PREDICTION OF LACTIC ACID CONCENTRATION USING ARTIFICIAL NEURAL NETWORK

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A thesis submitted in fulfilment of the
requirements for the award of the degree of
Master of Engineering (Bioprocess)

Faculty of Chemical Engineering
Universiti Teknologi Malaysia

April 2012

To my beloved mother and father

ACKNOWLEDGEMENT

“In the name of Allah (God) Most Gracious Most Merciful”

I seek blessing from Allah, praise to Him the Almighty for His guidance throughout this work. In completing this thesis, I have been indebted to many particular persons for their assistance, guidance and patience for me to fully understand and bring out the best result for my thesis. Primarily, I would like to express my deepest gratitude towards Dr. Roslina Rashid, for being there as an understanding supervisor and her patience during the period of my study. Her guidance, critics and encouragement also never to fail reminds me for what is importance are things that will always be there for me to cherished and use them as my future guidelines.

Furthermore, my whole life gratefulness for my parents, Almarhum Haji Mohamed Esivan and Hajah Seri Ngatin Shamsuri for their never ending prays and support. In addition, my appreciation towards my brothers and sisters that constantly being there for me and had given their supports regardless the situation. Thanks to my postgraduates colleagues that help me in understanding the process throughout this work not to mention a lot of encouragement for me to finish this project. May Allah will bless all your kindness. Last but not the least, many thanks towards my dearest friends, Amir Haziq and friends of their willingness to help me to reach the final line to complete this journey.

ABSTRACT

This study investigates the application of artificial neural network in model development for lactic acid production. The current measurement of lactic acid concentrations is conducted offline, resulting in time delay in obtaining the results, not to mention that current analysis method is expensive and in need of specially trained personnel. In view of this, two model of artificial neural network; multilayer perceptron (MLP) and radial basis function (RBF) network, have been employed. For the development of MLP model, normalization method, the size of input layer, size of hidden layer and activation function have been varied. Effects of input combinations on the MLP performance have also been investigated. For RBF model development, effects of the tolerance (MSE), radius (σ) value, the number of input variables and input combinations on the RBF performance have been investigated. The results show that the optimum structure of MLP has four input variables (biomass concentration, glucose concentration, temperature and reaction time) and a transfer function of log sigmoid in the hidden layer and linear in the output layer. This model is capable of producing the error index (*EI*) test of 7.26% and R-value test of 0.9909 with seven nodes in the hidden layer. Also, the RBF model was able to obtain *EI* test of 6.48% and R-value of 0.9926 with a model of three input variables (biomass concentration, glucose concentration and reaction time) and a radius (σ) equal to 1.5. The optimum structure of the RBF model was 3-7-1. Both models exhibit comparable and good generalization ability. However, the RBF model out-performed the MLP model with regard to its generalization ability and reproducibility but overall both models have displayed satisfying ability in estimation of lactic acid concentration for the identified process.

ABSTRAK

Penyelidikan ini mengkaji aplikasi rangkaian neural buatan untuk digunakan dalam pembangunan model pengeluaran asid laktik. Ketika ini, proses analisis pengiraan untuk mendapatkan kepekatan asid laktik selalunya dilakukan di luar talian dan ini menyebabkan masa yang banyak terbuang, serta kaedah analisis yang mahal dan memerlukan kakitangan yang terlatih untuk mengendalikan alatan itu. Maka dengan itu, dua model neural buatan, rangkaian peseptron berbilang-lapis (MLP) dan fungsi asas jejarian (RBF); telah digunakan dalam pembangunan ini. Dalam pembangunan MLP, kaedah normalisasi yang berbeza, saiz lapisan input, saiz lapisan tersembunyi dan fungsi pengaktifan telah dikaji. Kesan kombinasi input berlainan ke atas prestasi model MLP juga dikaji. Bagi pembangunan model RBF, kesan nilai MSE, nilai radius (σ), bilangan input dan kombinasi input juga turut dikaji. Keputusan kajian menunjukkan model MLP yang optimum ialah model dengan struktur empat input (kepekatan biojisim, kepekatan glukosa, suhu dan masa reaksi) dan penggunaan fungsi pengaktifan *log sigmoid* dan *linear* pada lapisan tersembunyi dan lapisan output. Model ini berkebolehan untuk mencapai nilai indek ralat (*EI*) sebanyak 7.26% dan nilai-R sebanyak 0.9909 dengan tujuh neuron di dalam lapisan tersembunyi. Di samping itu, model RBF yang mempunyai struktur tiga input (kepekatan biojisim, kepekatan glukosa dan masa reaksi) dan nilai radius (σ) bersamaan dengan 1.5 memungkinkan model itu untuk mencapai nilai indek ralat sebanyak 6.48% dan nilai-R sebanyak 0.9926. Struktur yang optimum untuk model RBF ialah 3-7-1. Oleh sebab itu, kajian mendapati kedua-dua model mempunyai keupayaan penyeluruhan yang bagus. Walaubagaimanapun, kajian juga mendapati model RBF lebih sesuai digunakan kerana keupayaannya yang lebih baik dari model MLP dan juga dari segi kadar keupayaannya yang tinggi untuk mendapatkan nilai anggaran kepekatan asid laktik untuk proses yang dikenal pasti.

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N_p	-	number of pattern
$\hat{y}$	-	estimated value of lactic acid concentration
Δw	-	weight and bias update vector
a_{kl}	-	actual (calculated output) at the output neuron *l* for the input *k*
Al	-	alginate
ANN	-	artificial Neural Network
ATP	-	adenosine triphosphate
b	-	bias
B	-	normalized biomass concentration
BP	-	back-propagation training algorithm
C	-	carbon
Ca	-	calcium
cfu/L	-	colony forming unit per liter
c_i	-	center of RBF
C_p	-	specific heat (J/mole/ºC)
d_{kl}	-	desired (target) output neuron *l* for the input *k*
e	-	residual between the estimated and observed value
e	-	calculated MSE
EI	-	error index
FFNN	-	feedforward neural network
g/L	-	gram per liter
Gl	-	normalized glucose concentration
H	-	hydrogen
HPLC	-	high performance liquid chromatography
I	-	identity matrix
J	-	Jacobian matrix

K	-	temperature
L	-	liter
Lai	-	normalized lactic acid concentration
LM	-	Levenberg-Marquardt training algorithm
mL	-	milliliter
MLP	-	Multilayer Perceptron
mm	-	millimeter
MSE	-	mean square error
n	-	total number of neurons in the output layer of network
Na	-	sodium / natrium
n_h	-	number of hidden nodes of RBF
Np	-	total number of training patterns
O	-	oxygen
OD	-	optical density
OLS	-	Orthogonal Least Square training algorithm
PCA	-	principle component analysis
pH	-	pH value
PLS	-	Partial least square
RBF	-	Radial Basis Function
rpm	-	rotation per minute
RSM	-	response surface methodology
R-value	-	coefficient of determination for regression analysis
t	-	reaction time
w	-	weights and biases of the network
x	-	variable x
$x\ max$	-	maximum value of variable x
$x\ min$	-	minimum value of variable x
$x\ norm$	-	normalized value of variable x
y	-	observed value of lactic acid concentration

Greek letters

σ	-	radius or width parameter of RBF
μ	-	adaptive learning rate
β_j	-	bias parameter for the *j*th output node of RBF
$\|\ast\|$	-	Euclidean norm
$\emptyset_i$	-	output of the *i*th hidden node of RBF

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CHAPTER I

INTRODUCTION

1.1 Background of Study

Production of lactic acid is conducted either by a chemical synthesis process or by carbohydrate fermentation. The chemical process is done commercially based on lactonitrile (Marques *et al.*, 2008, Narayanan *et al.*, 2004,). The chemical synthesis is performed by the hydrolysis of lactonitrile by strong acids. Base-catalyzed degradation of sugars, oxidation of propylene glycol, reaction of acetaldehyde, carbon monoxide and water at elevated temperature and pressure, nitric acid oxidation of propylene and hydrolysis of chloropropionic acid are also alternative routes to the chemical synthesis of the lactic acid (Mussatto *et al.*, 2008). Unfortunately, this process depends on by-products from other industries and it produces a mixture of L (+) and D (-) lactic acid isomers (Nandasana and Kumar, 2008, Pal *et al.*, 2009).

The other route to produce lactic acid is through fermentation. Fermentation of lactic acid is a carbohydrate fermentation whereby sugar is converted by the microorganism known as lactic acid bacteria (LAB). The typical sugar used in the fermentation is glucose. The most common LAB used for lactic acid fermentation is from *Lactobacillus* strains such as *Lactobacillus amylophilus, Lactobacillus bulgaricus, Lactobacillus delbreuckii, Lactobacillus leichmanii and Lactobacillus plantarum* and others from fungal strains such as *Aspergillus niger* and from *Rhizopus* species (Pal *et al*., 2009). Production of lactic acid from the carbohydrate fermentation is preferred because it is less expensive compared to the chemical synthesis. This process has the advantage of selectively producing either of the single lactic acid enantiomers.

Fermentation of lactic acid can be carried out either by free cell fermentation or by immobilization. Immobilization involves entrapping the lactic acid bacteria (LAB) in beads under mildly confined conditions. These LABs are separated from their environment by a protective matrix, film or bead ensuring the extension of shelf life and also preventing exposure to the surround environment, in other words, the beads provide protection coats for these LABs.

In fermentation of lactic acid, the desired variable is the lactic acid concentration that shows how efficient the fermentation is. The key parameters of the fermentation are the substrate concentration, pH (Wee *et al*., 2004; Ye *et al*., 1996; Altaf *et al*., 2006; Huang *et al*., 2005; Marták *et al*., 2003), temperature (Huang *et al*., 2005; Idris and Suzana 2006) and the biomass concentration.

Instead of undergoing tedious analytical method in measuring of lactic acid and biomass concentrations, which results in delay of information, there is a need for a model to estimate and predict the concentration of lactic acid and biomass. Software sensors make use of easily available process knowledge, including a secondary process variables or a process model, to estimate primary variables of interest (Chatterjee and Saraf, 2004; Araúzo-Bravo *et al*., 2004; Facco *et al*., 2009). Software sensors are typically developed or designed from mathematical models based on growth kinetics or statistical analysis [such as multi-linear regression (MLR) or principal component analysis (PCA)], a 'black box' neural networks or combinations of all of these (Kiviharju *et al*., 2008).

Software sensors work by cause and effect; hence the inherent biologic relation between measured and unmeasured states can significantly affect the predictive accuracy (Chen, 2006). Software sensors are also known as virtual sensors (Dai *et al*., 2006); which is a software that processes several measurements together (Gonzaga *et al*., 2009) by using the history of the available data (Kadlec *et al*., 2009). In the process, each variable, also known as a signal, is interacting with each other, producing the desired responses by the end of the process. These kinds of interactions are used for calculating or to estimate new quantities that cannot otherwise be measured (Gonzaga *et al*., 2009). Some attributes of software sensors are as follows (Fortuna *et al*., 2005):

1. Software sensors recommend a low cost alternative to expensive hardware sensors.
2. Software sensors are able to work in parallel with hardware sensors giving useful information for fault detection tasks.
3. The sensors can easily be implemented on existing hardware (e.g. microcontrollers) and can easily be returned when system parameters change.
4. The sensors overcome the time delays introduced by slow hardware sensors (e.g. gas chromatography), allowing real time of data estimation thus improving the performance of the control algorithms.

Software sensors have been used in many different processes. Gonzaga *et al*. (2008) constructed a software sensor to provide a reliable real time of polyethylene terephthalate (PET) viscosity to be used in controlling polymerization process. Lee *et al*. (2008) used soft sensors in wastewater treatment plants (WWTPs) to control variables in order to monitor the plants' status and to support the operation of local wastewater systems.

In wine stills, software sensors are applied to estimate the distillate ethanol concentration on-line, thus enabling predefined ethanol profiles to be tracked throughout a distillation run (Osorio *et al*., 2008). Many studies have been conducted regarding the applications of software sensor to enhance, improve, optimize, monitor, predict, classify, and control (Kadlec *et al*., 2009) certain process. Therefore, the use of software sensors is a reasonable approach in order to make good estimations and predictions of product concentration in lactic acid production. Accordingly, it is practical to build a software sensor that is applicable to different conditions of the fermentation including the unseen data. Furthermore, software sensors that are well trained are capable of giving estimations for unseen data as long as the variables have been covered during training phase.

1.2 Problem Statement

Fermentation is a nonlinear, complex process. The complexity of the process includes the interrelation between each of variables. This process is also known as nonlinear process. Thus, supervision of the fermentation process must maintain certain variables within strict limits, since biological systems are highly sensitive to abnormal changes in operation conditions (Araúzo-Bravo *et al*., 2004). Meanwhile, the analysis of the lactic acid concentration in the fermentation is conducted by using high pressure liquid chromatography (HPLC) (Hábová *et al*., 2004; Marták *et al*., 2003; Resa *et al*., 2007; Shibata *et al*., 2007; Gao *et al*., 2009; Ding and Tan, 2006). These analysis methods are time consuming, tedious, and the apparatus is expensive (Rivier, 2000).

Traditionally, the optimizations of biology processes are based on mathematical models described by a set of differential equations derived from mass balances. There are models of lactic acid fermentation based on the mathematical models (Nandasana and Kumar, 2008; Schepers *et al*., 2000), yet due to the physiological complexity of the microorganisms, these models lack robustness and accuracy due to the physiological complexity of the microorganisms (Gueguim-Kana *et al*. 2007). Fermentation processes are difficult and complex, hence mathematical models find it difficult to represent the interrelations in the process itself. Moreover, the mathematical models are built with such complexes that they produce difficulties in estimation.

Most of the biology processes involve a nonlinear activity and this is the limitation to the classical modeling technique to describe the evolution of microorganisms (Esnoz *et al*., 2006). Considering these problems, using the artificial intelligence approach in estimating lactic acid concentration seems reasonable, since this approach requires less time for development and it has the capability of simulating nonlinear processes. Thus, artificial intelligence tools such as neural networks provide a new and better approach (Gueguim-Kana *et al*., 2007).

Experimental work for lactic acid production using cheap substrates can be found widely in literature. However, the modeling process using artificial intelligence (AI) has not been extensively explored. Nandasana and Kumar (2008) had developed mathematical modeling for lactic acid production from cheap substrate. The model was developed for the fermentation of cane sugar molasses for lactic acid production by *Enterococcus faecalis* RKY1. The model takes into account the substrate limitation and inhibition, growth- and non-growth associated lactic acid production and cell death rate and highly dependent on pH value.

Schepers *et al.* (2000) have developed a simple descriptive neural network model for *Lactobacillus helveticus* growth in pH controlled batch cultures, but the developed model was lacking in robustness and generalization. Acuña *et al*. (1998) have also performed work on the modeling of lactic acid production. They have developed two models, static modeling and dynamic modeling, which estimate the cell concentration of lactic acid fermentation. Though it was found out that, this model is able to give good estimates, but it was specifically modeled to estimate the cell number of fermentation.

1.3 Objective

Lactic acid is one of the foremost raw materials that have applications in many end-products, especially in foods. Therefore, an easy and rapid method of measurement should be employed as a way of maneuvering a productive fermentation. The general aim of this study can therefore be phrased as the desire to develop data based models to estimate the lactic acid concentration in lactic acid production as one of the analytical method in fermentation.

The objectives of this research are as follows:

1. To develop software sensor model to predict the lactic acid concentration from available process measurements (glucose concentration, biomass concentration, initial pH, temperature and reaction time) using Artificial Neural Network.
2. To evaluate a suitable scaling or normalization method for the data under consideration.
3. To design an optimum structure or model of the Multilayer Perceptron (MLP) and Radial Basis Function (RBF).
4. To compare both Multilayer Perceptron and Radial Basis Function neural network models in terms of their predictive performances on lactic acid concentrations.

Although this study's approach is similar to Acuña *et al*. (1998), the system employed is different. Acuña *et al*. (1998) studied the growth of *Lactobacillus* bacteria, while in this study; the focus is on the formation product by *Lactobacillus delbrueckii* in an immobilization system. The developed models are of a great importance due to its capability to predict lactic acid concentration under varying operating conditions.

1.4 Scope of Study

In order to achieve those objectives, simulation work was conducted based on the following limitations.

i. This study is limited to the fermentation of lactic acid with pineapple waste as the substrate. In this work, data were obtained from work done by Idris and Suzana (2006).

ii. In the first stage of software sensor development, all raw data used underwent pre-processing. Three different normalization methods were used in order to scale the data to the same units and range.

iii. Multilayer Perceptron (MLP) models were developed under varying conditions. The learning algorithm used in this study was Levenberg Marquardt (LM) training algorithm. The MLP structures were optimized in regards to the performance goal, input number, input variables, the size of hidden nodes and the combinations of transfer function.

iv. Then, Radial Basis Function (RBF) based models were developed and optimized. RBF model was considered because of its performance, which is fast and has linear learning. The input layers were varied in terms of input numbers and the combination of variables used in input layer. Other features being varied were the radius and MSE value.

v. The predictive performances of each model were evaluated based on mean square error (MSE), error index (*EI*), regression analysis, graphical plot and residual plot.

vi. Finally, the performances of the best predictive ability between MLP and RBF structures were compared, and the one that had the better generalization and predictive ability was employed as the software sensor in the lactic acid production.

1.5 Thesis Outline

The outline of the thesis is arranged as follows. The literature review is presented in the Chapter 2 and it includes the review of lactic acid production and software sensors. This chapter also includes reviews on current applications of Multilayer Perceptron and Radial Basis Function, and the chapter ends by discussing the factors that affect the performances of a neural network models.

In Chapter 3, an explanation and overview of the fermentation process is presented extensively. This is followed by step-by-step development of the artificial neural network model covering both of MLP and RBF. The chapter gives a detailed, stage-by-stage description of each model development, including data normalization, input variables selection, training and testing.

The findings of the MLP and RBF model are discussed in Chapter 4. The effects of the normalization method, input number on MLP and RBF performances are presented. In this chapter, the effects of the normalization method, hidden nodes, model structure size and transfer function of MLP performances are discussed. Meanwhile for RBF, findings of the effects of tolerance goal (MSE), radius and goal value are also included in this chapter. These two models are compared at the end of the chapter. Lastly, in Chapter 5, general conclusions are drawn from this research and some recommendations for future work are suggested.

REFERENCES

Acuña, G., Latrille, E., Béal, C., and Corrieu, G. (1998). Static and Dynamic Neural Network Models for Estimating Biomass Concentration during Thermophilic Lactic Acid Bacteria Batch Cultures. *Journal of Fermentation and Bioengineering*. 85(6): 615 – 622.

Akhlagi, Y. and Kompany-Zareh, M. (2005). Comparing Radial Basis Function and Feed-Forward Neural Networks assisted by Linear Discriminant or Principal Component Analysis for Simultaneous Spectrophotometric Quantification of Mercury and Copper. *Analytica Chimica Acta*. 537: 331-338.

Akratos, C. S., Papaspyros, J. N. E., and Tsihrintzis, V. A. (2008). An Artificial Neural Network Model and Design Properties for BOD and COD Removal Prediction in Horizontal Subsurface Flow Constructed Wetlands. *Chemical Engineering Journal*. 143: 96-110.

Albert, S., Hiden, H., Conlin, A., Martin, E.B., Montague, G. A., and Morris, A. J. (2001). Inferential Quality Assessment in Breakfast Cereal Production. *Journal of Food Engineering.* 50: 157-166.

Aleksendrić, D., Barton, D.C. and Vasić, B. (2010). Prediction of Brake Friction Materials Recovery Performance Using Artificial Neural Networks. *Tribology International*. 43: 2092-2099.

Altaf, M., Naveena, B. J. and Reddy, G. (2005). Screening of Inexpensive Nitrogen Sources for Production of L (+) Lactic Acid from Starch by Amyllytic *Lactobacillus amylophilus* GV6 in Single Step Fermentation. *Food technol. Biotechnol.* 43(3): 235-239.

Altaf, M., Naveena, B. J., and Reddy, G. (2007). Use of Inexpensive Nitrogen Sources and Starch for L (+) Lactic Acid Production in Anaerobic Submerged Fermentation. *Bioresource Technology*. 98: 498-503.

Altaf, M., Naveena,, B. J., Venkateshwar, M., Kumar, E. V., and Reddy, G. (2006). Single Step Fermentation of Starch to L(+) Lactic Acid by *Lactobacillus amylophilus* GV6 in SSF Using Inexpensive Nitrogen Sources to Replace Peptone and Yeast Extract – Optimization by RSM. *Process Biochemistry*. 41: 465-472.

Amanian, K., Salasshoor, K., Jafari, M.F., and Mosallaei, M. (2007). Soft Sensor Based on Dynamic Principal Component Analysis and Radial Basis Function Neural Network for Distillation Column. *Proceedings of the World Congress on Engineering and Computer Science 2007 (WCECS 2007)*. October 24-26, 2007, San Francisco, USA.

Araúzo-Bravo, M.J., Cano-Izquierdo, J.M., Gómez-Sánchez, E., López-Nieto, M.J., Dimitriadis, Y.A., and López-Coronado, J. (2004). Automatization of a Penicilin Production Process with Soft Sensors and an Adaptive Controller Based on Neuro Fuzzy Systems. *Control Engineering Practice*. 12: 1073-1090.

Argyri, A. A., Panagou, E. Z., Tarantilis, P. A., Polysiou, M., and Nychas, G. –J.E. (2010). Rapid Qualitative and Quantitative Detection of Beef Fillets spoilage based on Fourier transform infrared spectroscopy data and Artificial Neural Networks. *Sensors and Actuators B: Chemical*. 145: 146-154.

Ascencio, R. R. L., Reynaga, F., Herrera, E., and Gschaedler, A. (2001). Artificial Neural Network as a Biomass Virtual Sensor for a Batch Process. *Proceedings of the 2001 IEEE International Symposium on Intelligent Control*. September 5-7, 2001, Mexico City, Mexico.

Ayala H., L. F., Alp, D., and Al-Timimiy, M. (2009). Intelligent Design and Selection of Natural Gas Two-Phase Separators. *Journal of Natural Gas Science and Engineering*. 1: 84-94.

Babaoglu, I., Baykan, O. K., Aygul, N., Ozdemir, K. and Bayrak, M. (2009). Assessment of Exercise Stress Testing with Artificial Neural Network in Determining Coronary Artery Disease and Predicting Lesion Localization. *Expert Systems with Applications*. 36: 2526-2566.

Bar, N., Bandyopadhyay, T. K., Biswas, M. N., and Das, S. K. (2010). Prediction of Pressure Drop Using Artificial Neural Network for Non-Newtonian Liquid Flow Through Piping Components. *Journal of Petroleum Science and Engineering*. 71: 187-194.

Baş, D., and Boyacı,, İ. H. (2007). Modeling and Optimization II: Comparison of Estimation Capabilities of Response Surface Methodology with Artificial Neural Networks in a Biochemical Reaction. *Journal of Food Engineering*. 78: 846-854.

Basheer, I. A., and Hajmeer, M. (2000). Artificial Neural Networks: Fundamentals, Computing, Design, and Application. *Journal of Microbiological Methods*. 43: 3-31.

Bhattacharya, N., Tudu, B., Jana. A., Ghosh, D., Bandhopadhyaya, R., and Bhuyan, M. (2008). Preemptive Identification of Optimum Fermentation time Black Tea Using Electronic Nose. *Sensors and Actuators B.* 131:110-116.

Bogaerts, P., and Wouwer, A. V. (2004). Parameter Identification for State Estimation – Application to Bioprocess Software Sensors. *Chemical Engineering Science*. 59: 2465-2476.

Cabrera, A. C., and Prieto, J. M. (2010). Applications of Artificial Neural Networks to the Prediction of the Antioxidant Activity of Essentials Oils in Two Experimental *In-vitro* Models. *Food Chemistry*. 118: 141 – 146.

Chakrabarti, N. C., Sahasrabudine, R., and Bhuyarkar, T. (2006). Virtual Sensors for Advanced Pharmaceutical Process Control. *Process Analytical*. http://www.pharmamanufacturing.com/articles/2006/063.html

Charaniya, S., Hu, W. S., and Karypis, G. (2008). Mining Bioprocess Data: Opportunities and Challenges. *Trends in Biotechnology*. 26(12): 690 – 699.

Charlier, C., Cretenet, M., Even, S., and Le Loir, Y. (2009). Interactions Between *Staphylococcus aureus* and Lactic Acid Bacteria: An Old Story with New Perspectives. *International Journal of Food Microbiology*. 131: 30-39.

Chatterjee, T., and Saraf, D.N. (2004). On-Line Estimation of Product for Crude Distillation Units. *Journal of Process Control*. 14: 61 – 77.

Chegini, G. R., Khazaei, J., Ghobadian, B., and Goudarzi, A. M. Prediction of Process and Product Parameters in an Orange Juice Spray Dryer Using Artificial Neural Networks. *Journal of Food Engineering*. 84: 534-543.

Chen, L. Z. (2006). On-line Softsensor Development for Biomass Measurement using Dynamics Neural Network. *Modeling and Optimization of Biotechnology Processes*. Studies in Computational Intelligence (SCI). 15: 41-56.

Chen, X., Gao, F., Chen, G. (2004). A Soft-Sensor Development for Melt-Flow-Length Measurement During Injection Mold Filling. *Materials Science and Engineering.* 384: 245-254.

Cheroutre-Vialette, M., and Lebert, A. (2002). Application of Recurrent neural Network to Predict Bacterial Growth in Dynamic Conditions. *International Journal of Food Microbiology*. 73: 107-118.

Choi, D. J., and Park, H. (2001). A Hybrid Artificial Neural Network as a Software Sensor for Optimal Control of a Wastewater Treatment Process. *Wat. Res.* 35(16): 3959-3967.

Coleman, M. C., Buck, K. K. S., and Block, D. E. (2003). An Integrated Approach to Optimization of *Escherichia Coli* Fermentations Using Historical Data. *Biotechnology and Bioengineering*. 84(3): 274–285. doi: 10.1002/bit.10719.

Craninx, M., Fievez, V., Vlaemick, B., De Baets, B. (2008). Artificial Neural Network Models of Rumen Fermentation Pattern in dairy Cattle. *Computers and Electronics in Agriculture*. 60: 226-238.

Dacosta, P., Kordich, C., Williams, D., and Gomm, J. B. (1997). Estimation of Inaccessible Fermentation States with Variable Inoculum Sizes. *Artificial Intelligence in Engineering*. 11: 383-392.

Dai, Z., Wang, W., Ding, Y., and Sun, Z. (2006). “Assumed Inherent Sensor” Inversion Based ANN Dynamic Soft-Sensing Method and Its Application in Erythromycin Fermentation Process. *Computers and Chemical Engineering*. 30: 1203-1225.

Dam, M., and Saraf, D.N. (2006). Design of Neural Networks using Genetic Algorithm for On-Line Property Estimation of Crude Fractionator Products. *Computers and Chemical Engineering*. 30: 722-729.

Datta, R., and Henry, M. (2006). Lactic Acid: Recent Advances in Products, Processes and Technologies – A Review. *Journal of Chemical Technology and Biotechnology*. 81: 1119-1129.

Dias, L. G., Veloso, A. C. A., Correia, D. M., Rocha, O., Torres, D., Roscha, I., Rodrigues, L. R., and Peres, A. M. (2009). UV Spectrophotometry Method for the Monitoring of Galacto-Oligosaccharides Production. *Food Chemistry*. 113: 246-252.

Ding, S., and Tan, T. (2006). L–Lactic Acid Production by *Lactobacillus casei* Fermentation Using Different Fed-Batch Feeding Strategies. *Process Biochemistry*. 41: 1451-1454.

Dochain, D. (2003). State and Parameter Estimation in Chemical and Biochemical Processes: A Tutorial. *Journal of Process Control*. 13: 801-818.

Du, D., Wu, C., Luo, X., and Zuo, X. (2006). Delay Time Identification and Dynamic Characteristics Study on ANN Soft Sensor. *Proceedings of the Sixth International Conference on Intelligent Systems Design and Applications (ISDA '06)*.

Du, H., Wang, J., Zhang, X., Yao., and Hu, Z. (2008). Prediction of Retention Times of Peptides in RPLC by Using Radial Basis Function Neural Networks and Projection Pursuit Regression. *Chemometrics and Intelligent Laboratory Systems*. 92: 92-99.

Dufour, P., Bhartiya, S., Dhurjati, P. S., and Doyle III, F. J. D. (2005). Neural Network Based Software Sensor: Training Set Design and Application to Pulp Digester. *Control Engineering Practice*. 13: 135-143.

Dutta, J. R., Dutta, P. K., and Banerjee, R. (2004). Optimization of Culture Parameters for Extracellular Protease Production From a Newly Isolated *Pseudomonas* sp. Using Response Surface and Artificial Neural Network Models. *Process Biochemistry.* 39: 2193-2198.

Esnoz, A., Periago, P.M., Conesa, R., and Palop, A. (2006). Application of Artificial Neural Networks to Describe the Combined Effect of pH and NaCl on the Heat Resistance of *Bacillus stearothermophilus*. *International Journal of Food Microbiology*. 106: 153-158.

Facco, P., Doplicher, F., Bezzo, F., Barolo, M. (2009). Moving Average PLS Soft Sensor for Online Product Quality Estimation In and Industrial Batch Polymerization Process.

Fadda, S., López, C., and Vignolo, G. (2010). Role of Lactic Acid Bacteria during Meat Conditioning and Fermentation: Peptides Generated as Sensorial and Hydienic Biomarkers. *Meat Science*. 86: 66-79.

Fan, L., and Xu, Y. (2007). A PCA-Combined Neural Network Software Sensor for SBR Processes. In D. Liu et al. (Eds.). *ISNN 2007, Part II, LNCS 4492*. (pp. 1042-1047). Berlin Heidelberg: Springer-Verlag.

Fan, Y., Takayama, K., Hattori, Y., and Maitani, Y. (2004). Formulation Optimization of Paclitaxel Carried by PEGylated Emulsions Based on Artificial Neural Network.

Fernández-Navarro, F., Hervás-Martínez, C., Cruz-Ramírez, M., Gutiérrez, P. A., and Valero, A. (2011). Evolutionary q-Gaussian Radial Basis Function Neural Network to Determine the Microbial Growth / No Growth Interface of *Staphylococcus aureus*. *Applied Soft Computing*. 11: 3012-3020.

Fitzpatrick, J. J., Murphy, C., Mota, F. M., and Pauli, T. (2003). Impurity and Cost Considerations for Nutrient Supplementation of Whey Permeate Fermentations to Produce Lactic Acid for Biodegradable Plastics. *International Dairy Journal*. 13: 575-580.

Flood, I. (2008). Towards the Next Generation of Artificial Neural Network for Civil Engineering. *Advanced Engineering Informatics*. 22: 4-14.

Fogelman, K.D., Wikfors, E. E., and Chen, R. (2009). Time Delay for Sample Collection in Chromatography Systems. http://www.faqs.org/patents/app/20090050568.

Fortuna, L., Graziani, S., and Xibilia, M. G. (2005). Soft Sensors for Product Quality Monitoring in Debutanizer Distillation Columns. *Control Engineering Practice*. 13 : 499-508.

Gago, J., Landín, M. and Gallego, P.P. (2010a). Artificial Neural Networks Modeling the *In Vitro* Rhizogenesis and Acclimatization of *Vitis vinifera* L. *Journal of Plant Physiology*. 167: 1226-1231.

Gago, J., Martínez-Núñez, L., Landín, M., and Gallego, P. P. (2010b). Artificial Neural Networks as an Alternative to the Traditionally Statistical Methodology in Plant Research. *Journal of Plant Physiology*. 167: 23-27.

Gao, M. T., Shimamura, T., Ishida, N., and Takahashi, H. (2009). Application of Metabolically Engineered *Saccharomyces cerevisae* to Extractive Lactic Acid Fermentation. *Biochemical Engineering Journal*. 44: 251-255.

García-Gimeno, R. M., Hervás-Martínez, C., Rodríguez-Pérez, R., and Zurera-Cosano, G. (2005). Modelling the Growth of *Leuconostoc mesenteroids* by Artificial Neural Network. *International Journal of Food Microbiology*. 105: 317-332.

Garg, T., Ramam, M., Pasricha, J. S., and Verma, K. K. (2002). Long Term Topical Application of Lactic Acid / Lactate Lotion as a Preventive Treatment for

Acne Vulgaris. *Indian Journal of Dermatology, Venereology and Leprology*. 68(3): 137-139.

Garlotta, D. (2001). A Literature Review of Poly(Lactic Acid). *Journal of Polymers and the Environment*. 9(2): 63-83.

Gernaey, K. V., van Loosdrecht, M. C. M., Henze, M., Lind, M., and Jørgensen, B. (2003). Activated Sludge Wastewater Treatment Plant Modelling and Simulation: State of The Art. *Environmental Modelling & Software*. 19: 763-783.

Ghobadian, B., Rahimi, H., Nikbakht, A. M., Najafi, G., and Yusaf, T. F. (2009). Diesel Engine Performance and Exhaust Emission Analysis Using Waste Cooking Biodiesel Fuel with an Artificial Neural Network. *Renewable Energy*. 34: 976-982.

Godini, H. R., Ghadrrdan, M., Omidkhah, M. R., and Madaeni, S. S. (2011). Part II: Prediction of the Dialysis Process Performance using Artificial Neural Network (ANN). *Desalination (2010).* doi:10.1016/j.desal.2010.04.039.

Goñi, S. M., Oddone, S., Segura, J. A., Mascheroni, R. H., and Salvadori, V. O. (2008). Prediction of Foods Freezing and Thawing Times*:* Artificial Neural Networks and Genetic Algorithm Approach. *Journal of Food Engineering.* 84: 164-178.

Gonzaga, J. C. B., Meleiro, L. A. C., Kiang, C., Maciel Filho, R. (2009). ANN-Based Soft-Sensor for Real-time Process Monitoring and Control of an Industrial Polymerization Process. *Computers and Chemical Engineering*. 33: 43 – 49.

González, M. I., Alvarez, S., Riera, F. A., and Alvarrez, R. (2008). Lactic Acid Recovery from Whey Ultrafiltrate Fermentation Broth and Artificial Solutions by Nanofiltration. *Desalination.* 228: 84-96.

Gonzalez-Vara Y R, A., Pinelli, D., Rossi, M., Fajner, D., Magelli, F., and Matteuzzi, D. (1996). Production of L(+) and D(-) Lactic Acid Isomers by *Lactobacillus casei* subsp. *casei* DSM 20011 and *Lactobacillus coryniformis* subsp. *torquens* DSM 20004 in Continuous Fermentation. *Journal of Fermentation and Bioengineering*. 81(6): 548-552.

Gueguim-Kana, E. B., Oloke, J. K., Lateef, A., and Zebaze-Kana, M. G. (2007). Novel Optimal Temperature Profile for Acidification Process of *Lactobacillus bulgaricus* and *Streptococcus thermophilus* in Yoghurt

Fermentation Using Artificial Neural Network and Genetic Algorithm. *Journal of Industrial Microbiology and Biotechnology*. 34: 491-496.

Gupta, B., Revagade, N., and Hilborn, J. (2007). Poly(Lactic Acid) Fiber: An Overview. *Progress in Polymer Science*. 32:455-482.

Gupta, S., Cox, S., and Abu-Gannam, N. (2010). Process Optimization for the Development of a Functional Beverrage Based on Lactic Acid Fermentation of Oats. *Biochemical Engineering Journal.* 52: 199-204.

Hábová, V., Melzoch, K., Rychtera, M., and Sekavová, B. (2004). Electrodialysis as a Useful Technique for Lactic Acid Separation from a Model Solution and a Fermentation Broth. *Desalination*. 163: 361-372.

Hagan, M. T., and Menhaj, M. B. (1994). Training Feedforwards Networks with the Marquardt Algorithm. *IEEE Transactions on Neural Networks*. 5: 989-993.

Hamzaoui, R., Cherigui, M., Guessasma, S., Elkedim, O., and Fenineche, N. (2009). Artificial Neural Network Methodology: Application to Predict Magnetic Properties of Nanocrystalline Alloys. *Materials Science and Engineering B*. 163: 17-21.

Hao, W., Li, X. and Zhang, M. 2008. Application of RBF Neural Network to Temperature Compensation of Gas Sensor. *International Conference on Computer Science and Software Engineering.* IEEE Computer Society. 839-842.

Haykin, S. (1994). Neural Networks – A Comprehensive Foundation. Macmillan College Publishing Company, USA.

Herzog, M. A., Marwala, T., and Heyns, P. S. (2009). Machine and Component Residual Life Estimation through the Application of Neural Networks. *Reliability Engineering and System Safety*. 94: 479-489.

Hirata, M., Gaoo, M. T., Toorisaka, E., Takanashi, H., and Hano, T. (2005). Production of Lactic Acid by Continuous Electrodialysis Fermentation with a Glucose Concentration Controller. *Biochemical Engineering Journal.* 25: 159-163.

Hocalar, A., Türker, M., Karakuzu, C., and Yüzgeç, U. (2011). Comparison of Different Estimation Techniques for Biomass Concentration in Large Scale Yeast Fermentation. *ISA Transactions*. 50: 303-314.

Honda, H., Toyama, Y., Takahashi, H., Nakazeko, T., and Kobayashi, T. (1995). Effective of Lactic Acid Production by Two-Stage Extractive Fermentation. *Journal of Fermentation and Bioengineering.* 79(6): 589-593.

Hong, S. H., Lee, M. W., Lee, D. S., and Park, J. M. (2007). Monitoring of Sequencing Batch Reactor for Nitrogen and Phosphorus Removal Using Neural Networks. *Biochemical Engineering Journal.* 35: 365-370.

Huang, L. P., Jin, B., Lant, P., and Zhou, J. (2005). Simultaneous Sacchariffication and Fermentation of Potato Starch Wastewater to Lactic Acid by *Rhizopus oryzae* and *Rhizopus arrhizus*. *Biochemical Engineering Journal.* 23: 265-276.

Idris, A., and Suzana, W. (2006). Effect of Sodium Alginate Concentration, Bead Diameter, Initial pH and Temperature on Lactic Acid Production from Pineapple Waste using immobilized *Lactobacillus delbrueckii*. *Process Biochemistry*. 41: 1117 – 1123.

Ignova, M., Paul, G.C., Glassey, J., Ward, A.C., Montague, G.A., Thomas, C.R. and Karim, M.N. (1996). Towards Intelligent Process Supervision: Industrial Penicillin Fermentation Case Study. *Computers Chem. Engng*. 20: S545-S550.

Jafar, R., Shahrour, I., and Juran, I. (2010). Applications of Artificial Neural Networks (ANN) to Model the Failure of Urban Water Mains. *Mathematical and Computer Modelling*. 51: 1170-1180.

Jain, P., Rahman, I., and Kulkarni, B. D. (2007). Development of a Soft Sensor for a Batch Distillation Column using Support Vector Regression Techniques. *Trans ICheme, Part A, Chemical Engineering Research and Design*. 85(A2): 283-287.

John, R. P., Anisha, G. S., Nampoothiri, K. M., and Pandey, A. (2009). Direct Lactic Acid Fermentation: Focus on Simultaneous Saccharification and Lactic Acid Production. *Biotechnology Advances*. 27: 145-152.

John, R. P., Nampoothiri, K. M., and Pandey, A. (2006). Solid-State Fermentation for L–Lactic Acid Production From Agwo Wastes using *Lactobacillus delbrueckii*. *Process Biochemistry*. 21: 759-763.

John, R. P., Nampoothiri, K. M., And Pandey, A. (2007a). Fermentative Production of Lactic Acid from Biomass: An Overview on Process Developments and

Future Perspectives. *Applied Microbiology and Biotechnology*. 74(3): 524-534.

John, R. P., Sukumaran, R. K., Nampoothiri, K. M., and Pandey, A. (2007b). Statisical Optimization of Simultaneous Saccharification and L(+)–Lactic Acid Fermentation from Cassava Bagasse Using Mixed Culture of Lactobacilli by Response Surface Methodology. *Biochemical Engineering Journal*. 36: 262-267.

John, R.P., and Nampoothiri, K.M. (2008). Strain Improvement of *Lactobacillus delbrueckii* using Nitrous Acid Mutation for L-Lactic Acid Production. *World Journal of Microbiology and Biotechnology*. 24(12): 3105-3109.

Joo, D. S., Choi, D. J. and Park, H. (2000). The effects of Data Preprocessing in the Determination of Coagulant Dosing Rate. *Wat. Res.* 34(13): 3295-3302.

Jorjani, E., Asadollahi Poorali, H., Sam, A., Chehreh Chelgani, S., Mesroghli, S., and Shayestehfar, M. R. (2009). Prediction of Coal Response to Froth Flotation based on Coal Analysis using Regression and Artificial Neural Network. *Minerals Engineering*. 22: 970-976.

Kadlec, P., Gabrys, B., and Strandt, S. (2009). Data-Driven Soft Sensors in The Process Industry. *Computers and Chemical Engineering*. 33: 795-814.

Kamoshita, Y., Ohashi, R., and Suzuki, T. (1998). Improvement of Filtration Performance of Stirred Ceramic Membrane Reactor and Its Application to Rapid Fermentation of Lactic Acid by Debse Cell Culture of *Lactococcus lactis*. *Journal of Fermentation and Bioengineering.* 85(4): 422-427.

Kang, S. G., Kenyon, R. G. W., Ward, A. C., and Lee, K. J. (1998). Analysis of Differentiation State in *Streptomyces albidoflavus* SMF301 by the Combination of Pyrolysis Mass Spectrometry and Neural Networks. *Journal of Biotechnology*. 62: 1-10.

Karim, M. N., Yoshida, T., Rivera, S. L., Saucedo, V. M., Eikens, B., and Oh, G. S. (1997). Global and Local Neural Network Models in Biotechnology: Application to Different Cultivation Processes. *Journal of Fermentation and Bioengineering.* 83(1): 1-11.

Kashaninejad, M., Dehghani, A. A., and Kashiri, M. (2009). Modeling of Wheat Soaking Using Two Artificial Neural Networks (MLP and RBF). *Journal of Food Engineering*. 91: 602-607.

Kavaklioglu, K., Ceylan, H., Ozturk, H. K., and Canyurt, O. E. (2009). Modeling and Prediction of Turkey's Electricity Consumption using Artificial Neural Networks. *Energy Conversion and Management*. 50: 2719-2727.

Khashei, M., and Bijari, M. (2010). An Artificial Neural Network (*p,d,q*) Model for Timeseries Forecasting. *Expert Systems with Applications*. 37: 479-489.

Khayet, M., Cojocaru, C., and Essalhi, M. (2011). Artificial Neural Network Modeling and Response Surface Methodology of Desalination by Reverse Osmosis. *Journal of Membrane Science*. 368: 202-214.

Kiani, M. D. K., Ghobadian, B., Tavakoli, T., Nikbakht, A. M., and Najafi, G. (2010). Application of Artificial Neural Networks for the Prediction of Performance and Exhaust Emissions in SI Engine Using Ethanol-Gasoline Blends. *Energy*. 35: 65-69.

Kim, B. and Kim, S. (2009) Modeling of a Hemispherical Inductively Coupled Plasma using Neural Network. *Current Applied Physics*. 9: 13-17.

Kiviharju, K., Salonen, K., Moilanen, U., and Eerikäinen, T. (2008). Biomass Measurement Online: The Performance of In Situ Measurements and Software Sensors. *J. Ind. Microbiol. Biotechnol*. 35: 657 – 665.

Kothari, M. L., Madnani, S. and Segal, R. (1997). Orthogonal Least Squares Learning Algorithm Based Radial Basis Function Network Adaptive Power System Stabilizer. *Proceedings of the IEEE International Conference on Systems, Man and Cybernetics*. 1: 542-547.

Ławryńczuk, M. (2008). Modelling and Nonlinear Predictive Control of a Yeast Fermentation Biochemical Reactor Using Neural Networks. *Chemical Engineering Journal*. 145: 290-307.

Lee, E., Seong, C., Kim, H., Park, S., and Kang, M. (2010). Predicting the Impacts of Climate Change on Nonpoint Source Pollutant Loads from Agricultural Small Watershed Using Artificial Neural Network. *Journal of Environmental Sciences*. 22(6): 840-845.

Lee, J., Lee, S. Y., Park, S., and Middelberg, A. P. J. (1999). Research Review Paper: Control of Fed-batch Fermentations. *Biotechnology Advances*. 17: 29-48.

Lennox, B., Montague, G. A., Frith, A. M., Gent, C., and Bevan, V. (2001). Industrial Application of Neural Networks – An Investigation. *Journal of Process Control*. 11: 497-507.

Lertworasirikul, S., and Tipsuwan, Y. (2008). Moisture Content and Water Activity Predition of Semi-Finished Cassava Crackers From Drying Process Artificial Neural Network. *Journal of Food Engineering*. 84: 65-74.

Li, B., and Li, L. (2006). Artificial Neural Network Based Software Sensor for Yeast Biomass Concentration during Industrial Production. *Computational Intelligence and Security, 2006 International Conference*. 3-6 November. Guangzhou: IEEE, 955-958.

Li, G., and Shi, J. (2010). On Comparing Three Artificial Neural Networks for Wind Speed Forecasting. *Applied Energy*. 87: 2313-2320.

Lin, B., Recke, B., Knudsen, J. K. H., and Jørgensen, S. B. (2007). A Systematic Approach for Soft Sensor Development. *Computers and Chemical Engineering*. 31: 419-425.

Lin, M., Tsai, K., and Su, B. (2009). Estimating the Sound Absorption Coefficients of Perforated Wooden Panels by Using Artificial Neural Networks. *Applied Acoustics*. 70: 31-40.

Linko, S., Luopa, J., and Zhu, Y.-H. (1997). Neural Networks as 'Software Sensor' in Enzyme Production. *Journal of Biotechnology*. 52: 257-266.

Liu, L., Sun, J., Zhang, D., Du, G., Chen, J. and Xu, W. (2009). Culture Conditions Optimization of Hyaluronic Acid Production by *Streptococcuss zoepidemicus* Based on Radial Basis Function Neural Network and Quantum-Behaved Particle Swarm Optimization Algorithm. *Enzyme and Microbial Technology*. 44: 24-32.

Maeda, T., Yoshimura, T., Shimazu, T., Shirai, Y., and Ogawa, H. I. (2009). Enhanced Production of Lactic Acid with Reducing Excess Sludge by Lactate Fermentation. *Journal of Hazardous Materials*. 656-663.

Mandal, S., Sivaprasad, P. V., Venugopal, S., and Murthy, K. P. N. (2009). Artificial Neural Network Modeling to Evaluate and Predict the Deformation Behavior of Stainless Steel type AISI 304L during Hot Torsion. *Applied Soft Computing*. 9: 237-244.

Marchitan, N., Cojocaru, C., Mereuta, A., Duca, Gh., Cretescu, I., and Gonta, M. (2010). Modeling and Optimization of Tartaric Acid Reactive Extraction from Aqueous Solutions: A Comparison Between Response Surfacce Methodology and Artificial Neural Network. *Separation and Purification Technology*. 75: 273-285.

Marini, F. (2009). Artificial Neural Networks in Foodstuff Analyses: Trends and Perspectives A Review. *Analytica Chimica Acta.* 635: 121-131.

Marques, S., Santos, J. A. L., Gírio, F. M. and roseiro, J. C. (2008). Lactic Acid Production from Recycled Paper Sludge by Simultaneous Saccharification and Fermentation. *Biochemical Engineering Journal*. 41: 210-216.

Marták, J., Schlosser, Š., Sabolová, E., Krištofíková, L., and Rosenberg, M. (2003). Fermentation of Lactic Acid with *rhizopus arrhizus* in a Stirred Tank Reactor with a Periodical Bleed and Feed Operation. *Process Biochemistry*. 38: 1573-1583.

Masson, M. H., Canu, S., and Grandvalet, Y. (1999). Software Sensor Design Based on Empirical Data. *Ecological Modelling*. 120: 121-139.

Mehrabi, S., Maghsoudloo, M., Arabalibeik, H., Noormand, R., and Nozari, Y. (2009). Application of Multilayer Perceptron and Radial Basis Function Neural Networks in Differentiating Between Chronic Obstructive Pulmonary and Congestive Heart Failure Diseases. *Expert Systems with Applications*. 36: 6956-6959.

Mehta, R., Vineet, K., Haripada, B., and Upadhyay, S. (2005). Synthesis of Poly(Lactic Acid): A Review. *Journal of Macromolecular Science*. 45(4): 325-349.

Mitra, S., Pal, S., and Mitra, P. (2002). Data Mining in Soft Computing Framework: A Survey. *IEEE Trans. Neural Network.* 13(1): 3-14.

Miura, S., Arimura, T., Hoshino, M., Kojima, M., Dwiarti, L., and Okabe, M. (2003). Optimization and Scale-Up of L–Lactic Acid Fermentation by Mutant Strain *Rhizopus* sp. MK-96-1196 in Airlift Bioreactors. *Journal of Bioscience and Bioengineering*. 96 (1): 65-69.

Moore, C. M. (1996). Drug testing in the 90s. In Leikin SB & Paloucek FP (eds) Poisoning and Toxicology Handbook, 2nd edn., pp 1162 - 1175. Hudson (Cleveland): Lexi-Comp Inc. and American Pharmaceutical Association.

Mujtaba, I. M., Edreder, E. A., and Emtir, M. (2012). Significant Thermal Energy Reduction in Lactic Acid Production Process. *Applied Energy.* 89(1): 74-80.

Musatto, S. I., Fernandes, M., Mancilha, I. M. and Roberto, I. C. (2008). Effects of Medium Supplementation and pH Control on Lactic Acid Production from Brewer's Spent Grain. *Biochemical Engineering Journal*. 40: 437-444.

Najafi, G., Ghobadian, B., Yusaf, T. F., and Rahimi, H. (2007). Combustion Analysis of a CI Engine Performance Using Waste Cooking Biodiesel Fuel with and Artificial Neural Network Aid. *American Journal of Applied Sciences*. 4(10): 756-764.

Nandasana, A. D. and Kumar, S. (2008). Kinetic Modeling of Lactic Acid Production from Molasses using *Enterococcus faecalis* RKY1. *Biochemical Engineering Journal*. 38: 277-284.

Narayanan, N., Roychoudhury, P. K. and Srivastava, A. (2004). L (+) Lactic Acid Fermentation and Its Product Polymerization. *Electronic Journal of Biotechnology*. 7(2): Issue of August 15. http://www.ejbiotechnology.info/content/vol7/issue2/full/7/.

Nayak, R., and Gomes, J. (2009). Sequential Adaptive Networks: An Ensemble of Neural Networks for Feedforward Control of L–Methionine Production. *Chemical Engineering Science*. 64: 2401-2412.

Neelamegam, P., Jamaludeen, A., and Rajendran, A. (2011). Prediction of Calcium Concentration in Human Blood Serum Using and Artificial Neural Network. *Measurement*. 44: 312-319.

Nikfetrat, A., Vali, A. R., and Babaeipour, V. (2009). Neural Network Modeling and Nonlinear Predictive Control of a Biotechnological Fed-Batch Process. *International Conference on Control and Automation*. 9-11 December. Christchurch, New Zealand: IEEE, 2366-2370.

Norgaard, M., Ravn, O., Poulsen, N., and Hansen, L. (2000). *Neural Networks for Modelling and Control of Dynamic Systems*. UK: Springer-Verlag, London.

Nour, V., Trandafir, I., and Ionica, M. E. (2010). HPLC Organic Acid Analysis in Different Citrus Juices under Reversed Phase Conditions. *Notulae Botanicae Horti Agrobotanici Cluj-Napoca*. 38(1): 44-48.

Oğŭz, H., Sarıtas, I., and Baydan, H. E. (2010). Prediction of Diesel Engine Performance Using Biofuels with Artificial Neural Network. *Expert Systems with Applications*. 37: 6579-6586.

Osorio, D., Pérez-correa, J. R., Agosin, E., and Cabrera, M. (2008). Soft-sensor for On-line Estimation of Ethanol Concentrations in Wine Stills. *Journal of Food Engineering*. 87: 571-577.

Ozerdem, M. S., and Kolukisa, S. (2009). Artificial Neural Network Approach to Predict the Mechanical Properties of Cu-Sn-Pb-Zn-Ni Cast Alloys. *Materials and Design*. 30: 764-769.

Pal, P., Sikder, J., Roy, S., and Giorno, L. (2009). Process Intensification in Lactic Acid Production: A review of Membrane Based Processes. *Chemical Engineering and Processing*. 48: 1549-1559.

Palancar, M. C., Aragón, J. M., and Torrecilla, J. S. (1998). pH-Control System Based on Artificial Neural Networks. *Industrial and Engineering Chemistry Research.* 37(7): 2729–2740.

Panagou, E. Z., and Kodogiannis, V. S. (2009). Application of Neural Networks as a Non-Linear Modelling Technique in Food Mycology. *Expert Systems with Applications*. 36: 121-131.

Panagou, E. Z., Kodogiannis, V., and Nychas, G. H. –E. (2007). Modelling Fungal Growth Using Radial Basis Function Neural Networks: The Case of the Ascomycetous fungus *Monascus ruber* van Tieghem. *International Journal of Food Microbiology.* 117: 276-286.

Parlos, A.G., Chong, K.T. and Atiya, A.F. (1994). Application of the Recurrent Multilayer Perceptron in Modeling Complex Process Dynamics. *IEEE Transactions on Neural Network*. 5(2): 255-266.

Parthiban, R., Iyer, P. V. R., and Sekaran, G. (2007). Anaerobic Tapered Fluidized Ned Reactor for Starch Wastewater Treatment and Modeling Using Multilayer Perceptron Neural Network. *Journal of Environment Sciences*. 19: 1416-1423.

Pedreño-Molino, J. L., Pinzolas, M., and Monzó-Cabrera, J. (2006). A New Methodology for In Situ Calibration of Neural Network-Based Software Sensor for S-parameter prediction in Six-Port Reflectometers. *Neurocomputing*. 69: 2451-2455.

Petrov, K., Urshev, Z., and Petrova, P. (2008). L(+)–Lactic Acid Production From Starch by a Novel Amylolytic *Lactococcus lactis* subsp. *lactis* B84. *Food Microbiology*. 25: 550-557.

Piraino, P., Ricciardi, A., Salzano, G., Zotta, T., and Parente, E. (2006). Use of Unsupervised and Supervised Artificial Neural Networks for the Identification of Lactic Acid Bacteria on the Basis of SDS-PAGE Patterns of Whole Cell Proteins. *Journal of Microbiological Methods*. 66: 336-346.

Plessas, S., Bosnea, L., Psarianos, C., Koutinas, A. A., Marchant, R., and Banat, I. M. (2008). Lactic Acid Production by Mixed Cultures of *Kluyveromyces marxiamus*, *Lactobacillus delbrueckii* ssp. *bulgaricus* and *Lactobacillus helveticus*. *Bioresource Technology*. 99: 5951-5955.

Potočnik, P. and Grabec, I. (1999). Empirical Modeling of Antibiotic Fermentation Process using Neural Networks and Genetic Algorithms. *Mathematics and Computers in Simulation*. 49: 363-379.

Rafiq, M. Y., Bugmann, G., and Easterbrook, D. J. (2001). Neural Network Desogn for Engineering Applications. *Computers and Structures*. 79: 1541-1552.

Rao, C.S., Prakasham, R.S., Rao, A.B., and Yadav, J.S. (2008). Production of L (+) Lactic Acid by *Lactobacillus delbrueckii* Immobilized in Functionalized Alginate Matrices. *World Journal of Microbiology and Biotechnology*. 24: 1411-1415.

Rashid, R., Jamaluddin, H., Saidina Amin, N.A. (2006). Empirical and Feed Forward Networks Models of Tapioca Starch Hydrolysis. *Applied Artificial Intelligence*. 20: 79-97.

Reddy, G., Alttaf, M., Naveena, B. J., Venkateshwar, M., and Kumar, E. V. (2008). Amylolytic Bacterial Lactic Acid Fermentation – A Review. *Biotechnology Advances*. 26: 22-34.

Resa, P., Bolumar, T., Elvira, L., Pérez, G., and de Espinosa,, F. M. (2007). Monitoring of Lactic Acid Fermentation in Culture Broth Using Ultrasonic Velocity. *Journal of Food Engineering.* 78: 1083-1091.

Rivas, B. M., Moldes, A. B., Domínguez, J. M., and Parajó, J. C. (2004). Lactic Acid Production from Corn Cobs by Simultaneous Saccharification and Fermentation: A Mathematical Interpretation. *Enzyme and Microbial Technology*. 34: 627-634.

Rivier, L. (2000). Techniques for Analytical Testing of Unconventional Samples. *Bailliére's Clinical Endocrinology and Metabolism*. 14(1): 147-165.

Roslina binti Rashid (2004). *Genetic Algorithm and Neural Networks Modeling of Tapioca starch Hydrolysis Process*. Philosophy of Doctorate. Universiti Teknologi Malaysia.

Rustum, R., Adeloye, A.J., and Scholz, M. (2008). Applying Kohonen Self-Organizing Map as a Software Sensor to Predict Biochemical Oxygen Demand. *Water Environment Research*. 80(1): 32-40.

Sakai, K., Mori, M., Fujii, A., Iwami, Y., Chukeatirote, E., and Shirai, Y. (2004). Fluorescent *In situ* Hybridiazation Analysis of Open Lactic Acid Fermentation of Kitchen Refuse Using rRNA-Targeted Oligonuclleotides Probes. *Journal of Bioscience and Bioengineering*. 98(1): 48-56.

Sargolzaei, S., Faez, K., and Sargolzaei, A. (2007). Predicting Total Hydro Carbons Amount of Air using Artificial Neural Network. *Proceeding of Third International Conference on Natural Computation – Volume 3 (ICNC 2007)*. Vol. 3, 323-327, IEEE Computer Society, Washington, DC, USA,

Schepers, A. W., Thibault, J., and Lacroix, C. (2000). Comparison of Simple Neural Networks and Nonlinear Regression Models for Descriptive Modeling of *Lactobacillus helveticus* growth in pH-controlled Batch Cultures. *Enzyme and Microbial Technology*. 26: 431-445.

Schepers, A. W., Thibault, J., and Lacroix, C. (2002). *Lactobacillus helveticus* Growth and Lactic Acid Production During pH-Controlled Batch Cultures in Whey Permeate/Yeast Extract Medium. Part I. Multiple Factor Kinetic Analysis. *Enzyme and Mibrobial Technology*. 30: 176-186.

Seckin, G., Akoz, M. S., Cobaner, M., Haktanir, T. Application of ANN Techniques for Estimating Backwater Through Bridge Constrictions in Mississippi River Basin. *Advances in Engineering Software*. 40: 1039-1046.

Shahsavand, S. (2009). An Optimal Radial Basis Function (RBF) Neural Network for Hyper-Surface Reconstruction. *Transactions C: Chemistry and Chemical Engineering* . 16(1): 41-53.

Shene, C., Diez, C., and Bravo, S. (1999). Neural Networks for the Prediction of the State of *Zymomonas mobilis* CP4 Batch Fermentations. *Computers and Chemical Engineering*. 23: 1097-1108.

Shibata, K., Flores, D. M., Kobayashi, G., and Senomoto, K. (2007). Direct L-Lactic Acid Bacterium, *Enterococcus faecium*. *Enzyme and Microbial Technology*. 41: 149-155.

Si, F., Romero, C.E., Yao, Z., Xu, Z., Morey, R.L., and Liebowitz, B.N. (2009). Inferential Sensor for On-Line Monitoring of Ammonium Bisulfate Formation Temperature in Coal-Fired Plants. *Fuel Processing Technology*. 90: 56-66.

Tanrikulu, A. H. (2009). Application of ANN Techniques for Estimating Modal Damping of Impact-Damped Flexible Beams. *Advances in Engineering Software*. 40(10): 986-990.

Tetko, I. V., Livinstone, D. J., and Luik, A. I. (1995). Neural Network Studies. 1. Comparison of Overfitting and Overtraining. *Journal of Chemical Information and Computer Sciences*. 35: 826-833.

Tong, W. Y., Fu, X. Y., Lee, S. M., Yu, J., Liu, J. W., Wei, D. Z., and Koo, Y. M. (2004). Purification of L(+) – Lactic Acid From Fermentation Broth with Paper Sludge as a Cellulosic Feedstock Using Weak Anion Exchanger Amberlite IRA-92. *Biochemical Engineering Journal.* 18: 89-96.

Topuz, A. (2010). Predicting Moisture Content of Agricultural Products Using Artificial Neural Networks. *Advances in Engineering Software*. 41: 464-470.

Torrecilla, J. S., Mena, M. L., Yáñez-Sedeño, P., and García, J. (2007). Application of Artificial Neural Network to the Determination of Phenolic Compounds in Olive Oil Mill Wastewater. *Journal of Food Engineering*. 81: 544-552.

Torrecilla, J. S., Otero, L., and Sanz, P. D. (2005). Artificial Neural Network: A Promising Tool to Design and Optimize High-Pressure Food Processes. *Journal of Food Engineering*. 69: 299-306.

Tripathy, P. P., and Kumar, S. (2009). Neural Network Approach for Food Temperature Prediction during Solar Drying. *International Journal of Thermal Sciences*. 48: 1452-1459.

Tsaptsinos, D., and Leigh, J. R. (1993). Modelling of a Fermentation Process Using Multi-Layer Perceptrons: Epochs vs Pattern Learning, Sigmoid vs Linear Transfer Function. *Journal of Microcomputer Applications.* 16: 125-136.

Tudu, B., Jana, A., Metla, A., Ghosh, D., Bhattacharyya, N., and Bandyopadhyay, R. (2009). Electronic Nose for Black Tea Quality Evaluation by an Incremental RBF Network. *Sensors and Actuators B: Chemical*. 138: 90-95.

Valente, E., Rocha, M., Ferreira, E.C., and Rocha, I. (2009). Modelling of Biotechnology Processes – An Approach Based on Artificial Neural Network. *Comp. Intel. Tech. for Bio. Mod.*SCI 218: 311-332.

Valous, N. A., Mendoza, F., Sun, D. W., and Allen, P. (2010). Supervised Neural Network Classification of Pre-Sliceed Cooked Pork Ham Images Using Quaternionic Singular Values. *Meat Science*. 84: 422-430.

van Maris, A. J. A., Konings, W. N., van Dijken, J. P., and Pronk, J. T. (2004). Microbial Export of Lactic and 3-hydroxypropanoic Acid: Implications afor industrial Fermentation Processes. *Metabolic Engineering*. 6: 245-255.

Veloso, A. C. A., Rocha, I., and Ferreira, E. C. (2009). Monitoring of Fed-Batch *E. coli* Fermentations with Software Sensor. *Bioprocess Biosyst Eng.* 32: 381-388.

Wang, Q., Chen, G., Sun, X., and Jin, B. (2006). Recovery of Lactic Acid from Kitchen Garbage Fermentation Broth by Four-Compartment Configuration Electrodialyzer. *Process Biochemistry*. 41: 152-158.

Wee, Y. J., Kim, J. N., and Ryu, H. W. (2006). Biotechnological Production of Lactic Acid and Its Recent Applications. *Food Technol. Biotechnol.* 44(2): 163-172.

Wee, Y. J., Kim, J. N., Yun, J. S., and Ryu, H. W. (2004). Utilization of Sugar Molasses for Economical L(+)–Lactic Acid Production by Batch Fermentation of *Enterococcus faecalis*. *Enzyme and Microbial Technology*. 35: 568-573.

Xiong, Z., Huang, G., and Shao, H. (2005). On-line Estimation of Concentration Parameters in Fermentation Processes. *Journal of Zhejiang University Science*. 6B(6): 530-534.

Xu, G., Chu, J., Wang, Y., Zhuang, Y., Zhang, S., and Peng, H. (2006). Development of a Continuous Cell-Recycle Fermentation System for Production of Lactic Acid by *Lactobacillus paracasei*. *Process Biochemistry*. 41: 2458-2463.

Ye, K., Jin, S., and Shimizu, K. (1996). Performance Improvement of Lactic Acid Fermentation by Multistage Extractive Fermentation. *Journal of Fermentation and Bioengineering*. 81(3): 240-246.

Yin, Y., and Ding, Y. (2009). A Close to Real-Time Prediction Method of Total Coliform Bacteria in Foods Based on Image Identification Technology and Artificial Neural Network. *Food Research International*. 42: 191-199.

Yun, J., Wee, Y., and Ryu, H. (2003). Production of Optically pure L (+) – Lactic Acid from Various Carbohydrrates by batch Fermentation of *Enterococcus faecalis* RKY1. *Enzyme and Microbial Technology*. 33: 416-423.

Zamprogna, E., Barolo, M., and Seborg, D. E. (2005). Optimal Selection of Soft Sensor Inputs for Batch Distillation Columns Using Principal Component Analysis. *Journal of Process Control*. 15: 39-52.

Zhang, B., He, P. J., Ye, N. F., and Shao, L. M. (2008). Enhanced Isomer Purity of Lactic Acid from the Non-Sterile Fermentation of Kitchen Wastes. *Bioresource Technology*. 99: 855-862.

Zhang, Y., Shao, C., and Wu, Q. (2004). RBF Neural Network-Based Software Sensor for Aluminum Powder Granularity Distribution Measurement. *Springer-Verlag Berlin Heidelberg*. LNCS 3174: 860-865.

Zhang, Y., Xu, J., Yuan, Z., Xu, H., and Yu, Q. (2010). Artificial Neural Network-Genetic Algorithm Based Optimization for the Immobilization of Cellulose on the Smart Polymer Eudragit L-100.

Zhao, B., Wang, L., Li, F., Hua, D., Ma, C., Ma, Y., and Yu, P. (2010a). Kinetics of D-Lactic Acid Production by *Sporolactobacillus* sp. Strain CASD Using Repeated Batch Fermentation. *Bioresource Technology*. 101: 6499-6905.

Zhao, B., Wang, L., Ma, C., Yang, C., Xu, P., and Ma, Y. (2010b). Repeated Open Fermentative Production of Optically Pure L-Lactic Acid using a Themophilic *Bacillus* sp. Strain. *Bioresource Technology*. 101: 6494-6498.