total seven experiments were performed for validation.

(PT<sub>2</sub> element) [52]. The general transfer function of such a system is

$$G(s) = \frac{K_p}{(1 + T_1s) \times (1 + T_2s)} \quad (15)$$

The time constants  $T_1$  and  $T_2$  can be calculated by drawing the inflectional tangent and determining delay time  $T_w$  and transition time  $T_g$ . A detailed description is given in [52].

The resulting transfer function is

$$G(s) = \frac{-13.48}{(1 + 231.2s) \times (1 + 4928.4s)} \quad (16)$$

A PID controller was designed and tested using Matlab<sup>®</sup>. The general equation is

$$G(s) = K_p \left( 1 + \frac{1}{T_i s} + T_d s \right) \quad (17)$$

The resulting PID parameters are  $K_p = 0.44$ ,  $T_i = 0.16$  ms and  $T_d = 0.5$  ms. The closed loop response to a unit step results in an overshoot of 7.1%. This is acceptable, since the output settles down within a tolerance band of  $\pm 0.1^\circ\text{C}$ .

## 2.4 Neural network model for the prediction of yeast cell concentration (YCC)

### 2.4.1 Neural network model

The yeast cell concentration cannot be sensed directly. Therefore, a software sensor was built using on-line sensor data of OD, pH value, and density in order to predict the YCC. The feed-forward neural network consists of an input layer with three inputs (OD, pH value, density), a hidden layer with three nodes and an output layer providing the estimated cell concentration. The net was trained using backpropagation Levenberg-Marquardt algorithm [53–55].

As a performance index the mean square error is taken. It is used by the algorithm to adjust the network parameters [56]:

$$F(x) = E \left[ (t_q - a_q)^2 \right] \quad (18)$$

Here,  $p_q$  is an input to the network,  $t_q$  is the corresponding target output, and  $x$  denotes a vector containing the network's weights  $w$  and biases  $b$ . The Hessian matrix can be approximated as

$$H = J^T J \quad (19)$$

The gradient is computed as

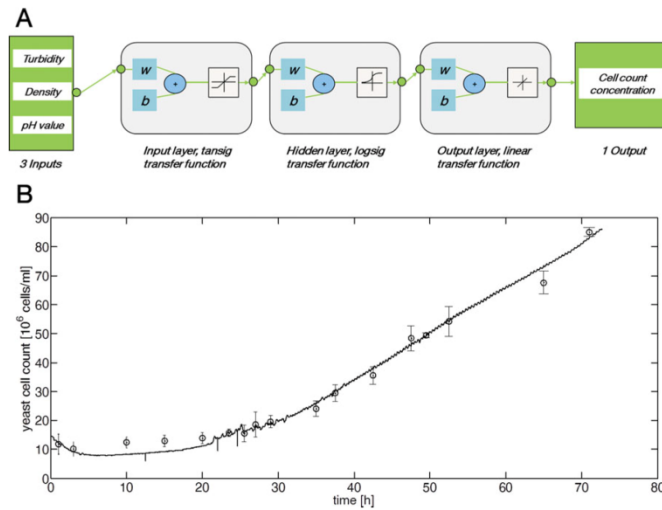
$$g = J^T e \quad (20)$$

In this regard,  $J$  denotes the Jacobian matrix, which contains the first derivatives of the network errors  $e$ , with respect to the weights and biases. In one iteration step, this approximation to the Hessian matrix is used in a Newton-like update:

$$x_{k+1} = x_k - [J^T J + \mu I]^{-1} J^T e \quad (21)$$

Here,  $x_k$  is a vector of current weights and biases,  $I$  is the unity matrix, and  $\mu$  a scalar. A detailed description of the algorithm is given in [56].

For training, testing, and validation a dataset comprising 64 off-line samples and corresponding on-line data from four complete batches was used (70% training, 15% testing, and 15% validation). Additionally, the net was simulated and validated using the on-line sensor signals (26 815 data points) of a separate batch. The architecture and validation of the network is shown in Fig. 5 (A, B). As it can be seen, the neural net is able to trace the trend of the process. However, of note is the decrease in the turbidity signal during the first 8 to 10 h, although the reference measurement of yeast cell concentration stays almost constant. Consequently, this kind of parabolic decrease is the main reason for the resulting root mean squared error of prediction (RMSEP) of  $4 \times 10^6$  cells/mL. It is assumed that a falling out of colloidal protein particles (cold trub) is occurring. However, this phenomenon has to be investigated in more detail in future work to reveal potential for nonlinear mathematical



**Figure 5.** (A) Schematic illustration of the neural network architecture.  $w$ 's are the distinct weights and  $b$  denotes the bias. (B) Prediction of yeast cell count using the 3-3-1 feedforward neural network. The solid line shows the prediction of the yeast cell count. The samples taken as reference measurements are shown as circles. The error bars represent the SD of threefold sampling. The data of four experiments (70% training, 15% testing, and 15% validation) was used to establish the neural network. Additionally, the neural net was validated with a separate experiment presented in (B).

compensation in order to further improve the RMSEP. Beside this, due to the formation of gas bubbles that particularly affect the signal of the bending vibrator, some outliers and oscillations are observed.

### 2.5 The fuzzy system

The main objective of the fuzzy expert system is to guide the process along a desired trajectory in order to produce sufficient biomass at the right time. Therefore, the system triggers the temperature and aeration intervals as the main influence parameters. The temperature controller consists of two inputs. The first input denoted as  $e_{YCC}$  is the difference between a reference biomass trajectory provided by the mathematical growth model (plant model) and the actually estimated biomass concentration. The second input is the first derivative over time of this difference denoted as  $\dot{e}_{YCC}$ . The output is a temperature increment  $\Delta T$  that is added to the initial temperature at the start of the process. The resulting temperature value is then forwarded as nominal value to the PID controller of the PLC. The sampling time for exchanging information with the PLC was fixed to 10 s. A schematic illustration of the inputs and the output fuzzy variables, respectively, fuzzy sets and the applied rule base of the temperature controller is given in Fig. 6A. For the linguistic partition of the inputs and outputs only piecewise linear membership functions are used. The fuzzy input variable  $e_{YCC}$  has the fuzzy sets *low*, *matched*, and *high*. The sets of  $\dot{e}_{YCC}$  are named as *slower*, *matched*, and *faster*. The output variable consists of five fuzzy sets *min*, *neg*, *zero*, *pos*, and *max*. The applied inference engine uses the well-established max-min-method. For defuzzification, centroid defuzzification is used. A detailed description of theoretical mechanisms of fuzzy logic controllers is given in [57].

The fuzzy aeration controller has the task to adjust the opening and closing times of a membrane valve that allows the yeast suspension to be provided with sufficient oxygen. Similar to the temperature approach the aeration controller is based on a reference trajectory. This is the decline of extract given by the plant model. The basic idea is that a consumption of more than 4 g/100 g from the beginning to the end of the process indicates that the culture has shifted too much to the anaerobic metabolism due to the lack of oxygen. Thus, if the actual extract concentration deviates from the desired path, the length of the aeration intervals (pulse and pause times) is adjusted. First of all, a fuzzy state variable *aeration\_state* is calculated within a range of  $-1$  and  $1$  to express the magnitude and direction of changing the duration of the aeration on a normalized scale. The fuzzy system's structure for that is similar to the temperature controller. Next, the state variable is taken as input in combination with the estimated cell concentration *YCC* to output a fuzzy number within the range of 0 to 1 for the aeration intervals *SP\_Pulse* and *SP\_Pause*. The defuzzified, numerical value is taken to get the new aeration setpoint in minutes and to scale it within predefined limits  $a$  and  $b$ :

$$Pulse\_setpoint = (a_1 - b_1) \times SP\_pulse + b_1 \quad (22)$$

$$Pause\_setpoint = (a_2 - b_2) \times SP\_pause + b_2 \quad (23)$$

Those limits  $a_1 = 10$  min,  $a_2 = 20$  min,  $b_1 = 4$  min, and  $b_2 = 10$  min are based on the experience of an expert. The reason for this expert knowledge approach is that there is only very sparse and uncertain information about kinetics of mass transfer, fluid dynamics in the reactor and bubble size distribution that would allow setting up a mechanistic model to calculate an adapted provision of oxygen. Figure 6B shows schematically the aeration controller for adjusting the pulse times. The adjustment of pause times (not shown) is analogue to the aforementioned.

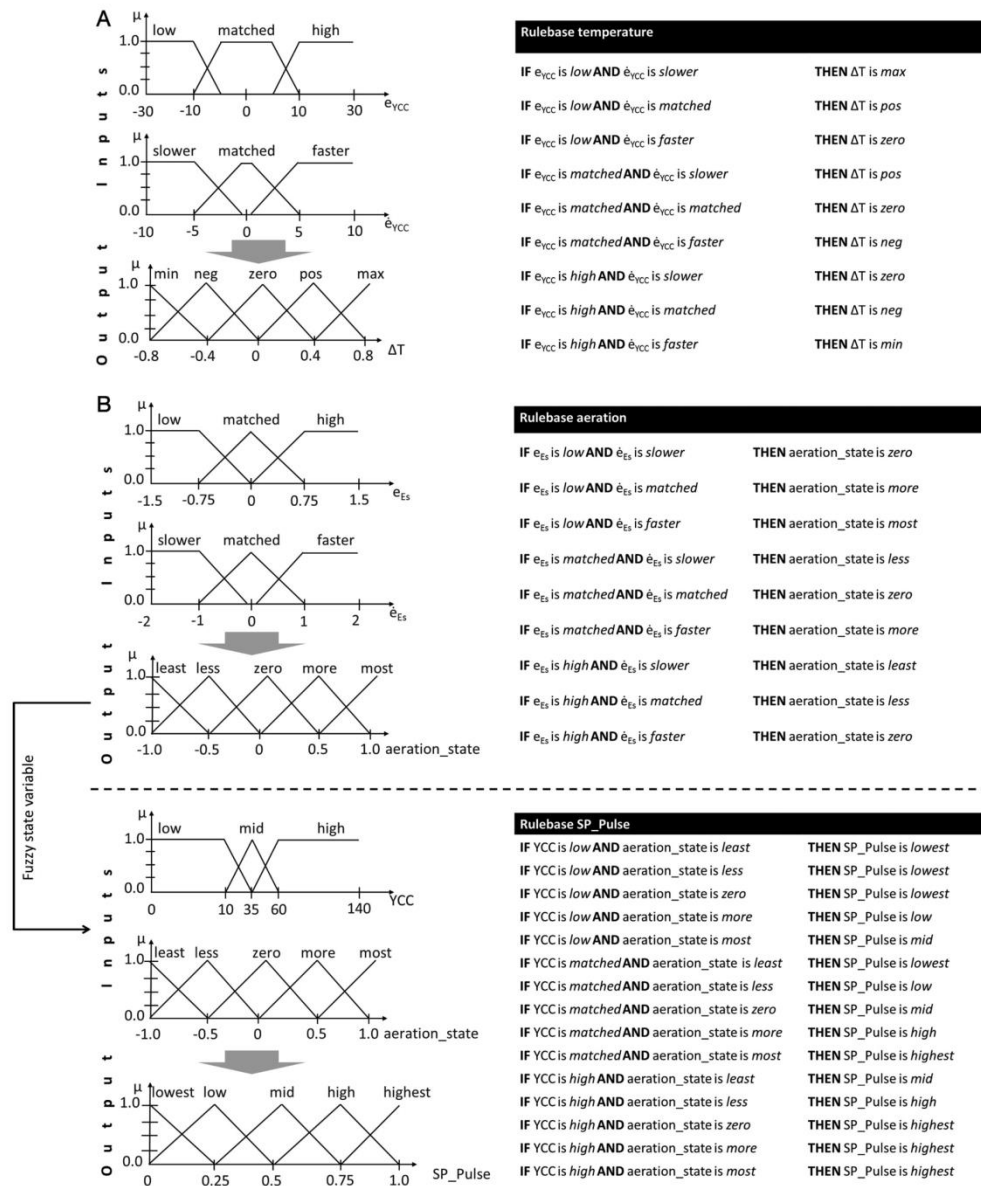
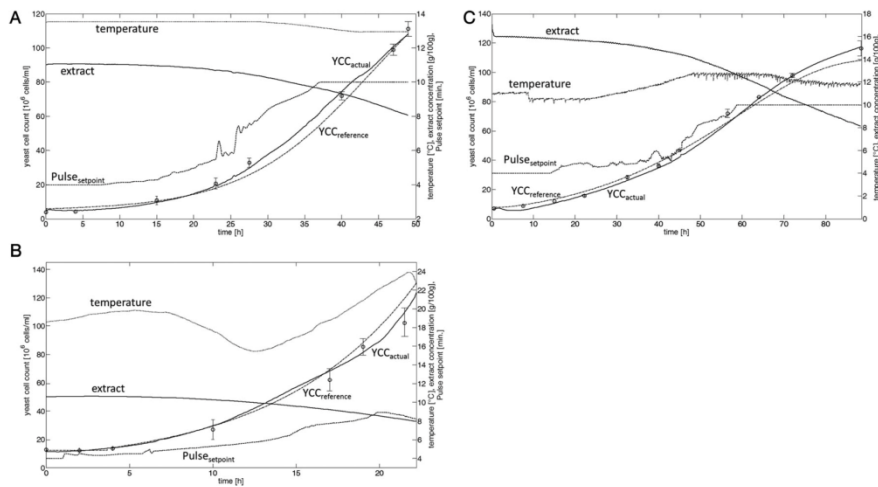


Figure 6. (A) Schematic outline of inputs, output, and rule base of the applied fuzzy temperature controller. (B) Schematic illustration of the aeration controller to adjust pulse times.





**Figure 7.** (A) An experimental run over two days. From the 22nd hour onwards, the cell count concentration ( $YCC_{actual}$ ) starts to deviate from the desired trajectory ( $YCC_{reference}$ ). In order to finish the process within 48 h, the temperature is gradually changed until both trajectories are matching within the allowed tolerance. The experiment was repeated four times resulting in similar trajectories. The off-line measurements are shown as circles. All off-line measurements were performed threefold. The error bars represent the SD of the off-line measurements. (B) One day experimental run. The upper temperature limit of 20°C was exceeded in order to counteract the deviations from the reference trajectory. One experiment was performed. The off-line measurements are shown as circles and were performed threefold. The error bars represent the SD of the off-line measurements. (C) Industrial scale run over 4 days. The controller parameters of the PLC system were not adjusted. This is reflected by the noisy temperature signal. Off-line measurements are shown as circles. All off-line measurements were performed threefold. The error bars represent the SD of the off-line measurements. The industrial experiment was performed three times.

However, instead of the cell concentration it uses the dissolved oxygen content as input.

### 3 Results and discussion

In this section results of the applied system are shown for small scale (70 L) and a test at industrial scale with a working volume of 8.500 L. In Fig. 7A and 7B experimental scale trials over a period of two and one day are presented. It can be observed that the temperature is increased and decreased depending on the divergence of the actual cell concentration to the reference trajectory. In consequence, the on-line predicted yeast cell count and the reference trajectory of the mathematical growth model are converging and the desired target of  $100\text{--}120 \times 10^6$  cells/mL is reached. The decline of extract concentration does not exceed a  $\Delta E$  of 4 g/100 g and it does not undergo the limit of 6 g/100 g at the end of the process. The RMSE of nominal and actual YCC trajectory is  $3.9 \times 10^6$  cells/mL. The deviation at the end of the process is negligible ( $0.3 \times 10^6$  cells/mL). This shows that the expert system is able to keep the process within the desired constraints. The batch presented in Fig. 7B is relatively short in comparison to industrial standards. There, batch cycles varying from 48–96 h are state of the art. However, the capability and productivity of the system had to be tested. The challenge with respect to process control and a short batch run time is the aforementioned intrinsic time-variant behavior of

the system until a clear growth reaction is observable due to an applied temperature change. Therefore, the propagation process was started on a higher temperature level. It can be seen that the desired final states of cell and extract concentration could be achieved, as well. However, the control had to compensate for the deviations of the actual cell count trajectory from its reference path occurring from the 12th h onwards. Thus, the suggested upper temperature range of 20°C was exceeded, violating the previously mentioned temperature corridor. For this reason, further investigations are carried out in order to analyze the consequences of this temperature exceedance on the sensory properties. The RMSE of on-line predicted YCC and its reference trajectory is  $4.0 \times 10^6$  cells/mL. The final deviation at the end of the process is  $7.0 \times 10^6$  cells/mL. Figure 7 C shows the system tested under industrial conditions. The extract concentration started on a very high level. This has influence on the growth behavior of the yeast and leads to limitations that can be observed toward the end of the process when the reference trajectory starts to flatten. Thus, more substrate than 4 g/100 g is consumed. The RMSE of actual and reference cell count is  $6.7 \times 10^6$  cells/mL. The deviation at the end of the batch is  $8.7 \times 10^6$  cells/mL. However, the desired residual extract value was achieved. It has to be mentioned that for the industrial testing a tuning of the underlying PLC controllers was not done. That can be seen in the noisy signal of the sensed temperature value. A generality of all presented batches is an over or undershooting of the reference trajectory. This is on the one hand due to a time delay of

information because of signal filtering (36 min) and on the other hand due to a time-variant delay of yeast growth with respect to a temperature change. The latter one was estimated to be within 2–3 h. A compensation of this combined effect using a one-step-ahead prediction could achieve better control performance and is currently being investigated.

#### 4 Concluding remarks

In this work a fuzzy-based expert system is presented for controlling the brewer's yeast propagation process. The proposed system uses a metabolic growth model in order to guide the process along reference trajectories of cell growth and substrate consumption. Beyond this, methods of data-pretreatment, signal processing, and soft sensing using a neural network were presented, as well as linear controller adjustment was addressed. The presented results show that the system is able to target the desired final state corridors for extract and yeast cell concentration within the desired duration. However, the system has space for future optimization. Although the final states are met, there is a deviation of  $7.0 \times 10^6$  cells/mL (Fig. 7B) and  $8.7 \times 10^6$  cells/mL (Fig. 7 C) at the end of the process. This indicates that the control performance can be improved. Therefore, methods of one-step-ahead prediction and tuning of fuzzy parameters are in the focus of future research. With respect to the predictive capability of yeast cell concentration, the effect and mechanisms causing a decrease of OD at the very beginning of the process has to be investigated. Compensating this effect would improve the accuracy and predicting performance of yeast growth. Furthermore, failure scenarios including sensor failures and process variations by changing the planned termination point in the middle of the process should be tested in order to guarantee process and product safety as well as to prove the system's robustness and limits. Additionally, scale-up studies should be investigated. The adaptation and recalibration of the model to industrial conditions is the focus of future work and would be a step forward to monitoring and control of large-scale production.

#### Practical application

In the food and beverage industry, the individual flavor, design, and final quality for a wide range of products is essentially determined by fermentation processes. In common practice, the observation and control of these processes is characterized by manual interventions and empirically determined process parameters. However, due to the intrinsic dynamic behavior of the used organisms, intelligent monitoring and control systems are required in order to avoid delayed reaction to process deteriorations. Particularly, fuzzy logic based expert systems are capable of mimicking human reasoning and therefore show a high potential to manage complex production processes by handling fragmental and uncertain process information.

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## 2.2.3 Management of uncertainty by statistical process control and a genetic tuned fuzzy system

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*Research Article*

### Management of Uncertainty by Statistical Process Control and a Genetic Tuned Fuzzy System

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In food industry, bioprocesses like fermentation often are a crucial part of the manufacturing process and decisive for the final product quality. In general, they are characterized by highly nonlinear dynamics and uncertainties that make it difficult to control these processes by the use of traditional control techniques. In this context, fuzzy logic controllers offer quite a straightforward way to control processes that are affected by nonlinear behavior and uncertain process knowledge. However, in order to maintain process safety and product quality it is necessary to specify the controller performance and to tune the controller parameters. In this work, an approach is presented to establish an intelligent control system for oxidoreductive yeast propagation as a representative process biased by the aforementioned uncertainties. The presented approach is based on statistical process control and fuzzy logic feedback control. As the cognitive uncertainty among different experts about the limits that define the control performance as still acceptable may differ a lot, a data-driven design method is performed. Based upon a historic data pool statistical process corridors are derived for the controller inputs control error and change in control error. This approach follows the hypothesis that if the control performance criteria stay within predefined statistical boundaries, the final process state meets the required quality definition. In order to keep the process on its optimal growth trajectory (model based reference trajectory) a fuzzy logic controller is used that alternates the process temperature. Additionally, in order to stay within the process corridors, a genetic algorithm was applied to tune the input and output fuzzy sets of a preliminarily parameterized fuzzy controller. The presented experimental results show that the genetic tuned fuzzy controller is able to keep the process within its allowed limits. The average absolute error to the reference growth trajectory is  $5.2 \times 10^6$  cells/mL. The controller proves its robustness to keep the process on the desired growth profile.

#### 1. Introduction

Generally, uncertainty can be considered as a result of some information deficiency of any problem-solving situation [1]. When dealing with bioprocesses under real conditions it is rarely impossible to completely avoid uncertainty. The reasons for uncertainty are quite diverse. On the one hand, there are large variations in raw material quality, especially in the food and beverage sector. On the other hand there is the intrinsic nonlinear behavior of the used microorganisms, which is in most cases still not fully understood. Therefore, existing process models are affected by incomplete or fragmentary knowledge about the underlying mechanisms. With respect to process monitoring and control, uncertainty is almost inseparable from any real-time measurement, resulting from a combination of inevitable measurement errors and

resolution limits of applied sensors. And at the cognitive level, uncertainty stems from the vagueness and ambiguity which is inherent in human language and the semantics of assessment [2]. Because of the fact that in most cases the sources of uncertainty cannot be easily solved from a physical point of view, several approaches are proposed in literature that allow handling uncertainties by the use of statistics. A general overview of (multivariate) statistical process control and quality control is given in [3–8] and with special focus on food by [9–11]. With respect to online process observation and quality monitoring the use of online control charts is emphasized [12, 13]. The use of online control charts is a very powerful tool in decision-making. It serves as human-machine interface and thus allows the operator to evaluate the process in real time. By means of simple statistics, they allow calculating and

graphically visualizing if the current process is running inside or outside its allowed limits. In order to represent the process, key performance indicators and critical quality attributes have to be defined on a univariate or multivariate basis. There are several charting techniques existing that ease the process of statistical quality control and on a single variable basis they are comprehensively reviewed by [14]. However, the majority of SPC approaches presented in literature consider SPC as a pure monitoring system. Although there has been done quite interesting work making use of fuzzy logic approaches in order to handle uncertainty that is related with the construction [15–20] or the evaluation of control charts with respect to quality attribute changes [21], there is only little investigation that actually takes into account how to integrate the information that is delivered by the SPC system into a feedback control system in order to keep the process within its statistical borders. This shortcoming is mentioned as well by Woodall, Montgomery, and Stoumbos [22–25].

With respect to automatic process control, fuzzy logic has also become a powerful tool in intelligent control of biological systems due to the capability to handle complex nonlinear processes and uncertainty in data [26–29]. The concept of fuzzy logic was first introduced by Zadeh [30]. It uses the principle of linguistic description by means of IF-THEN algorithms in order to mimic human reasoning and process assessment. Therefore, it is a good platform for controller design that is subjected to uncertain process behavior.

However, the classic fuzzy controller has several drawbacks. In particular, a major drawback is the lack of a learning capability. Classical fuzzy systems are static and their practical implementation and optimization is done by trial and error and based on the experience of an expert knowing the process and how it should be controlled. However, with respect to fast controller implementation and finding the optimal parameter configuration of the fuzzy sets in order to reach the required controller performance, the method of trial and error is quite cumbersome and often results in inefficient and suboptimal configurations of the control parameters. The optimal configuration can be “hidden” in the data. Therefore, in this work a genetic algorithm was used in order to provide additional intelligence and the ability of learning to the fuzzy controller. The genetic algorithm optimizes the control performance on a data-driven approach. The overall control strategy, which is represented by the rulebase, uses the cognitive knowledge of an expert.

In this approach, the process control architecture is realized by an automated feedback control system based on fuzzy logic. The fuzzy system is linked to SPC in order to control and monitor the process of yeast propagation. The developed fuzzy controller adjusts the process temperature in order to keep the process within statistical corridors of the controller input variables, which are the control error and the temporal control error derivative. Within the framework of SPC, the statistical corridors, respectively, upper and lower control limits of the input variables, are derived from historical data of batches that met the required quality specifications. Shewhart control charts ( $\bar{X}$ -charts) are used to calculate the ideal trajectory  $\bar{X}$ , the upper control (UCL) limit, and the lower

control limit (LCL) of the input variables. With respect to the control quality this means that if the control error stays within the statistical borders, the process and the control meet the required and predefined quality and performance criteria with a probability of 99.73%. The adjustment of the fuzzy controller parameters is done by a genetic algorithm. The heuristic search mechanism of the genetic algorithm is able to find the ideal parameter configuration of the fuzzy sets. The advantage therefore lies in the combination of fuzzy and genetic algorithms. The fuzzy system holds the principle expert knowledge of how to best control the process and the genetic algorithm is used to optimize the expert knowledge by providing learning capability and efficient solution finding in a big search space.

## 2. Materials and Methods

*2.1. Control Charts and Data Pool.* The standard Shewhart  $\bar{X}$ -chart consists of a centerline to monitor the process mean and the upper and lower control limit which are calculated from historic process data. The control limits are usually set at  $\pm 3$  times the standard deviation from the centerline, which is simply the arithmetic average. This expresses statistically that 99.73% of all batches that run within these limits are meeting the specified quality requirements and can be viewed to be in control.

The process for which the system was developed is the brewer's yeast propagation process, which is a typical and representative process biased by various sources of uncertainty. In general, yeast propagation is performed as a batch process, whereby the yeast undergoes the different growth phases of a static culture (lag phase, exponential phase, transition or deceleration phase, stationary phase, and degeneration). The individual phase duration and the transition time from one phase to another depend on various factors. For example, the lag phase depends on the physiological state of the inoculum and the specific growth medium [31]. The physiological state in turn depends on storage conditions and the upstream treatment of the yeast used as inoculum [32]. Furthermore, the growth behavior is influenced by the substrate, which is beer wort. Its composition again is dependent on natural variations of the used raw materials. In consequence, the effects of substrate limitations on the metabolic behavior due to unavoidable variations in available carbohydrates, nitrogen, zinc, or vitamins are subjected to uncertainty. Additionally, metabolic regulation effects occurring under brewing related conditions have to be taken into account. In this regard, the most important regulation mechanism affecting the different metabolic pathways is the Crabtree effect [33]. The Crabtree effect, which is also known as overflow metabolism, catabolite repression, aerobic fermentation, or oxidoreductive metabolism, leads to the formation of ethanol at exceedance of a critical glucose concentration in the substrate [34–36]. In summary, the process of oxidoreductive yeast propagation is affected by numerous sources of uncertainty that in consequence influence the observability and controllability of the process. Hence, in order to observe and control this kind of process an intelligent online monitoring and process control system is required.

In this work the data of 11 batches was used that met the following performance and quality requirements:

- (i) Cell count concentration at end of batch:  $\geq 100 \times 10^6$  cells/mL.
- (ii) Portion of dead cells at end of batch:  $\leq 1\%$ .

For the experimental work, beer wort produced from standard malt extract (Weyermann®, “Bavarian Pilsner”) was used as substrate for the propagation of *Saccharomyces cerevisiae* sp. (strain W34/70). A detailed description of the technical plant configuration, experimental procedure, and analytics is given in [37]. For the performance analysis, calculation of control charts, and the later controller design, a temperature dependent growth model by [38] was implemented. The model is based on known stoichiometric turnover and Michaelis-Menten kinetics of yeast [35, 36, 39]. In addition, it considers growth limitations like the Crabtree effect that occur by feeding substrate sugar concentrations above 100 g/L [33]. The effect of temperature on yeast growth, respectively, the substrate uptake, is modeled by implementing an additional temperature factor  $f_{temp}$  that is expressed by a square root term that was originally developed to describe the temperature effect on the growth of specific bacteria [40, 41]. The specific substrate uptake  $q_S$  can be represented by the following equations:

$$\begin{aligned}
 q_S &= q_{S,max} * \min\left(\frac{S}{S + K_s}, \frac{N}{N + K_n}\right) * \frac{K_{i,eth}}{K_{i,eth} + E} \\
 &\quad * L_t * f_{temp}, \\
 f_{temp} &= \langle b * (T - T_{min}) * \{1 - \exp[c * (T - T_{max})]\} \rangle^2.
 \end{aligned} \tag{1}$$

Applied half saturation constants for limitations or inhibition were  $K_s = 2.8$  mmol/L [36],  $K_n = 2$  mmol/L [42], and  $K_{i,eth} = 500$  mmol/L [43]. Furthermore,  $q_{S,max} = 0.486$  mol/mol/h [36] denotes the maximum specific substrate uptake rate,  $S$  is the substrate concentration in mmol/L,  $N$  is the nitrogen concentration in mmol/L expressed as  $\text{NH}_3$  equivalents, and  $E$  is the ethanol concentration in mmol/L. The lag time  $L_t$  is determined by a sigmoid function  $L_t = 1/(1 + e^{-(t-t_{lag})})$ , where  $t_{lag}$  was set to 5.6 h.  $T$  is the temperature in K and the mathematical regression coefficients were determined to be  $b = 0.03296$  and  $c = 11.98$  in this work.  $T_{min} = 270.7616$  K and  $T_{max} = 308.1539$  K are temperatures where no further growth is observed.

Figure 1 displays the comparison of yeast cell counts (YCC) in mmol/L between the model outputs and the corresponding experimental runs (that were judged as “good” batches from a qualitative point of view) for different temperature profiles. The YCC of the batches was measured online using a turbidity sensor (optek-Danulat, AF 16). The model has a root mean squared error (RMSE) of 7.4 mmol/L and therefore shows good accuracy in predicting the cell concentration. The error  $e_{YCC}$  between model and real trajectory, as

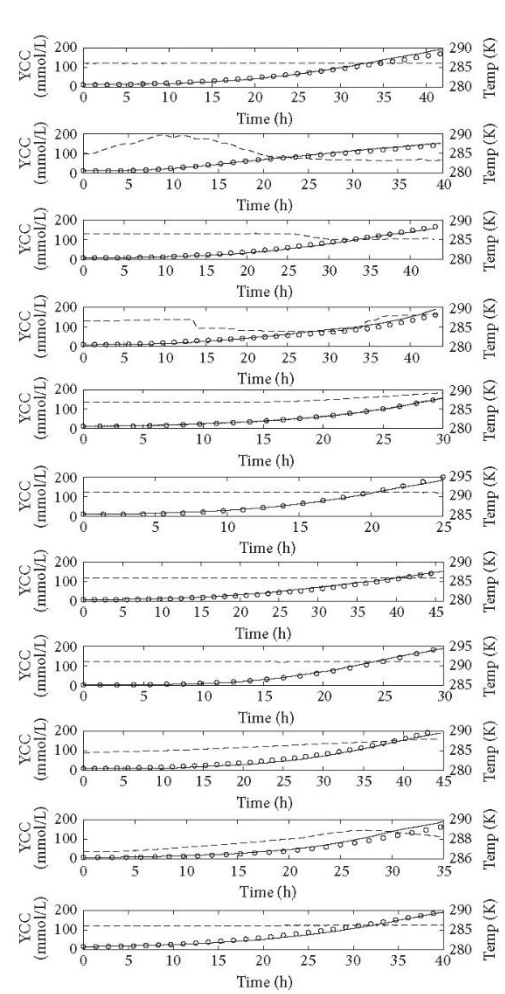


FIGURE 1: Comparison of cell count (YCC) of historical batches and model output. The circles (o) show the YCC model output in mmol/L, the solid line (—) is the experimental trajectory of YCC in mmol/L, and the dashed line (- -) denotes the temperature in K. The duration, respectively, batch length, varied between 24 and 46 hours. Initial conditions of yeast cell concentration varied in between 4.1 mmol/L and 14.9 mmol/L. The final state of the yeast cell concentration showed a range from 146.3 mmol/L to 191.9 mmol/L. The temperature varied from 283 K to 291 K.

well as its temporal derivative  $\dot{e}_{YCC}$ , is then calculated in order to establish the control charts:

$$\begin{aligned}
 e_{YCC} &= YCC_{real} - YCC_{model}, \\
 \dot{e}_{YCC} &= \frac{de_{YCC}}{dt}.
 \end{aligned} \tag{2}$$

Due to the varying individual batch length, the batches were uncoupled from time. To achieve this, batch evening was performed by resampling the batches and mapping them to the shortest number of  $J = 9120$  sampling instances. Then, after mean centering and normalization with the standard deviation, for  $N_k$  batches with  $i = 1 : J$  sampling instances, the control charts are calculated as follows:

$$\begin{aligned}
 \bar{X}_{e_{YCC},i} &= \frac{1}{N_k} \sum_{k=1}^{N_k} e_{YCC,i,k}, \\
 \bar{X}_{\dot{e}_{YCC},i} &= \frac{1}{N_k} \sum_{k=1}^{N_k} \dot{e}_{YCC,i,k}, \\
 UCL_{e_{YCC},i} &= \bar{X}_{e_{YCC},i} + 3 * \sigma_{e_{YCC},i} \\
 &= \bar{X}_{e_{YCC},i} + 3 * \sqrt{\frac{1}{N_k - 1} \sum_{k=1}^{N_k} (X_{k,i} - \bar{X}_{e_{YCC},i})^2}, \\
 LCL_{e_{YCC},i} &= \bar{X}_{e_{YCC},i} - 3 * \sigma_{e_{YCC},i} \\
 &= \bar{X}_{e_{YCC},i} - 3 * \sqrt{\frac{1}{N_k - 1} \sum_{k=1}^{N_k} (X_{k,i} - \bar{X}_{e_{YCC},i})^2}, \\
 UCL_{\dot{e}_{YCC},i} &= \bar{X}_{\dot{e}_{YCC},i} + 3 * \sigma_{\dot{e}_{YCC},i} \\
 &= \bar{X}_{\dot{e}_{YCC},i} + 3 * \sqrt{\frac{1}{N_k - 1} \sum_{k=1}^{N_k} (X_{k,i} - \bar{X}_{\dot{e}_{YCC},i})^2}, \\
 LCL_{\dot{e}_{YCC},i} &= \bar{X}_{\dot{e}_{YCC},i} - 3 * \sigma_{\dot{e}_{YCC},i} \\
 &= \bar{X}_{\dot{e}_{YCC},i} - 3 * \sqrt{\frac{1}{N_k - 1} \sum_{k=1}^{N_k} (X_{k,i} - \bar{X}_{\dot{e}_{YCC},i})^2}.
 \end{aligned} \tag{3}$$

**2.2. The Fuzzy Controller.** The applied fuzzy temperature controller is a Mamdani type controller [44, 45] that consists of the standard components of fuzzification, inference engine with rulebase, and defuzzification. The fuzzification of the input variables  $e_{YCC}$  (difference in biomass concentration between the reference process model and the real measurement) and the temporal derivative  $\dot{e}_{YCC}$  is done via piecewise linear functions, respectively, trapezoidal fuzzy sets. In this context, the fuzzy variable  $e_{YCC}$  is assigned to the linguistic expressions *low*, *matched*, and *high*. Similarly, the fuzzy variable  $\dot{e}_{YCC}$  is linked to the verbal terms *slower*, *matched*, and *faster*. The fuzzy output variable comprises three fuzzy sets, namely, *neg*, *zero*, and *pos*. Here, the output is a temperature increment  $\Delta T$  that is added to the initial temperature at the start of the process. The inference engine has the task to match the input variables to the output variable of the controller by taking into account the logical statements defined in the rulebase. In this case a standard max-min method was applied [46]. The rulebase contains the rules in "IF-THEN" form that determine the basic control strategy in order to follow an optimal growth trajectory delivered by the process

model. The rulebase of the fuzzy temperature controller is shown as follows:

- IF  $e_{YCC}$  is *low* AND  $\dot{e}_{YCC}$  is *slower* THEN  $\Delta T$  is *pos*.
- IF  $e_{YCC}$  is *low* AND  $\dot{e}_{YCC}$  is *matched* THEN  $\Delta T$  is *pos*.
- IF  $e_{YCC}$  is *low* AND  $\dot{e}_{YCC}$  is *faster* THEN  $\Delta T$  is *zero*.
- IF  $e_{YCC}$  is *matched* AND  $\dot{e}_{YCC}$  is *slower* THEN  $\Delta T$  is *pos*.
- IF  $e_{YCC}$  is *matched* AND  $\dot{e}_{YCC}$  is *matched* THEN  $\Delta T$  is *zero*.
- IF  $e_{YCC}$  is *matched* AND  $\dot{e}_{YCC}$  is *faster* THEN  $\Delta T$  is *neg*.
- IF  $e_{YCC}$  is *high* AND  $\dot{e}_{YCC}$  is *slower* THEN  $\Delta T$  is *zero*.
- IF  $e_{YCC}$  is *high* AND  $\dot{e}_{YCC}$  is *matched* THEN  $\Delta T$  is *neg*.
- IF  $e_{YCC}$  is *high* AND  $\dot{e}_{YCC}$  is *faster* THEN  $\Delta T$  is *neg*.

At first, the fuzzy set parameterization for each variable was done uniformly across the individual universe of discourse. Therefore, the set parameters were assigned as follows:

- (i)  $e_{YCC}$ :
  - (a) *low* := [-100 -30 -5 0],
  - (b) *matched* := [-5 -0.01 0.01 5],
  - (c) *high* := [0 5 30 100];
- (ii)  $\dot{e}_{YCC}$ :
  - (a) *slower* := [-100 -10 -5 0],
  - (b) *matched* := [-5 -0.01 0.01 5],
  - (c) *faster* := [0 5 10 100];
- (iii)  $\Delta T$ :
  - (a) *neg* := [-1.2 -0.8 -0.6 -0.2],
  - (b) *zero* := [-0.6 -0.1 0.1 0.6],
  - (c) *pos* := [0.2 0.6 0.8 1.2].

Here, the numbers denote the characteristic points of the piecewise linear membership functions used to define the individual fuzzy sets. For example, the support (the set of points on the variable domain, where the membership function value is greater than zero) and slopes of the trapezoidal fuzzy set *matched* are characterized by the four points -5, -0.01, 0.01, and 5. In general the membership function  $\mu_{A_i^j}(u_i)$  of a trapezoidal set is given by [46]

$$\mu_{A_i^j}(u_i) = \begin{cases} 0: & u_i \leq \bar{l}; u_i \geq r \\ 1: & m_1 \leq u_i \leq m_2 \\ \frac{u_i - \bar{l}}{m_1 - \bar{l}}: & \bar{l} < u_i < m_1 \\ \frac{m_2 - u_i}{r - m_2} + 1: & m_2 < u_i < r. \end{cases} \tag{4}$$



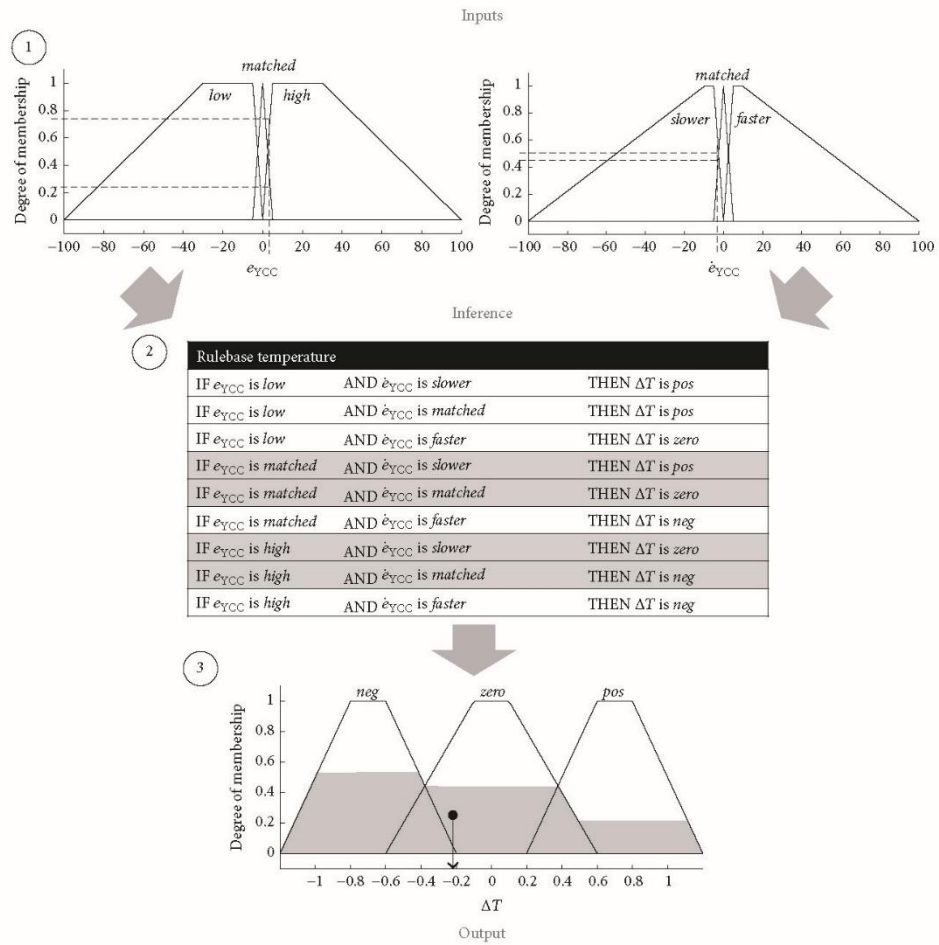


FIGURE 2: Schematic representation of the nontuned fuzzy controller structure and the flow of information. The first step shows the fuzzy partition and the fuzzification of the input variables  $e_{YCC}$  and  $\dot{e}_{YCC}$  into their specific fuzzy sets. The second step diagrammatically shows the inference mechanism and the activation of the corresponding rules in the rulebase. The third step illustrates the set partition of the fuzzy output variable  $\Delta T$  and the accumulation and COG defuzzification of the overall implied fuzzy set into a crisp output.

Here,  $\mu_{A_i^j}(u_i)$  is a membership function associated with fuzzy set  $A_i^j = \{(u_i, \mu_{A_i^j}(u_i)) \mid u_i \in \mathcal{U}_i\}$ , which maps  $\mathcal{U}_i$  to  $[0, 1]$ .  $\mathcal{U}_i$  is the universe of discourse,  $l$  denotes the leftmost point of the trapezium,  $m_1$  is the left center point,  $m_2$  is the right center point, and  $r$  represents the rightmost point. Figure 2 gives a schematic representation of the fuzzy temperature controller.

The defuzzification uses the center of gravity method (CoG) [46] in order to do the back transformation from the linguistic to the numerical domain and to calculate a crisp output value. The crisp output value of  $\Delta T$  is then used as

an incremental change of process temperature  $T$  at the current point in time  $t$ ,

$$T(t+1) = T(t) + \frac{\Delta T}{\text{cph}}. \quad (5)$$

Here, cph is equal to 360 and it denotes the cycles per hour. This results from the chosen sampling time of 10 s.

2.3. Genetic Tuning of Fuzzy Sets. There is a wide range of bioengineering and food related applications, where fuzzy

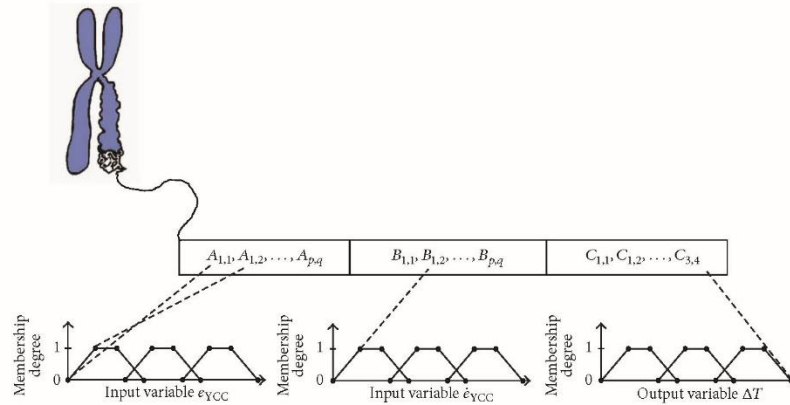


FIGURE 3: Illustrative representation and coding scheme of input and output fuzzy set parameters on a chromosome. For example,  $A_{1,1}$  is the first parameter of the fuzzy set low of the input variable  $e_{YCC}$  and  $A_{1,2}$  is the second parameter. Following this, all parameters are coded on a chromosome, where  $B$  denotes the second input variable  $e_{YCC}$  and  $C$  represents the output variable.

logic controllers and expert systems have been successfully used [26–28, 47–53]. However, they show a deficiency in knowledge acquisition and their parameterization relies to a great extent on empirical and heuristic knowledge. Moreover, in-field tuning and performance adjustment is mostly done by trial and error, which can be very inefficient and time-consuming depending on the complexity of the process to be controlled. The combination of evolutionary optimization methods and fuzzy logic allows incorporating information that is present in the process data in order to automatically adjust the controller parameters and to add a certain degree of intelligence. In this case, genetic algorithms play a significant role, as search techniques for handling complex spaces, and were successfully applied in many fields such as artificial intelligence, (bio)engineering, and robotics [54–57]. In this work, a genetic algorithm (GA) was used in order to tune the input and output membership functions in order to make the control error stay within its statistical borders. The genetic algorithm consists of initialization, rank-based selection, crossover, and mutation. In the beginning the settings of the GA are initialized. A population size of  $j = 40$  individuals was chosen. The selection rate was set to 0.5 and the mutation rate was fixed to 0.02. The maximum number of iterations was set to 120. Instead of binary coding, real coding of fuzzy set parameters on the chromosomes was applied. A similar method as suggested by [58, 59] was chosen to encode the fuzzy parameters. Trapezoidal fuzzy sets were used because this allows the GA to change the set form also into triangular sets as a special form of a trapezium if the two center points are allowed to take equal values. With respect to the coding scheme some restrictions have to be made in order to maintain the order of the linguistic labels. Each trapezoidal shaped membership function or label of a fuzzy

variable is parameterized by a 4-tuple of real values. Therefore, an individual of the population or chromosome  $P_j$  is encoded as follows:

$$P_j = (A_{1,1}, A_{1,2}, A_{1,3}, A_{1,4}, \dots, A_{p,q}, B_{1,1}, B_{1,2}, B_{1,3}, B_{1,4}, \dots, B_{p,q}, C_{1,1}, C_{1,2}, C_{1,3}, C_{1,4}, \dots, C_{p,q}). \quad (6)$$

In this assignment,  $A$  denotes the first fuzzy variable  $e_{YCC}$ ,  $B$  represents  $e_{YCC}$ , and  $C$  is the output variable  $\Delta T$ . Each variable has 3 labels and each label consists of 4 characteristic points (alleles). Thus  $p = (1, \dots, 3)$  and  $q = (1, \dots, 4)$ . In the beginning, the GA is initialized. For this, the first individual was fixed and the set parameters of the original fuzzy controller were encoded on the chromosome. The residual population was initialized randomly within each variables domain. However, some constraints with respect to the semantics of ordering relation and completeness have to be considered [58]. In this context, the ordering of the labels was fixed and for each fuzzy set the sequence of the characteristic points was fixed in order to maintain the order of the linguistic labels. For example, in the case of  $A$ ,  $low < matched < high$  for label ordering and  $A_{p,1} < A_{p,2} \leq A_{p,3} < A_{p,4}$  for the sequence of set points. This boundary condition is valid for the mutation operation, as well. Figure 3 shows how the fuzzy set parameters are coded on the chromosomes.

Including a priori knowledge, the set parameters  $A_{1,1}$ ,  $A_{1,2}$ ,  $A_{3,3}$ ,  $A_{3,4}$ ,  $B_{1,1}$ ,  $B_{1,2}$ ,  $B_{3,3}$ ,  $B_{3,4}$ ,  $C_{1,1}$ , and  $C_{3,4}$  were hard coded with their initial values in order to cover the whole universe of discourse. Thus, they are not altered by crossover and mutation. The residual parameters of the trapezoidal

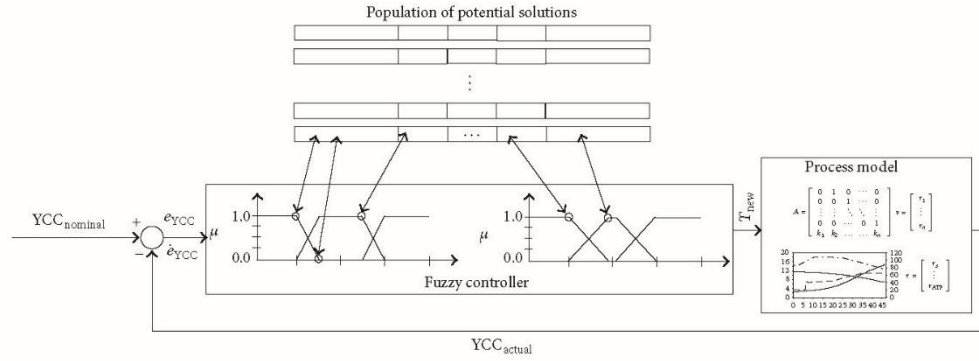


FIGURE 4: After initialization each individual of the population passes its parameter vector to the fuzzy controller. The controller is then simulated using the process model described in Section 2.1. Following the principle of elitism, the best solutions of each iteration are kept in order to create the next population.

fuzzy sets were allowed to take values in the possible intervals of adjustment as follows:

$$\begin{aligned}
 \Gamma_{1,4} &\in [\Gamma_{1,2}, \Gamma_{3,3}], \\
 \Gamma_{1,3} &\in [\Gamma_{1,2}, \Gamma_{1,4}], \\
 \Gamma_{2,1} &\in [\Gamma_{1,2}, \Gamma_{3,3}], \\
 \Gamma_{2,2} &\in [\Gamma_{2,1}, \Gamma_{3,3}], \\
 \Gamma_{2,3} &\in [\Gamma_{2,2}, \Gamma_{3,3}], \\
 \Gamma_{2,4} &\in [\Gamma_{2,3}, \Gamma_{3,3}], \\
 \Gamma_{3,1} &\in [\Gamma_{1,2}, \Gamma_{3,3}], \\
 \Gamma_{3,2} &\in [\Gamma_{3,1}, \Gamma_{3,3}].
 \end{aligned} \tag{7}$$

Here,  $\Gamma$  represents  $A$ ,  $B$ , and  $C$ , respectively. The whole population is simulated using the growth model and the cost, respectively, fitness of each individual, is calculated using the RMSE:

$$\text{RMSE} = \sqrt{\frac{\sum_{t=1}^n (\hat{y}_t - y_t)^2}{n}}. \tag{8}$$

Here,  $\hat{y}_t$  denotes the predicted YCC by the model at the sampling point  $t$  and  $y_t$  is the YCC of the reference trajectory at the same point of time. Rank-based selection [60] is used in order to choose the best solutions. The best 20 individuals are chosen to form the mating pool and the pairing is done randomly within the pool. The crossover operation is done by calculating the mean of the corresponding alleles of each mating pair, which corresponds to whole arithmetic crossover [61]. In this crossover method two offspring  $H_k = (h_1^k, \dots, h_i^k, \dots, h_n^k)$  and  $k = 1, 2$  are computed from two parental chromosomes  $C_1 = (c_1^1 \dots c_n^1)$  and  $C_2 = (c_1^2 \dots c_n^2)$

selected to apply the crossover operator, where  $h_i^1 = \lambda c_i^1 + (1 - \lambda)c_i^2$  and  $h_i^2 = \lambda c_i^2 + (1 - \lambda)c_i^1$ .  $\lambda$  is a constant (uniform arithmetical crossover) and was chosen to be equal to 0.5. According to this the population is filled up again with 20 new offspring. Finally, 2% of the new population is mutated by randomly alternating one allele on a chosen chromosome. The mutation alternation is done in compliance with the restrictions of ordering. Figure 4 shows schematically the flow of information during the genetic tuning process.

The control strategy was implemented using a PLC system (Beckhoff, CX9000) with standard I/O terminals for analogue inputs and outputs (4–20 mA). On the PLC a PID temperature controller was programmed. The fuzzy system, the genetic algorithm, and the SPC monitoring system run on a separate PC in a framework similar to a SCADA (Supervisory Control and Data Acquisition) system. The fuzzy system reads from the PLC, recalculates a new set point for temperature, and writes it to the PID controller on the PLC. The communication between the PLC system and the external PC, respectively, the SCADA system, is done via Ethernet (TCP/IP). The software used for the SCADA system is in-house developed C++ based software named Virtual Expert®.

### 3. Results and Discussion

After the genetic tuning process the best individual of the simulations (RMSE =  $4.03 \times 10^6$  mmol/L) was chosen for experimental validation. The obtained genetically tuned fuzzy sets are shown in Figure 5. The resulting set parameters are as follows:

- (i)  $e_{YCC}$ :
- (a) *low* := [-100 -30 -17.28 10.79],
  - (b) *matched* := [0.17 19.16 25.28 27.31],
  - (c) *high* := [12.90 18.95 30 100];



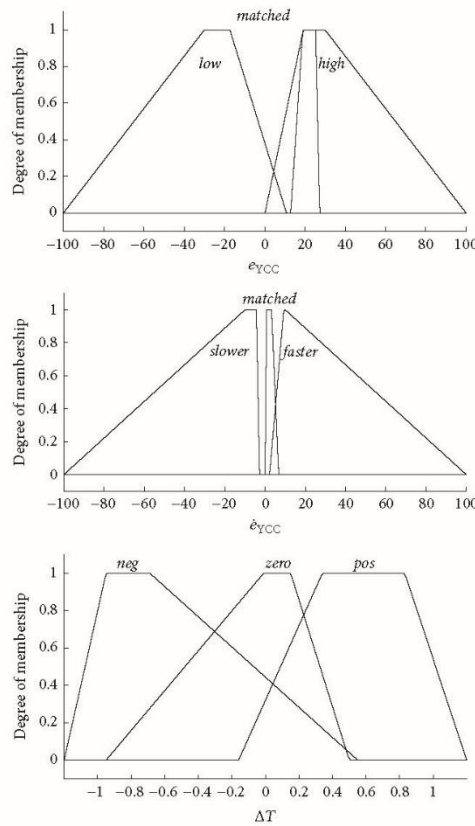


FIGURE 5: New set configuration of the fuzzy controller after the genetic tuning process. Slopes, shapes, and positions of the sets were changed. In particular, the sets denoted as *matched* were generally enlarged.

(ii)  $\dot{e}_{YCC}$ :

- (a) *slower* := [-100 -10 -4.31 -1.24],
- (b) *matched* := [-1.29 -0.61 3.24 6.72],
- (c) *faster* := [2.23 9.30 10 100];

(iii)  $\Delta T$ :

- (a) *neg* := [-1.2 -0.95 -0.69 0.55],
- (b) *zero* := [-0.95 -0.01 0.15 0.50],
- (c) *pos* := [-0.16 0.34 0.83 1.2].

It can be observed that the slopes, shapes, and positions of the different sets have been changed. In particular, the part of the fuzzy sets linked to the linguistic value *matched* with a membership value equal to one has been enlarged compared

to the original sets (almost triangular). This makes the controller behavior more robust against process disturbances and therefore leads to less fluctuation in temperature.

Prior to genetic tuning, the yeast propagation process was run with a nonadapted, uniformly parameterized fuzzy controller described in Section 2.2. As expected, the control performance of the fuzzy controller did not meet the requirements and exceeded the allowed control corridors. As a result, big changes in process temperature exceeding 10 K within 15 hours were recorded. As a consequence, the required performance specifications could not be met. After 2 days of propagation, less than  $70 \times 10^6$  cells/mL and around 5% of dead cells were detected by microscopic plate count [62]. The experiment was then repeated 4 times using the tuned fuzzy controller. The corresponding control charts are shown in Figure 6. As shown, the original controller exceeds the control limits, which is indicated by the arrows. In contrast, the adjusted fuzzy controller is able to keep the process within the statistical borders and therefore meets the performance requirements. Furthermore, by comparison of the controller outputs, in contrast to the nontuned fuzzy controller it alters the process temperature only when it is necessary. The original controller parameterization leads to a permanent change in temperature resulting in an oscillatory, unstable behavior. By applying the genetic tuning process this behavior could be avoided leading to a smoother change of the temperature. Using the tuned fuzzy controller, on average, a cell concentration of about  $185 \times 10^6$  cells/mL and less than 1% of dead cells were achieved after two days of cultivation. The RMSE of reference trajectory and online measured YCC is  $5.2 \times 10^6$  cells/mL. This shows that there is a good matching and that the fuzzy controller is able to lead the process along the desired growth profile. The control charts are projected online; thus the user is permanently informed if the process was in control or if there was any deterioration occurring. However, it has to be noted that the immediate and specific identification of the cause for undesired process behavior would need some additional process knowledge and experience. Here, the quality of the process is merely linked to the control performance. So, if there was, for example, contamination with another microorganism or an undersupply with oxygen, the process would go out of the corridors and one could directly observe this in the control charts, but one would not be able to tell the reason for that without having the corresponding experience and process knowledge. Therefore, a multivariate approach in combination with recent fuzzy control chart evaluation methods [21] is currently under investigation in order to link further quality attributes with the corresponding key performance indicators of the process. This would be a further step in combining online (multivariate) statistical process monitoring and direct, intelligent feedback process control techniques.

#### 4. Conclusion

In this work an approach is presented to couple statistical process monitoring with an intelligent feedback control based

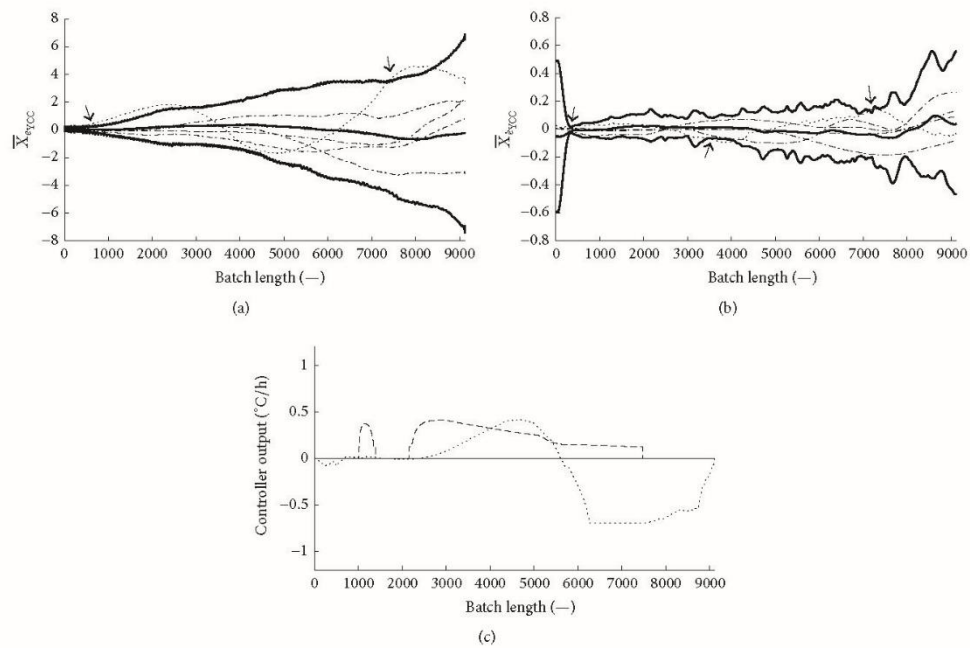


FIGURE 6: Online control charts for control error  $e_{YCC}$  (a) and its derivative  $\dot{e}_{YCC}$  (b). The solid bold lines (—) are the statistical values of the upper control limit, mean, and lower control limit. The dotted (···) curve is the trajectory that belongs to the nontuned fuzzy controller. The arrows mark where it leaves the statistical corridor. The residual lines (— · —) stay clearly within the control limits and show the error trajectories resulting from the genetic tuned fuzzy controller. Graph (c) shows the output of the nontuned fuzzy controller (···) in comparison to the output of the genetic tuned controller (— · —).

on fuzzy logic for handling uncertainty biased processes related to food production and fermentative processes in life sciences. The system is demonstrated by the process of brewer's yeast propagation. For that purpose, the fuzzy controller parameters are adjusted using a genetic tuning algorithm in order to meet the required quality and performance criteria. Subsequent to the simulations, an experimental verification was performed using a 120 L medium-scale propagation system. The obtained results show that the performance of the control system is directly linked to process quality. By staying within the statistical control limits, the required biomass concentration of  $100 \times 10^6$  cells/mL was exceeded reaching up to  $185 \times 10^6$  cells/mL, whereby the RMSE to the reference growth trajectory is  $5.2 \times 10^6$  cells/mL. However, the remaining future challenge is to specifically identify the cause of a process anomaly without having the corresponding experience or knowledge about the process. Therefore, current investigations strive for a combined approach of multivariate modeling and fuzzy control chart evaluation to link specific quality attributes and the control performance of the process, which would be a step forward in combining online (multivariate) statistical process

monitoring and direct, intelligent feedback process control techniques.

### Abbreviations

SD:	Standard deviation
YCC:	Yeast cell concentration
FLC:	Fuzzy logic controller
GA:	Genetic algorithm
SPC:	Statistical process control
Control error $e_{YCC}$ :	Change in control error $\dot{e}_{YCC}$ .

### Competing Interests

The authors declare that there are no competing interests regarding the publication of this paper.

### Acknowledgments

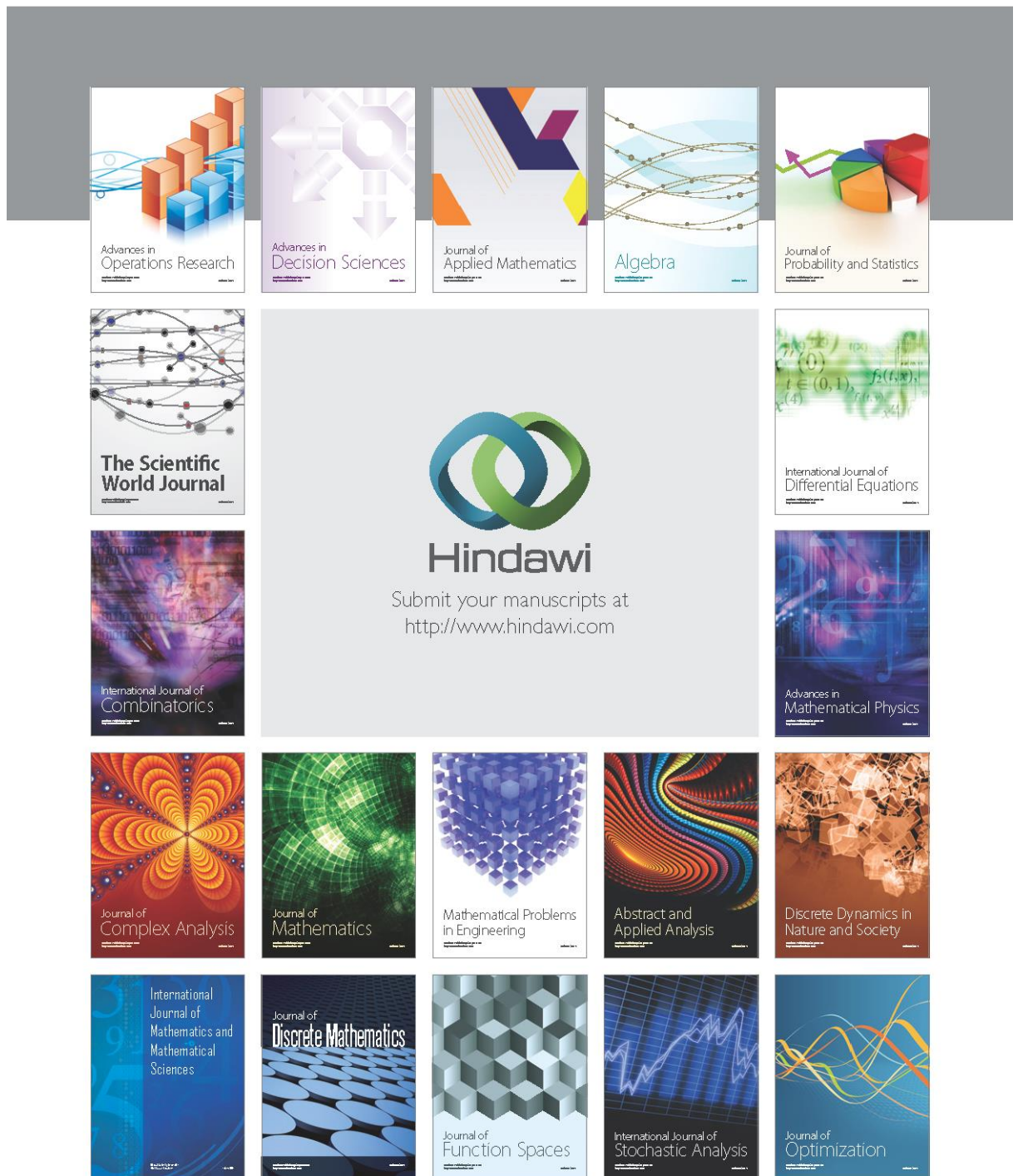
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## 2.2.4 Incorporation of negative rules and evolution of a fuzzy controller for yeast fermentation process

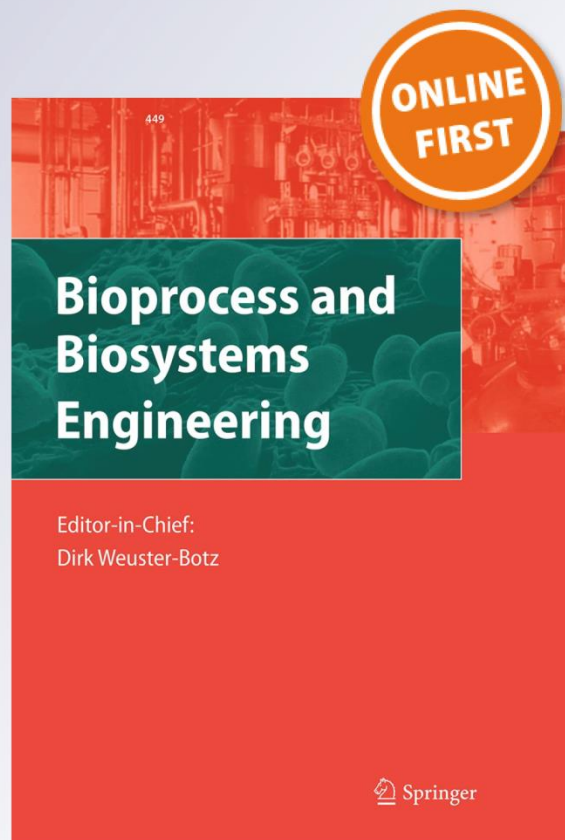
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## Incorporation of negative rules and evolution of a fuzzy controller for yeast fermentation process

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**Abstract** The control of bioprocesses can be very challenging due to the fact that these kinds of processes are highly affected by various sources of uncertainty like the intrinsic behavior of the used microorganisms. Due to the reason that these kinds of process uncertainties are not directly measurable in most cases, the overall control is either done manually because of the experience of the operator or intelligent expert systems are applied, e.g., on the basis of fuzzy logic theory. In the latter case, however, the control concept is mainly represented by using merely positive rules, e.g., “If A then do B”. As this is not straightforward with respect to the semantics of the human decision-making process that also includes negative experience in form of constraints or prohibitions, the incorporation of negative rules for process control based on fuzzy logic is emphasized. In this work, an approach of fuzzy logic control of the yeast propagation process based on a combination of positive and negative rules is presented. The process is guided along a reference trajectory for yeast cell concentration by alternating the process temperature. The incorporation of negative rules leads to a much more stable and accurate control of the process as the root mean squared error of reference trajectory and system response could be reduced by an average of 62.8 % compared to the controller using only positive rules.

**Keywords** Fuzzy logic control · Negative rules · Yeast fermentation · Prediction

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### Abbreviations

YCC	Yeast cell concentration
FLC	Fuzzy logic controller
RMSE	Root mean squared error
AFCE	Absolute final control error
P/N	Positive/negative

### Introduction

The behavior of bioprocesses like fermentations is biased by different sources of uncertainty. The causes for these process uncertainties are multidisciplinary, as well. So, e.g., initial process conditions can hardly be kept constant due to natural changes in the used raw materials, which have immediate effect on the metabolic behavior of the involved microorganisms. Additionally, there is also a lack of appropriate sensors that allow to reliably detect changes in the metabolic behavior in real-time and to take corrective action on the process. Therefore, the control of the process in practice is still performed by experienced human operators. However, during the last 10 years, various expert systems based on fuzzy logic have been proposed for the intelligent control of biological based processes due to the capability to mimic human reasoning and to handle uncertainty based complex nonlinear processes [1–6]. However, most of the proposed systems are solely based on positive knowledge or experience, that is formulated in a “If A then do B” manner. However, this is not straightforward, as countless situations exist not only with respect to control theory, but also in daily life where it is much more suitable to express a decision by negative experience. Using warnings and/or prohibitions in the form of negative rules like “If A then do not do B” leads to a much more transparent processing of practical knowledge and allows

expanding the application field of fuzzy logic control. In this context the incorporation of negative rules that have been identified and extracted from process operation by an expert can be very useful to change the system properties of a fuzzy control system and to form a more efficient process behavior. Following this hypothesis, the general approach should be to construct a fuzzy system that uses a combination of positive and negative rules in such a way that the negative rule-part leads the process away from situations that should be avoided and that, after passing the critical situation, the positive part of the fuzzy system takes over again and controls the process in the usual manner. In this regard, a very comprehensive approach is described by [7] who uses a double-stranded fuzzy controller architecture for separate processing of positive and negative rules. The positive and negative membership functions that have been created by the positive and negative rules then are set off against each other using a hyperinference module. Thereafter, the combined membership function is treated by a downstream hyperdefuzzification that outputs a crisp value. Another quite practical and an easy to implement approach is presented by [8, 9]. They present a novel method denoted as dot attenuation in which the processing of negative and positive rules, respectively their membership functions take place as part of the defuzzification process. Compared to Kiendl's approach, it has one restriction which is that the consequents of the negative rules have to be of the same type and shape as the ones of the positive rule consequents. In Kiendl's method the consequents can be of different type. However, this is not a serious disadvantage, as in most practical applications a mixture of the types is not required. There has been several control applications published in literature using negative rules and showing the superiority of the control performance in comparison to mere positive fuzzy rules. In [10], negative rules are used for the development of an obstacle avoidance controller for an autonomous vehicle. It is shown that the fuzzy system has fewer rules than would be required for a controller using purely positive fuzzy rules and, therefore, has better interpretability. A similar approach was also used by [11]. A combined positive and negative fuzzy rule system for machine learning and image classification was introduced and applied [12]. It could be shown that the proposed method achieved better results in learning performance and classification accuracy compared to a backpropagation based neural network and the fuzzy c means algorithm. Similar findings for image classification problems are presented by [13, 14]. However, there are no applications described in literature using the concept of positive/negative (P/N) fuzzy systems, for the control of uncertainty biased systems like bioprocesses.

In the present work, we apply a P/N-fuzzy system to the brewer's yeast propagation process. The objective is to

improve the performance of the control system, which is based on a classical fuzzy controller whose rulebase contains only positive rules. By incorporating negative rules to the classical Mamdani based fuzzy controller, its performance with respect to overshooting and process stability could be enhanced. The negative rules are formed using the predictions of yeast cell concentration (YCC) 3 h ahead of time which are provided by simple moving least squares estimator. This paper is arranged as follows. "Materials and methods" section presents the materials and methods used to build the system. Besides the process model which was used for later simulations of the process, this includes the description of the YCC one step-ahead predictor. Furthermore, the fuzzy controller is explained. "Results and discussion" section contains the results and discussion of simulations of the yeast propagation process using the P/N-fuzzy system. "Conclusion" section gives a conclusion and an outlook to ongoing work in that direction.

## Materials and methods

### Process model

For the later simulation studies, an adapted version of the black-box growth modeling approach of [15] was implemented. The model is based on known stoichiometric turnover rates and Michaelis–Menten kinetics of yeast [16–18]. In addition to that, it considers growth limitations like the Crabtree effect [19] that occurs under brewing specific circumstances of production. The Crabtree effect is a limiting growth phenomenon that takes place when feeding substrate sugar concentrations are above 100 g/l. Due to the fact that standard beer wort, which is used as substrate for yeast cultivation is generally above that threshold, the Crabtree effect cannot be avoided under brewing conditions and, therefore, shifts the metabolism partly to the anaerobic pathway limiting the growth rate. Besides this, the effect of temperature on yeast growth, respectively the substrate uptake is modeled by implementing an additional temperature factor  $f_{temp}$ . This parameter is expressed using a square root term that was originally developed to describe the temperature effect on the growth of specific bacteria [20, 21]. The specific substrate uptake  $q_S$  and the specific oxygen uptake rate can be represented by the following equations [15]:

$$q_S = q_{S,max} \times \min\left(\frac{S}{S + K_s}, \frac{N}{N + K_n}\right) \times \frac{K_{i,eth}}{K_{i,eth} + E} \times L_t \times f_{temp} \quad (1)$$

$$f_{temp} = \{b \times (T - T_{min}) \times [1 - \exp(c \times (T - T_{max}))]\}^2 \quad (2)$$

**Table 1** Parameters applied for use of the model

Parameter	Value	Unit	References
$q_{S,max}$	0.486	mol/mol/h	[17]
$K_S$	2.8	mmol/l	[17]
$K_O$	0.00121	mmol/l	[22]
$K_{eth}$	2.2	mmol/l	[16, 17]
$K_n$	2	mmol/l	[24]
$K_{i,eth}$	500	mmol/l	[25]
$K_{i,eth,o}$	217.39	mmol/l	[16]
$t_{lag}$	5.6	h	*
$t_{lag,eth}$	0	h	*
$b_{femp}$	0.0329632		*
$T_{min,femp}$	270.7616	K	[15]
$c_{femp}$	11.98		[15]
$T_{max,femp}$	308.1539	K	[15]
$b_{q_{O_2,max}}$	0.0283757		*
$T_{min,q_{O_2,max}}$	276.3958	K	[15]
$c_{q_{O_2,max}}$	0.0163645		*
$T_{max,q_{O_2,max}}$	295.8981	K	*

Parameters marked by \* were determined by a parameter estimation procedure

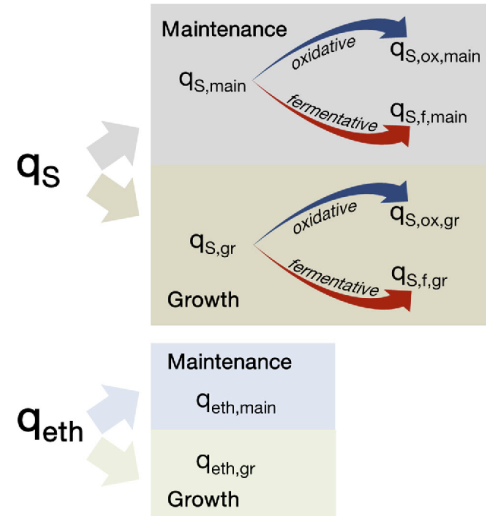
$$L_t = \frac{1}{1 + e^{-(t-t_{lag})}} \quad (3)$$

$$q_{O_2} \leq q_{O_2,max} \times \frac{O}{K_o + O} \times \frac{K_{i,eth,o}}{K_{i,eth,o} + E} \quad (4)$$

$$L_{t,eth} = \frac{1}{1 + e^{-(t-t_{lag,eth})}} \quad (5)$$

$$q_{eth} \leq q_{eth,max} \times \min\left(\frac{E}{K_{eth} + E}, \frac{N}{K_n + N}\right) \times L_{t,eth} \quad (6)$$

Here,  $S$  denotes the substrate concentration (glucose is assumed to be the preferred substrate),  $O$  is the oxygen concentration,  $N$  is the nitrogen concentration and  $E$  reflects the concentration in ethanol. All concentrations are in mmol/l. Furthermore,  $T$  represents the temperature in Kelvin,  $t$  is the time and  $L_t$  or  $L_{t,eth}$  are sigmoid lag-time functions for growth on glucose and ethanol, respectively. Analogue to  $q_S$ , the specific oxygen uptake rate  $q_{O_2}$  is determined by a temperature dependent maximum uptake factor  $q_{O_2,max}$  [22, 23], which is calculated similar to  $f_{emp}$ . All applied model parameters and half saturation constants are stated in Table 1. A partitioning of the substrate uptake flux is given in Fig. 1. The overall specific growth rate  $\mu$  is then calculated from the sum of the specific growth rates for oxidative and fermentative growth on glucose ( $\mu_{S,ox}$ ,  $\mu_{S,f}$ ) or ethanol ( $\mu_{eth}$ ) and the yield coefficients  $Y_{X/S_{ox}} = 3527$  mol BM/mol glucose,  $Y_{X/S_f} = 0,72$  mol BM/mol glucose and  $Y_{X/eth} = 1,12$  mol BM/mol ethanol [17] by the following equations [15]:



**Fig. 1** Flux division of substrate uptake corresponding to [15]. The flux is separated into divisions for cell growth and maintenance with respect to the growth on glucose or ethanol, respectively

**Table 2** Key data of the batches used for the validation of the model

Batch ID	Duration [h]	$T(t=0)$ [°C]	YCC ( $t=0$ ) [mmol/l]
Batch A	47	13.7	10.2
Batch B	32	12.6	7.5
Batch C	24	14.5	14.1

$$\mu_{S,ox} = q_{S,ox,gr} \times Y_{X/S_{ox}} \quad (7)$$

$$\mu_{S,f} = q_{S,f,gr} \times Y_{X/S_f} \quad (8)$$

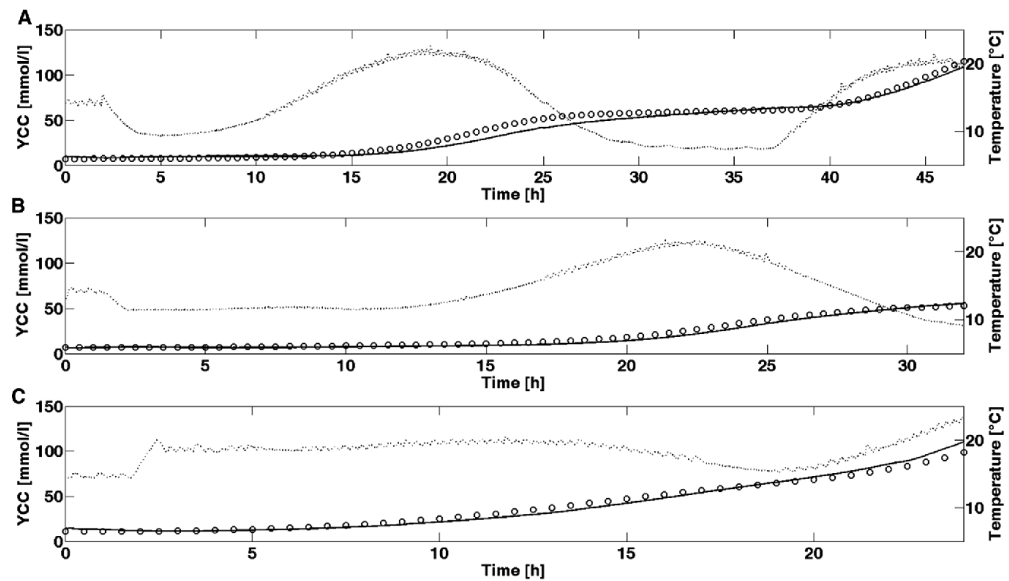
$$\mu_{eth} = q_{eth,gr} \times Y_{X/eth} \quad (9)$$

$$\mu = \mu_{S,ox} + \mu_{S,f} + \mu_{eth} \quad (10)$$

The intermediate steps of division and calculation of specific substrate uptake rates like  $q_{S,ox,gr}$ ,  $q_{S,f,gr}$  and  $q_{eth,gr}$  are not shown here and the reader is referred to [15] for a detailed and comprehensive description of the model.

The model was then validated using real process data of three different batches. The batches differ in batch length, initial temperature and YCC (Table 2).

For the validation, as an input, the temperature trajectories were fed into the model and the model output of the YCC was compared with the YCC of the experimental batches. The comparison of model output and experimental data is shown in Fig. 2 together with the corresponding temperature trajectories for each batch. The root mean squared error (RMSE) between experimental YCC and



**Fig. 2** Comparison of cell concentration from experimental results (solid line) and the yeast cell concentration provided by the model (circles) in  $10^6$  cells/ml. The temperature trajectories (dashed line)

that were fed as inputs to the model are plotted on the right axis in °C. The key data of the batches (A–C) is given in Table 2

model output is  $3.8 \times 10^6$  cells/ml. This shows that the model is capable to represent the growth dynamics due to temperature changes and therefore it is suitable to be used in further simulations and to serve as a model for plant response. The conversion from mmol/l to  $10^6$  cells/ml and vice versa is done via the following equation [15]:

$$\text{Biomass [mmol/l]} = \frac{\text{YDM [g/cell]} \times \text{YCC [Mio. cells/ml]}}{\text{BM [g/mol]}} \times 10^6 \frac{[\text{ml mmol}]}{[\text{l mol}]} \quad (11)$$

Here,  $YDM$  = yeast dry mass =  $4 \times 10^{-11}$  g/cell,  $BM$  (molar weight of the mean biomass composition) = 25.01 g/mol [17].

### The predictor

The predictor used in this work is based on a sliding window fifo buffer (first in–first out). The input is the actual YCC which is measured online using a turbidity sensor (optek-Danulat GmbH, AF 16). The turbidity signal is mapped to the YCC value using a simple second order polynomial regression. The sampling time is 3.6 s and the buffer size was chosen 1000 values, which corresponds to 1 h. As soon as the buffer has been filled, linear

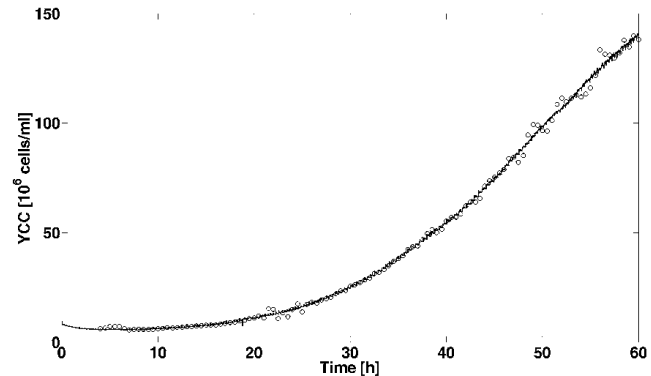
interpolation is done by minimizing the sum of squares of the buffer data (least-squares fit) and the coefficients of the best fit 2nd order polynomial are calculated. The resulting polynomial expression is then used for extrapolation and calculating the YCC 3 h in advance. Figure 3 shows exemplarily, the predictions of YCC using real batch data.

### The fuzzy controller

#### The basic fuzzy controller

In its basic version, the fuzzy controller that was applied in order to regulate the process temperature is a Mamdani type controller [26, 27]. It consists of the standard components, which are first the fuzzification, where crisp inputs are transformed into fuzzy sets and, respectively, linguistic labels by using membership functions. The linguistic labels or fuzzy sets are then used in the rulebase and the inference mechanism. The rulebase contains the knowledge, in the form of a set of “if–then”-rules, of how best to control the system. The inference mechanism emulates an expert’s decision-making, and evaluates which control rules are relevant at the current time, and then decides what the input to the plant should be. The defuzzification interface converts the conclusions drawn by the inference mechanism

**Fig. 3** Future predictions of YCC 3 h in advance. The *solid line* represents the online detected YCC. The *circles* are the predictor outputs at the corresponding time (only every 500st point plotted)



into crisp outputs. For a comprehensive description of fuzzy logic control, the reader is referred to [28]. In this work, only piecewise linear membership functions were used to create the fuzzy sets. For inferencing, the max–min method was used and center-of-gravity (COG) defuzzification is used to compute a numerical value from the resulting output fuzzy set. The input fuzzy variables are  $e_{YCC}$  and its temporal derivative  $\dot{e}_{YCC}$ . More clearly,  $e_{YCC}$  is the difference between the nominal YCC value (setpoint) and the actual YCC value. The actual YCC value is detected online using a turbidity sensor (Optek-danulat, AF 16). The YCC setpoint value is provided for each point in time, using a time-dependent 3rd order polynomial function (not shown here). In other words,  $e_{YCC}$  is the control error. Depending on  $e_{YCC}$  and  $\dot{e}_{YCC}$ , the fuzzy controller tries to keep the process as close as possible to the YCC reference trajectory by changing the temperature. The fuzzy variable  $e_{YCC}$  is assigned to the linguistic expressions low, matched and high. Similarly, the fuzzy variable  $\dot{e}_{YCC}$  is linked to the verbal terms slower, matched and faster. The fuzzy output variable  $dTemp$  consists of three fuzzy sets, namely neg, zero, and pos. The fuzzy output is a temperature increment  $\Delta T$  that is added to the initial temperature at the start of the process. The basic rulebase comprises nine simple rules:

- 1) **If**  $e_{YCC}$  is low and  $\dot{e}_{YCC}$  is slower **Then**  $dTemp$  is neg.
- 2) **If**  $e_{YCC}$  is low and  $\dot{e}_{YCC}$  is matched **Then**  $dTemp$  is neg.
- 3) **If**  $e_{YCC}$  is low and  $\dot{e}_{YCC}$  is faster **Then**  $dTemp$  is zero.
- 4) **If**  $e_{YCC}$  is matched and  $\dot{e}_{YCC}$  is slower **Then**  $dTemp$  is neg.
- 5) **If**  $e_{YCC}$  is matched and  $\dot{e}_{YCC}$  is matched **Then**  $dTemp$  is zero.

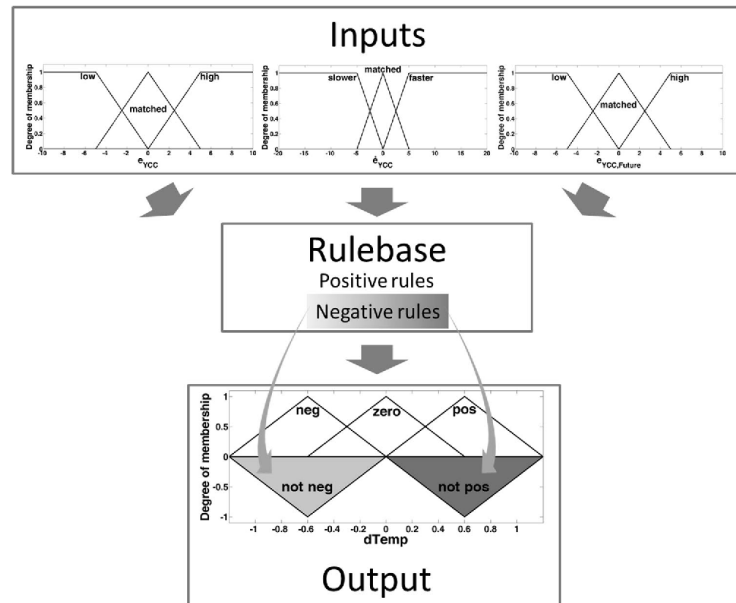
- 6) **If**  $e_{YCC}$  is matched and  $\dot{e}_{YCC}$  is faster **Then**  $dTemp$  is pos.
- 7) **If**  $e_{YCC}$  is high and  $\dot{e}_{YCC}$  is slower **Then**  $dTemp$  is zero.
- 8) **If**  $e_{YCC}$  is high and  $\dot{e}_{YCC}$  is matched **Then**  $dTemp$  is pos.
- 9) **If**  $e_{YCC}$  is high and  $\dot{e}_{YCC}$  is faster **Then**  $dTemp$  is pos.

The fuzzy set parameterization for each variable was assigned as follows:

- $e_{YCC}$ 
  - low =  $]-\infty -5 [0]$
  - matched =  $[-5 0 5]$
  - high =  $[0 5 \infty[$
- $\dot{e}_{YCC}$ 
  - slower =  $]-\infty -5 [0]$
  - matched =  $[-5 0 5]$
  - faster =  $[0 5 \infty[$
- $dTemp$ 
  - neg =  $[-1.2 -0.6 0]$
  - zero =  $[-0.6 0 0.6]$
  - pos =  $[0 0.6 1.2]$

Here, the numbers denote the characteristic points of the piecewise linear membership functions used to define the individual fuzzy sets. E.g., the support (the set of points on the variable domain, where the membership function value is greater than zero) and slope of triangular fuzzy set matched is characterized by the three points  $-5$ ,  $0$  and  $5$ . Besides triangular shaped sets, left open and right open sets (“bisected trapezoidal sets”) were used. Note, as  $-\infty$  and  $\infty$  are no finite, real numbers, the practical implementation of the corresponding sets is bound to the restriction, that for

**Fig. 4** Graphical representation of the P/N-fuzzy controller. The inputs show the fuzzy input variables  $e_{YCC}$ ,  $\dot{e}_{YCC}$  and  $e_{YCC,Future}$  and the partitioning into their distinct fuzzy sets. The output of the controller consists of the fuzzy output variable  $dTemp$ . For illustration purposes, the fuzzy sets which are fired by the negative rules are plotted on the negative ordinate



any crisp input value greater or smaller than the central point, the membership has full saturation. In other words, the membership value is equal to 1. If, e.g.,  $e_{YCC} \geq 5$ , then the membership degree of the right open fuzzy set high is  $\mu_{high} = 1$ . Conversely, the same counts for left open fuzzy sets.

*Incorporation of negative rules*

For the incorporation of the negative rules, the method of dot product attenuation described by [8, 9] is used. In this method, the part of defuzzification is modified and COG method becomes:

$$y(x) = \frac{\sum_{i=1}^R b_i \int \mu^{imp}(i) (1 - \hat{a}_i^T \mu^-)}{\sum_{i=1}^R \int \mu^{imp}(i) (1 - \hat{a}_i^T \mu^-)} \quad (12)$$

where  $T$  denotes transpose,  $\mu^-$  is the negative implied vector,  $\mu^{imp}(i)$  is the implied fuzzy set from rule  $i$ ,  $\hat{a}_i$  denotes a unit vector in the direction of the consequent of rule  $i$ ,  $R$  stands for the number of rules and  $b_i$  represents the center of the membership function determined by the consequent of rule  $i$ .

The rulebase is extended by two negative rules containing an additional fuzzy input variable denoted as  $e_{YCC,Future}$ , whose parameterization, respectively partitioning into fuzzy sets corresponds to  $e_{YCC}$ :

- 10) **If**  $e_{YCC}$  is low and  $e_{YCC,Future}$  is high **Then**  $dTemp$  is not neg.
- 11) **If**  $e_{YCC}$  is high and  $e_{YCC,Future}$  is low **Then**  $dTemp$  is not pos.

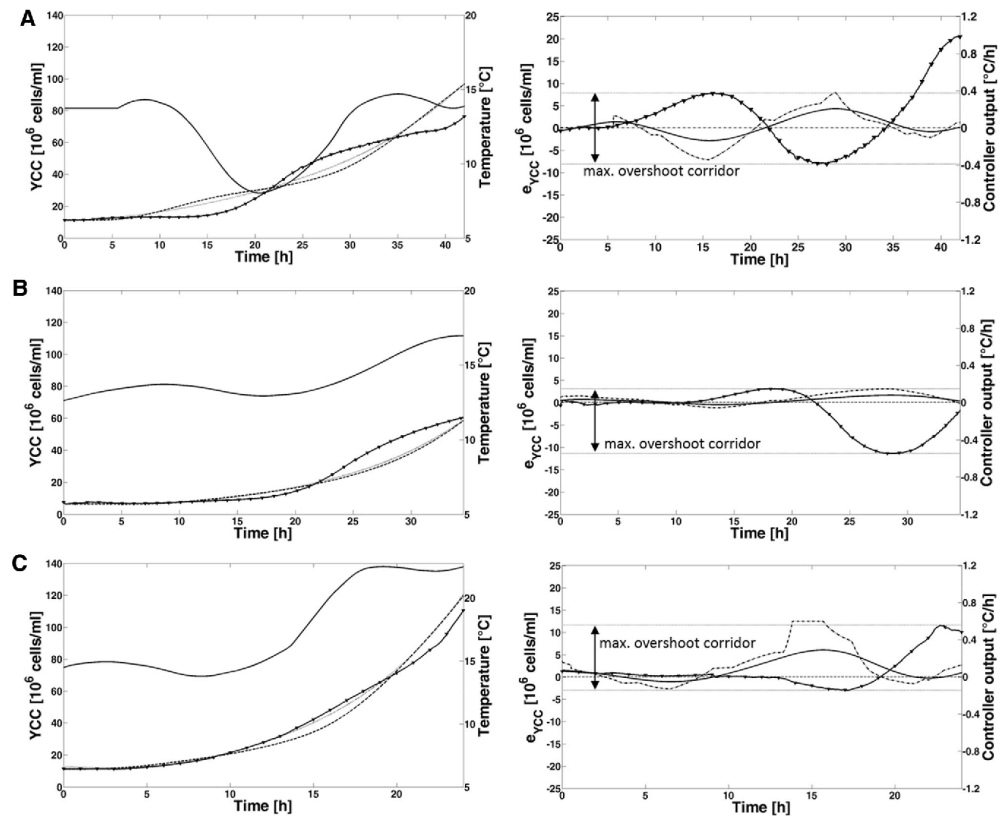
For all other fuzzy relations with the variable  $e_{YCC,Future}$  on the Cartesian product space (e.g., with the set matched), the output is mapped to zero, in order not to alter the behavior of the basic controller in regions that are not of interest.

Figure 4 gives a graphical representation of the fuzzy controller input and output variables. For illustration purposes, the fuzzy sets which are fired by the negative rules are plotted on the negative ordinate.

**Results and discussion**

In this section, the results from experimental runs without negative fuzzy rules, and the simulations using the combined rulebase of positive and negative rules are compared and presented. As the task of the fuzzy controller is to follow the reference trajectory as close as possible, the deviations expressed by the RMSE are used. All simulations were started with the same initial conditions as the corresponding experiment. Three different batches (A-C) were chosen for the simulations. The results are presented





**Fig. 5** Comparative results for the fuzzy controller having only positive rules and with inclusion of two negative rules. Three different batches (a–c) were chosen for the simulation study. On the *left hand side* are the resulting batch trajectories. The *solid line* is the resulting temperature trajectory for the P/N-fuzzy controller. (*Inverted closed triangle*) denotes the curve of yeast cell concentration without using negative rules. The *dashed line* shows the resulting cell concentration by using also negative rules. The reference trajectory is expressed as a *dotted line*. It can be seen that by incorporating negative rules, the

fuzzy controller is able to keep the process much closer to the desired trajectory. On the *right hand side*, the corresponding error trajectories and the controller output signal are shown. Here, the line marked by (*inverted closed triangle*) is the error trajectory using only positive rules, the *solid line* denotes the error by the P/N-fuzzy controller and the *dashed line* marks the controller output. The region of maximum overshooting occurring is marked by a corridor (see *arrows*) with *dashed lines*

in Fig. 5. The graphs on the left side show the trajectories for the cell growth. On the right hand side, the corresponding deviations, respectively the control errors ( $e_{YCC}$ ) to the reference trajectory are presented. The first batch (A) was started with an initial concentration of about  $11.3 \times 10^6$  cells/ml (18.1 mmol/l); the temperature at the beginning was 14 °C and the batch ran for 42 h. The resulting RMSE of the control error using only positive rules was  $9.1 \times 10^6$  cells/ml. By adding also negative rules, the RMSE could be reduced by 78 % to  $2.0 \times 10^6$  cells/ml and the absolute maximum overshoot was reduced

from 19.0 to 9.2 %. The second batch (B) had an initial YCC of  $6.4 \times 10^6$  cells/ml (10.2 mmol/l), was pitched at 14 °C and the duration was 34 h. The RMSE using only positive rules was determined as  $5.1 \times 10^6$  cells/ml and could be reduced by the incorporation of negative rules to  $0.9 \times 10^6$  cells/ml. Absolute maximum overshooting could be improved from 32.7 to 4.7 %. Batch C was started with a YCC of  $11.1 \times 10^6$  cells/ml (17.8 mmol/l),  $T(t = 0) = 14.5$  °C and it was run for 24 h. Using negative rules, the RMSE of the control error could be reduced from  $3.9 \times 10^6$  cells/ml to  $2.8 \times 10^6$  cells/ml, which is an



**Table 3** Fuzzy controller performance values without and with negative rules

	Batch A		Batch B		Batch C		Avg. improvement (%)
	Only pos. rules	P/N fuzzy system	Only pos. rules	P/N fuzzy system	Only pos. rules	P/N fuzzy system	
Max. overshoot (%)	19.0	9.2	32.7	4.7	11.2	13.8	11.7
RMSE (10 <sup>6</sup> cells/ml)	9.1	2.0	5.1	0.9	3.9	2.8	62.8
AFCE (10 <sup>6</sup> cells/ml)	20.5	0.2	1.7	0.3	10.0	0.9	90.8

improvement of around 28 %. However, with respect to maximum absolute overshooting occurring between the 10th and 20th hour (maximum at 16th hour), this was slightly higher with 13.8 % compared to 11.2 % using only positive rules. It is assumed that this could be avoided by further tuning of the fuzzy set parameters. Therefore, future investigations are carried out in order to automatically tune the set parameters using evolutionary optimization techniques like particle swarm optimization or genetic algorithms. This would allow to further improve the control performance and beyond this, it would allow to carry out quick controller prototyping that leads to a reduction of practical controller implementation and evaluation time. However, as a general and probably the most important finding, it can be noted that the fuzzy controller using solely positive rules is not really able to stabilize the process. In contrast to the P/N-fuzzy controller, it could not make the cell concentration to target the reference trajectory at the end of the process, which could be observed for all batches. However, this was achieved by incorporating two additional negative rules that reduce gradually, the output of the corresponding positive rules. In other words, if in future the control performance, respectively the control error deteriorates, then the decision that is made by the positive rules at the current point of time will be attenuated gradually. A comparative summary of maximum overshoot, RMSE and absolute final control error (AFCE) at the end of the batch is given in Table 3.

## Conclusion

In this work, an approach is presented for improving the control performance of the process of brewer's yeast propagation using a fuzzy controller based on negative and positive rules. The control performance of experimental batches that were controlled using only positive rules is compared to the same controller with two additional negative rules. The comparison is drawn upon evaluation of RMSE of the control error and the absolute maximum overshoot occurring during the process. The negative control rules were built on a moving least squares predictor

that outputs future values of YCC and which are taken to gradually prohibit or reduce the output of positive fuzzy rules, referring to the current point of time in the process. It could be shown that the incorporation of negative rules can be used to achieve a more stable control performance than by only using positive rules. Furthermore, it shows to potential to specifically reduce overshooting and to achieve smaller control errors. In this regard, an average improvement of 11.7 % in overshooting, 62.8 % reduction of RMSE and 90.8 % decrease of AFCE could be achieved by the proposed P/N-fuzzy controller. Therefore, fuzzy inference systems, especially when applied to complex systems that are difficult to control, can benefit from the incorporation of negative experience into the decision-making process. Hence, warnings, respectively prohibitions can be turned into concrete actions and interventions, to modify the controller behavior where it is necessary. This confirms the findings of [7] and [9, 10] that the inclusion of negative experience can significantly improve the quality of the control performance. However, as the input and output fuzzy sets of the controller were parameterized in a very uniform manner, there exists further potential for performance optimization by fine tuning of the parameter configuration of the fuzzy sets. In that respect, current investigations strive for including a data-driven automatic approach for fine tuning of the premise and consequent fuzzy set parameters by the use of evolutionary computing.

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## Compliance with ethical standards

**Conflict of interest** The authors have declared no conflict of interest.

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### 3 Discussion and outlook

The online supervision and control of biologically based processes is generally a challenging task. Besides varying quality of raw materials and nonlinear and dynamic metabolic behavior there are multidisciplinary sources of uncertainty that have to be taken into consideration for the successful development of an online monitoring and control system. In this regard one also has to be aware of a certain deduction of measurement accuracy when dealing with online applications. In addition to measurement noise, limitations in the temporal, spatial, physical, or chemical resolution of available sensors commonly lead to a lack of information that cannot be avoided completely. Furthermore, in many cases crucial quality attributes or process parameters or variables cannot even be measured in a direct way. Therefore, indirect methods or soft sensors built upon some kind of (multivariate) regression model are used in order to provide an estimate of the required variable of interest. However, it is clear that the detour via indirect, model-based measurement inevitably includes supplementary information uncertainty. Hence, in terms of the scope of this work an approach based on fuzzy logic was investigated and developed which is capable of handling these kinds of uncertainty within an online framework for monitoring and process control. In this regard, several solutions and optimization methods like genetic algorithms or the incorporation of negative rules were explored in order to enhance the system's flexibility and to meet the required performance. In that context a comprehensive screening of the state of the art in terms of fuzzy logic control and soft sensing applications in the food and beverage sector was performed in order to evaluate current trends and challenges in that direction. In this perspective, the founding principle is to provide comprehensive process intelligence by using innovative sensor concepts to improve process continuity, process safety, and process efficiency. In order to achieve that objective, innovative sensor principles are combined with modern methods of data analysis and modeling using process and product knowledge (Krause, Birle et al. 2011). Hence, software sensors constitute useful tools for the indirect supervision of necessary process variables. Recent approaches in food-related processing use the concept of fuzzy reasoning and its potential to implement expert knowledge along with numerical information. In that context the fuzzy symbolic approach makes heavy use of expert knowledge with respect to quality evaluation of food (Mauris, Benoit et al. 1994; Ioannou, Mauris et al. 2003; Ioannou, Perrot et al.

2004). However, this approach relies exclusively on human assessment and is still in need of human control action. Therefore, the online capability is limited and the system's stability in the case of variable sampling instances is difficult to judge. However, fuzzy controllers generally possess a series of advantages. First, they are now quite fast, problem-related, and meaningful tools for a smart control of complex, non-linear system behavior as the description of the system's behavior can be achieved by means of linguistic expressions and the integration of expert knowledge. Under consideration of rapid controller design and from a practical engineering perspective that approach is very focused on problem-solving and simpler than using methods of complex mathematics. Equally positive is the traceability and interpretability of the obtained results and controller outputs. In addition to that, fuzzy controllers can be used as a universal approximator of any nonlinear system. Therefore, the control algorithm can be designed for the whole working range. By choosing appropriate definitions of fuzzy sets and fuzzy rule bases a fine-tuning of the controller behavior and adjustment of the desired control performance can be achieved with the necessary sensitivity for the whole operating range. Due to that, controllers based upon the principle of fuzzy inference are suitable for formulating nonlinear and robust control rules. However, there exist several practicable and scientific shortcomings of classical fuzzy inference control systems. One major drawback is the lack of learning ability. An automated adaptation to a steadily changing environment is not possible and it is difficult to repair errors implanted in the initial design phase at a later point in time. In other words, if for example the quality or composition of used raw materials changes due to yearly variations of harvest conditions, or if the intrinsic metabolic behavior of microorganisms is altered by any kind of mutation, then a static fuzzy control system will not be able to compensate for that kind of diversification. Furthermore, the parameterization of the fuzzy system, applying the appropriate fuzzy operators, and the methods of implication and defuzzification are of crucial importance for the system's performance. Due to the high degree of freedoms that can be adjusted, the still dominant in-field method of trial and error is not constructive from a scientific point of view. Besides, without further optimization methods, a trade-off between computation performance and quality of the result has to be dealt with. Consequently, the suitability of fuzzy logic in the sense of software sensors is rather limited. Hence, hybrid systems of fuzzy logic and computational optimization methods like evolutionary

computing have emerged. This allows the advantages of both systems to be made use of. Heuristic optimization methods are acknowledged to be very efficient and fast in finding the optimal solution for a distinct problem. Different approaches are tested simultaneously to reach the optimum, providing several potential solutions. As they are able to cope with ill-behaved problem domains, exhibiting attributes such as multimodality, discontinuity, time-variance, randomness, and noise, they seem to be particularly suitable for parameter optimization of fuzzy logic based control systems and enhancing their learning capability. However, applications and experience with these optimization tools in the field of food and beverage production barely exist. This might be mainly due to the fact that, depending on the problem space, evolutionary optimization like genetic algorithms can be computationally intensive and frequently require massive parallel implementations in order to deliver usable results within an acceptable timeframe. Hence, their online application to real-time control has been rather limited up to now. However, this circumstance opens up space for further scientific research. In general, the combination or tuning of fuzzy inference systems has the advantage that the inputs and outputs can be linguistic expressions maintaining the interpretability of the system, while optimization and inference is accomplished by the flexibility of the heuristic optimizer. Therefore, the intelligent combination of these two technologies into an integrated system seems to be a promising direction to optimized process control reducing development time and improving the accuracy of the underlying fuzzy system. Looking at the landscape of soft sensing approaches present in the field of food and beverage processing there is a need for more investigation particularly with respect to robustness and sensitivity analysis to error-prone input data in order to compete with the steadily changing process conditions and satisfy the high quality demands in the case of large-scale production. Especially in the case of the predicting and determination of crucial quality parameters of fermentation processes there is a need for statistically based methods that allow the handling of information uncertainty stemming from sensor data for the purpose of online process supervision. In this context approaches based on (multivariate) statistical process control offer an intelligent method for treating process-related uncertainties by the use of statistically based process and quality corridors. Moreover, control charts can then be used as an adequate tool for online visualization and monitoring of the process evolution. In consequence, with respect to the

observability and controllability of biologically based processes, uncertainty should be treated on two levels. For the part of process monitoring and supervision the uncertainty of process variability (process variance) can be charted by means of statistical process control. The subsequent processing of this information and its incorporation into a feedback control system in order to stay within statistical ranges of certitude is then performed via fuzzy logic control.

In this work the brewer's yeast propagation process was used in order to evaluate the developed methods. Therefore a basic monitoring and control system was designed and evaluated in the first instance. The proposed system consists of a classical fuzzy logic control system and a metabolic growth model (Kurz, Mieleitner et al. 2002) in order to guide the process along reference trajectories of cell growth and substrate consumption. In addition, methods of data pretreatment, signal processing, and soft sensing of yeast cell concentration using a neural network were applied. In order to adjust the underlying PID controllers in the basic PLC system classical methods of linear controller design were applied. In order to evaluate the performance of the system and the quality of the produced yeast suspension target values of the final process states were defined consisting of target yeast cell concentration, final substrate concentration, percentage of dead cells, and the intracellular pH value. These target values had to be achieved for varying process run times. The presented results show that the system is able to target the desired final state corridors for extract and yeast cell concentration within the desired duration. However, the system also shows potential for further optimization. Although the final states are met, a deviation of  $7.0 \times 10^6$  cells/mL and  $8.7 \times 10^6$  cells/mL at the end of the process was observed. This indicates that the control performance can be improved. Therefore, the next step was to apply further optimization methods of evolutionary tuning of fuzzy parameters. In order to handle the aforementioned uncertainty with respect to the part of process monitoring, the concept of statistical process control was introduced using statistically predefined process corridors as a measure of uncertainty. Hence, statistical process monitoring was coupled with an intelligent feedback control based on fuzzy logic for handling uncertainty-biased processes related to food production and fermentative processes in life sciences. The system was also demonstrated by the process of yeast propagation. In that section of this work, the fuzzy controller parameters were tuned using a genetic algorithm in order to meet the required quality and performance criteria.

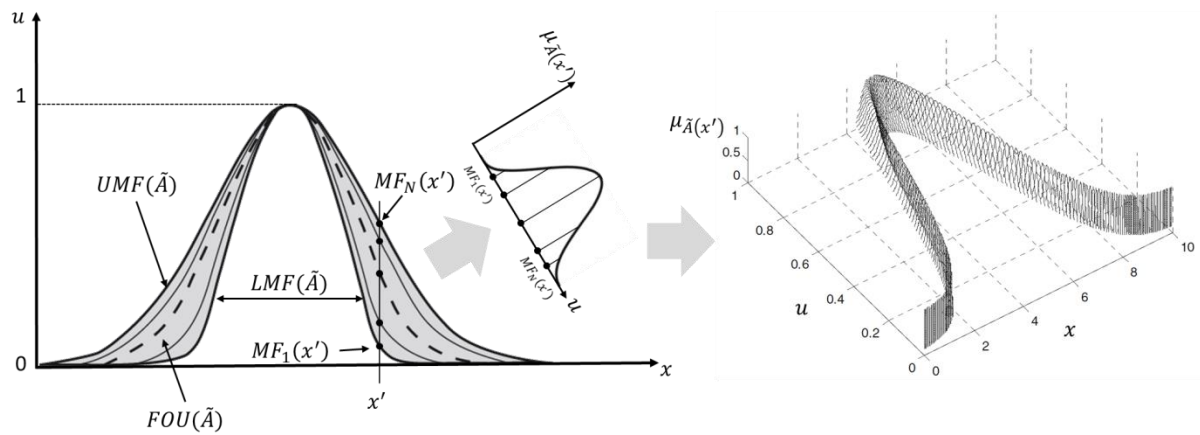
Prior to the experimental verification using the 120 L medium-scale propagation system the tuning was performed by simulation. For this, a growth model according to (Kurz 2002) was used to serve as the system response. The results show that the performance of the control system is directly linked to the quality of the process. It could be shown that if the statistical control limits were not exceeded, the target yeast cell concentration of  $100 \times 10^6$  cells/ml was outperformed reaching up to  $185 \times 10^6$  cells/ml and having less than 1% dead cells. The RMSE to the reference growth trajectory was  $5.2 \times 10^6$  cells/ml. However, the remaining future challenge is to specifically identify changes in the trend of the control chart and to identify the cause of a process anomaly without having the corresponding experience or knowledge about the process. Therefore, a combined approach of multivariate modeling and fuzzy control chart evaluation, e.g. (Sorooshian 2013), should be explored in order to link specific quality attributes and the control performance of the process. Considering the semantics of human decision making it is not straightforward to only use positive experience when corrective action is required. The way how we make decisions also includes negative experience, which can lead to more efficient assessment or actions. However, this is not the case in most of the existing fuzzy inference systems, especially when applied to control tasks. Generally, the standard modus ponens, or only positive rule formulation, is applied. For this reason, the incorporation of negative experience into a fuzzy controller was studied and evaluated. Following the concept of modus tollens, an approach was used for improving the control performance of the process of brewer's yeast propagation by implementing a fuzzy controller based on negative and positive rules. The control performance of a fuzzy controller using only positive rules is compared to the same controller with two additional negative rules. The comparison is made upon the evaluation of RMSE of the control error and the absolute maximum overshoot occurring during the process. The negative control rules were established by designing a moving least squares predictor. It outputs future values of the yeast cell concentration which are used to gradually reduce the corresponding output of positive fuzzy rules referring to the current point of time in the process. The results show that the incorporation of negative rules can be used to achieve a more stable control performance than what is obtained when only positive rules are used. Furthermore, the method has the potential to specifically reduce overshooting and to achieve smaller control errors. This is emphasized by an average improvement of 11.7% in

overshooting, a 62.8% reduction of RMSE, and a 90.8% decrease in the absolute final control error, which was achieved by the proposed P/N-fuzzy controller. It is shown that fuzzy inference systems applied to complex biologically based systems can be improved by the incorporation of negative experience into the decision-making process. Warnings and prohibitions can be transformed into specific control actions to modify the controller behavior where it is required. The results are in accordance with the findings of (Kiendl 1997) and (Branson and Lilly 2001; Lilly 2007). They state that the inclusion of negative experience can significantly improve the quality of the control performance.

However, there is further potential for performance optimization as the input and output fuzzy sets of the controller were parameterized in a uniform way. This could be achieved by fine-tuning the parameter configuration of the fuzzy sets. A data-driven approach for automatically updating and fine-tuning the premise and consequent fuzzy set parameters (e.g. through the use of evolutionary computing) should therefore be investigated. Beyond this, there is another topic that should be examined in future work, which is the treatment of the cognitive uncertainty that emerges from the ambiguity or vagueness inherent in natural language. Based on the thesis that words mean different things to different people the classical fuzzy logic systems, also denoted as type-1 fuzzy logic systems, were extended to the concept of type-2 fuzzy logic systems by (Karnik and Mendel 1998; Karnik and Mendel 1998; Karnik, Mendel et al. 1999; Liang and Mendel 2000; Karnik and Mendel 2001; Karnik and Mendel 2001; Mendel 2001) for practical use within an efficient computational framework. In a classical fuzzy system uncertainties about the meaning of linguistic expressions are defined via precise membership functions one believes to capture the uncertainty of the words. However, by defining those membership functions the uncertainty about the meaning of the words completely disappears due to the preciseness of the membership function. In a type-2 fuzzy system this kind of uncertainty is modeled by expanding the boundaries of type-1 membership functions to the left and to the right. Consequently, a type-2 membership function is defined by an upper membership function (UMF) and a lower membership function (LMF) enclosing the so-called footprint of uncertainty (FOU). The FOU itself can be modeled by any kind of membership function. This extends the classical two-dimensional representation to a



three-dimensional form allowing the uncertainty linked to computing with words to be handled. Figure 15 shows the concept of a type-2 Gaussian-shaped fuzzy set.



**Figure 15:** Illustration of the concept of a Gaussian type-2 fuzzy set  $\tilde{A}$ . The grey region is the footprint of uncertainty (FOU) defined by the upper membership function (UMF) and the lower membership function (LMF). The third dimension is illustrated by the vertical slice through the FOU and is defined by a Gaussian membership function  $\mu_{\tilde{A}}(x')$ , as well. In consequence a three-dimensional fuzzy set is created, which is illustrated in the right-hand side of the figure.

By incorporating uncertainty directly into the design of the fuzzy sets, new doors in the design of fuzzy logic based control systems are opened. In particular their stability and robustness (Biglarbegian, Melek et al. 2011; Mendel, Hagrass et al. 2014) make the concept very attractive for a broad field of control applications, classification, and pattern recognition (Dereli, Baykasoglu et al. 2011; Melin and Castillo 2013; Castillo and Melin 2014).

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