An Improved MICA Approach with Applications to Batch Process Monitoring

HONGGUANG LI^a, HUI GUO^{a,b,*}

^a School of Information Science and Technology Beijing University of Chemical Technology Chaoyang District, Beijing, 100029 CHINA

^b School of Mathematics and Computer Science Ningxia University Xixia District, Yinchuan, 750021 CHINA

* guohui@grad.buct.edu.cn (Corresponding author)

Abstract: - On-line monitoring of batch processes using multi-way independent component analysis has attracted much attention in both academia and industry. This paper focuses on two knotty issues concerning selecting dominant independent components without a standard criterion and determining the control limits of monitoring statistics in the presence of non-Gaussian distribution. To optimize the number of key independent components, we introduce a novel concept of system deviation which is able to evaluate the reconstructed observations with different independent components. Additionally, the monitored statistics are transformed to Gaussian distribution data by means of Box-Cox transformation, which helps readily determine the control limits. Finally, the proposed method is applied to on-line monitoring of a fed-batch penicillin fermentation simulator, giving rise to satisfied results.

Key-Words: - Batch process monitoring, MICA, System deviation, Box-Cox transformation, Contribution plots, Fed-batch fermentation

1 Introduction

Batch operations are quite popular for low-volume and high valued-added products manufacturing, targeting high reproducibility and quality subject to possible low cost. Practically, most batch processes present batch-to-batch variations due to composition disturbances, equipment defects and process deviations (Lee et al., 2005) [1], together with high nonlinearity and uncertainty as well as insufficient measurement, which are responsible for the great challenge to process control and monitoring.

During the last decade, multivariate statistical process control (MSPC) has been applied to

monitoring, fault detection and diagnosis of batch processes. Nomikos & MacGregor (1995a, b) [2,3] employed multi-way principal component analysis (MPCA) and multi-way partial least squares (MPLS) to monitor batch processes. Subsequently, numerous studies were carried out on extensions of MPCA and MPLS, such as nonlinear MPCA (Dong & McAvoy, 1996; Lee et al., 2004) [4,5], dynamic MPCA (Chen & Liu, 2002) [6], multi-scale MPCA (Bakshi, 1998; Wang & Romagnoli, 2005) [7,8], hierarchical MPCA (R änner et al., 1998) [9] and multi-block MPCA or MPLS (Lee & Vanrolleghem, 2003; MacGregor et al., 1994; Kourti et al., 1995) [10,11,12]. However, the approaches aforementioned are confined with an assumption that considered process variables should be consistent with Gaussian distribution, which rarely holds in practical processes. To solve this problem, independent component analysis (ICA) becomes increasingly attractive for multivariate non-Gaussian process monitoring. ICA is considered as a useful extension of PCA which could deal with statistically independent data sources. Yoo et al. (2004a, b) [13,14] introduced multi-way independent component analysis (MICA) to batch process monitoring. After that, several extensions of MICA were circulated in the literature, such as multi-way kernel independent component analysis (MKICA) employed to monitor nonlinear processes (Tian et al., 2009, Wang & Shi, 2010) [15,16], dynamic MICA concerning process dynamics (Albazzaz & Wang, 2006, Stefatos & Hamza, 2010) [17,18], and MICA methods incorporated external information (Kano et al., 2004) [19]. In addition, several other variants of MICA were discussed by Xia & Howell (2005) [20], Ge & Song (2008) [21] and Zhang & Zhang (2009) [22].

Two problems emerged from the conventional ICA approaches have been intractable. First, in order to improve the robust performance and reduce analysis complexity of MICA, a small number of key independent components (ICs) should be cautiously selected from all the independent components extracted from original observed variables (Lee et al., 2004b) [23].Even though researchers proposed various approaches to establish a standard criterion, such as L_{∞} norm of each individual component (Back & Weigend, 1997) [24], Euclidean norm of each row of the de-mixing matrix (Cardoso & Soulomica, 1993) [25], and others (Cheung & Xu, 2001, Lee et al., 2004b) [26,23], they could calculate percentage of various norms of de-mixing vectors or ICs themselves only. Consequently, unilateral results happened due to taking less measurements and ICs in all rounds. The second problem lies in the fact that the control limits of ICA statistics cannot be determined directly from a particular approximate distribution because that the ICs rarely follow a normal distribution. Despite

that the kernel density estimation (KDE) was recognized as a popular method to deal with this issue, it still suffers very time-consuming and highly sensitive to the smoothing parameter (Yoo et al., 2004a) [13].

Inspired by these observations, some improvements associated with MICA are performed in this paper. Initially, a novel concept of system deviation quantifying the differences between the original measurements and those of reconstructed with ICs according to leaving-one method is introduced, optimizing the number of dominant independent components. After that, the ICA statistics data are transformed to approximate Gaussian distribution by means of Box-Cox transformations (Box & Cox, 1964) [27]. contributing to easy calculations of the control limits.

The remainder of this paper is organized as follows. Section 2 outlines fundamentals of ICA and MICA. In section 3, the improved MICA approach is introduced, together with its application framework for fault detection and diagnosis of batch processes. In section 4, an experiment consisting in penicillin fermentation monitoring is carried out to demonstrate the applicability of the proposed approach. Section 5 gives conclusions.

2 Fundamentals

2.1 Basic ICA model

Independent component analysis is a statistical and computational technique to reveal unknown factors that underlie sets of random variables or measurements using only the assumption that the hidden factors are mutually independent (Comon, 1994, Hyvarinen & Oja, 2000) [28,29]. Suppose that a set of observations of random variables are generated as a linear mixture of ICs and expressed by vector-matrix notation:

$$X = AS \tag{1}$$

where $X \in \mathbb{R}^{n \times q}$ denotes the observed data matrix, $A \in \mathbb{R}^{n \times n}$ denotes the unknown mix matrix, $S \in \mathbb{R}^{n \times q}$ is the unknown ICs matrix, *n* is the variable index and *q* is the number of sample. The ICA model describes how the observed mixture signals are generated by a process that uses the mixing matrix *A* to linearly mix the latent source signals *S*. Alternatively, it could be specified to find a linear transformation given by a de-mixing matrix *W*, so that the random variables y_i ($i = 1, 2, \dots, n$) are as independent as possible.

$$Y = WX = \overset{\Lambda}{S} \tag{2}$$

where $\overset{\Lambda}{S}$ is the estimation of the ICs and W is the inverse of A.

To eliminate all the cross-correlation between random variables, whitening becomes a useful initial step of ICA (Lee, 1998) [30], which can be executed as follows: Observing x(k) at sample k, its covariance is $R_x = E(x(k)x^T(k))$. The eigendecomposition of R_x is given by $R_x = U\Lambda U^T$. The whitening transformation is expressed as

$$z(k) = Qx(k) = QAs(k) = Bs(k)$$
(3)

where, $Q = \Lambda^{-\frac{1}{2}}U^T$, *B* is an orthogonal matrix, *s*(*k*) is characterized by

$$\overset{\Lambda}{s(k)} = B^{T}Qx(k) \,. \tag{4}$$

Thus, we can obtain the equation

$$W = B^T Q \,. \tag{5}$$

The FastICA algorithm based on maximum likelihood estimation could be utilized to calculate ICA models and represented as follows:

- 1. Centering and whitening the sampled data;
- ②. Choice an initial (e.g. random) matrix *B*;
- ③. Compute y = BX

$$\beta_{i} = -E\{y_{i}g(y_{i})\} \text{ for } i = 1, \dots, n.$$

$$\alpha_{i} = -\frac{1}{(\beta_{i} + E\{g'(y_{i})\})} \text{ for } i = 1, \dots, n.$$

④. Update the matrix *B* by

$$B \leftarrow B + diag(\alpha_i)[diag(\beta_i) + E\{g(y)y^T\}]B$$

⑤. De-correlate and normalized by

$$B \leftarrow (BCB^T)^{-1/2} B$$

6. If not converged, go back to step 3.

Here, the nonlinear function g is the tanh function. The matrices $diag(\alpha_i)$ and $diag(\beta_i)$ are used to optimized the convergence speed of the algorithm. After every step, the matrix B must be projected on the set of sphere matrices; this is accomplished by step (5). After calculating B, we can respectively obtain $\stackrel{\Lambda}{s}(k)$ and de-mixing W. For more details see For more details see (Hyvärinen, 1999) [31].

2.2 MICA for Batch Data



Fig. 1 Unfolding of batch data

As an extension of ICA, multi-way ICA is usually suggested to deal with batch data. Fig.1 shows the basic idea behind MICA. The normal operating conditions (NOC) data from a historical database of batch runs are generally arranged into a three-way array \underline{X} ($I \times J \times K$) where I is the number of batches, J is the number of variables and the K is the number of sampling times in a given batch. A novel method of unfolding original data matrix proposed by Lee et al. (Lee et al., 2004a) [32] combines the advantages of batch-wise unfolding and variableunfolding. Therein, batch wise the data X ($I \times J \times K$) is unfolded batch-wise for eliminating the batch trajectory and scaling the variables at each time, and then, the unfolded matrix X ($I \times KJ$) is rearranged into the form of a variable-wise matrix $X (IK \times J)$ for extracting the major dynamic relations along both time and batch horizons. As long as the batch data is unfolded, the statistical process monitoring with basic ICA could be carried out.

3 Improved MICA Approach

3.1 Selection of ICs

As a new criterion, the system deviation is suggested to evaluate the reconstruction of ICA model by means of measured variables and estimated independent components based on leaving-one method. Assume that $s_{i,n\times m}(k)$ denotes the ICs vector at sample k in which the *i*-th independent component is omitted, i.e. the *i*-th row of the ICs vector equals to zero, and m and n are the number of samples and the ICs, respectively. In addition, $x_i(k)$ indicates the reconstructed measurements, defined by:

$$\hat{x}_{i}(k) = A_{n \times n} \hat{s}_{i,n \times m}(k)$$
(6)

where $A_{n \times n}$ is the mix matrix, which equals to the inverse of W. Thus, the system deviation (SD) is expressed as follows

$$SD(k) = e_{i}(k)^{T} e_{i}(k) =$$

$$(x(k) - \hat{x_{i}}(k))^{T} (x(k) - \hat{x_{i}}(k)) \quad (7)$$

Similarly, *m* system deviations are seriatim calculated when a different independent component is omitted in order. Obviously, a system deviation represents the reconstruction of the omitted IC in the *k*-th sample, which implies that the larger the system deviation the greater the effect of the IC. Alternatively, the average system deviation at different samples could be regarded as a steady measurement indicator. From a computational perspective, the system deviation is recognized as a global criterion, which, combining with a graphical technique, can provide an intuitive and reliable basis for the division of the ICs. The selected ICs become dominant ones which represent the paramount process variation, while the remains form the excluded part. Meantime, the de-mixing matrix Wis divided into the dominant section, abbreviated W_d which includes the selected rows corresponding the dominant ICs, and the excluded section, W_e which consists of the remaining rows. Accordingly, the orthogonal matrix B is cut into B_d and B_e portions by column.

3.2 Estimation of statistics

In general, the statistical distance, T^2 (D), represents the deviation within the model of the monitored process relative to the center point, while the squared prediction error, SPE, indicates the deviation from the model. As previously mentioned, these two types of statistics are accordingly separated as T_d^2 , T_e^2 and SPE_d , SPE_e , respectively. To facilitate the analysis, we exclude SPE_e statistic which contains relatively less information, and thereby rename SPE_d as SPE_d .

Thus, T_d^2 and T_e^2 statistics at sample k are expressed by

$$T_d^2(k) = \hat{s}_d(k)^T \hat{s}_d(k)$$
 (8)

$$T_{e}^{2}(k) = \hat{s}_{e}(k)^{T} \hat{s}_{e}(k)$$
(9)

where $\hat{s}_d(k) = W_d x_{new}(k)$ and $\hat{s}_e(k) = W_e x_{new}(k)$, respectively. Similarly, the statistic SPE at sample k is characterized by

$$SPE(k) = E(k)^{T} E(k) =$$

$$((x_{new}(k) - \hat{x}_{new}(k))^{T})(x_{new}(k) - \hat{x}_{new}(k)) \quad (10)$$

where

 $\hat{x}(k) = Q^{-1}B_d \hat{s}_d(k) = Q^{-1}B_d W_d x_{new}(k)$ according to Eqs. (4) and (5).

Before performing on-line monitoring, the control limits of T_d^2 , T_e^2 and SPE statistics should be specified, which demands the hypothesis that the normal operation data comply to certain distribution. However, it is acknowledged that ICs rarely follow Gaussian distribution. For adaptation, Box-Cox transformation (Box & Cox, 1964) [27] is suggested here. As a widespread tool in transforming non-Gaussian data, Box-Cox transformation is typically characterized by

$$z = y^{(\lambda)} = \begin{cases} \frac{y^{\lambda} - 1}{\lambda} & \text{if } \lambda \neq 0\\ 1n y & \text{if } \lambda = 0 \end{cases}$$
(11)

where y is the original variable, z is the transformation, and λ is a tuning parameter. To ensure positive original data, we substitute y with $y - y_0$, where y_0 is a threshold with $y_0 < y$. An appropriate value of λ that maximizes the normality of the transformed variable should be identified, for which some estimation methods are available, such as likelihood-based and Bayesian approaches (Carroll & Ruppert, 1988, Atkinson & Riani, 2000) [33,34]. Taking advantage of the simplicity in terms of principles and computations, the maximum likelihood estimation is employed here, in which the likelihood function with respect to arithmetic mean μ and standard deviation σ is expressed as

$$L(\mu,\sigma) = \frac{1}{(2\pi)^{N/2}\sigma^{N}} \cdot \prod_{i=1}^{N} e^{\frac{-(z_{i}-\mu)}{2\sigma^{2}}} \cdot \prod_{i=1}^{N} (y_{i})^{\lambda-1}$$
(12)

where N is the total number of samples, y_i and z_i are original data and corresponding transformation at sample k, respectively. Instead, we use

$$\mu = \frac{1}{N} \sum_{i=1}^{N} z_i$$
 and $\sigma = \sqrt{\frac{1}{N} \sum_{i=1}^{N} (z_i - \mu)^2}$ in Eq.

(12), making the likelihood function depend only on λ so that the estimation problem could be readily resolved by a maximization approach. Once the optimal estimation of the transformation parameter is obtained and the two types of statistics are transformed to normal or approximately normal distribution data, then the traditional technique, such as $\mu \pm 3\sigma$ (99%), can be used for determining the control limits of the transformed data. Subsequently, the control limits of the original data are computed according to the inverse of transformation function.

3.3 Applications in process monitoring

While a new batch is running, the T_d^2 , T_e^2 and SPE statistics can be calculated and any violations of their control limits could be utilized to indicate deviations beyond the normal operating conditions of the process. Additionally, contribution plots are traditionally suggested to identify the assignable causes, revealing the process variables that most influence the model or the residuals (Westerhuis et al., 2000) [35]. The contributions of x(k) for the statistics are given by

$$x_{d}(k) = \frac{Q^{-1}B_{d}\hat{s}_{d}(k)}{\left\|Q^{-1}B_{d}\hat{s}_{d}(k)\right\|} \cdot \left\|\hat{s}_{d}(k)\right\|, \quad (13)$$

$$x_{e}(k) = \frac{Q^{-1}B_{e}\hat{s}_{e}(k)}{\left\|Q^{-1}B_{e}\hat{s}_{e}(k)\right\|} \cdot \left\|\hat{s}_{e}(k)\right\|,$$
(14)

$$x_{SPE}(k) = x(k) - Q^{-1}BWx(k)$$
. (15)

In concluding, two main phases are involved in the framework of the improved MICA for batch process monitoring, as presented in Fig.2. In the first phase, off-line MICA modeling including the unfolding NOC data, dividing data and determining control limits of the statistics is performed. While the second phase is concerned with on-line monitoring procedure composed of detecting the fault and identifying the causes.



Fig. 2 Schematic of improved MICA monitoring

Hongguang Li, Hui Guo

4 Implementation

The efficiency of the proposed method will be demonstrated through an application of a simulation example: fed-batch penicillin fermentation.

4.1 Fed-batch fermentation

The modularized simulator for penicillin production, PenSim v2.0, which is based upon a series of detailed mechanistic models, is used as a test-bed for carrying out the study (Birol et al., 2002a) [36], as described in Fig.3. Penicillin fermentation is the synthesis of secondary metabolites operated in the mechanically agitated bioreactor with appropriate levels of nutrients at suitable conditions such as aeration rate, concentrations of dissolved gases, pH and temperature etc. Slight changes in operating conditions during critical periods may significantly differentiation impact on growth and of microorganisms, as well as final product quality and throughput. In order to maintain the circumstances required by penicillin fermentation, acid or base additions are allowed to control pH at a certain value, while cooling or heating water are used to make the cultivation temperature stay constant. (Bajpai & Reuss, 1980; Birol et al., 2002b) [37,38].





4.2 Experiment and analysis

Table 1 presents 10 monitoring variables associated with the process. For the purpose of developing an off-line MICA model, the simulator operated repeatedly under normal operating conditions with the duration of each batch specified as 400 h. Therein, a NOC dataset of 60 batches was collected under the sampling interval of 0.5 h.

Table 1 Fermentation process variables used for monitoring

- 1 Aeration rate (l/h)
- 2 Agitator power (W)
- 3 Glucose feed temperature (K)
- 4 Dissolved oxygen concentration (% saturation)
- 5 Culture volume (1)
- 6 Carbon dioxide concentration (mmol/l)
- 7 pH
- 8 Temperature (K)
- 9 Generated heat (kcal)
- 10 Cooling water flow rate (l/h)

Initially, the dataset was unfolded into two-way matrix to formulate conventional ICA. The percentage of system deviation of each IC omitted in reconstructing the measurements was calculated, as shown in Fig.4. With relatively small system deviations, IC 1, 3 and 8 were regarded as the residual part. While the remainders turned out to be the dominant part able to characterizes the trait of the penicillin fermentation process.



Accordingly, T_d^2 , T_e^2 and *SPE* statistics were computed and transformed into normal distribution data by means of Box-Cox transformations, in which, the corresponding transformation parameters were specified as -1.4751, -1.0819 and -1.9755, respectively. Fig.5 shows the comparisons between the original statistics and their transformations in terms of normality check. The transformations of T_d^2 and *SPE* statistics are more strictly subject to Gaussian distribution than T_e^2 that could meet the requirements of practical statistical process control. Therefore, control limits of the two types of statistics were determined separately.

Fig. 5 Comparison on normality check of three statistics and their transformations

To exemplify the on-line monitoring, we disturbed the agitator power with a -0.1 slope change introduced at time 300 h and terminated at time 320 h over a new operating batch. Fig.6 shows the profiles of the improved MICA monitoring, in which the upper control limits were presented with red dashed lines (99%). It reveals that all of T_d^2 , T_e^2 and *SPE* statistics exceeded the control limits during sampling time 601 to 640. Then, contributions of 10 monitoring variables for T_d^2 , T_e^2 and *SPE* statistics were respectively calculated according to Eqs.(13)-(15) at sample 601, and the

contribution charts are depicted in Fig.7. The second variable, agitator power, conducted much higher values than those of other variables which implied the actual fault source consistent with the reality.

Fig. 6 MICA based on-line monitoring charts

Fig. 7 Variables contributing to statistics at sample 601

5 Conclusion

To effectively monitoring batch or semi-batch processes, an improved MICA approach is introduced in this paper. The contribution is twofold. First, the system deviation is proposed to evaluate the reconstructed observations with different ICs, which could provide a new global criterion of selecting dominant components and simplifying analysis. Second, Box-Cox transformation is employed to deal with monitoring statistics and determining control limits, demanding a little number of sampling data as well as enjoying simplicity. As a result, a monitoring scheme behind this novel idea is presented, along with a monitoring experiment consisting in a fed-batch penicillin benchmark problem, which demonstrates the effectiveness and potential of the contribution.

References:

- Lee, D.S., Park, J.M. & Vanrolleghem, P.A., Adaptive multiscale principal component analysis for on-line monitoring of a sequencing batch reactor. *Journal of Biotechnology*, Vol.116, No.2, 2005, pp. 195–210.
- [2] Nomikos, P. & MacGregor, J.F., Multivariate SPC charts for monitoring batch processes. *Technometrics*, Vol.37, No.1, 1995a, pp. 41–59.
- [3] Nomikos, P. & MacGregor, J.F., Multi-way partial least squares in monitoring batch processes. *Chemometrics and Intelligent Laboratory Systems*, Vol.30, No.1, 1995b, pp. 97–108.
- [4] Dong, D. & McAvoy, T.J., Batch tracking via nonlinear principal component analysis. *American Institute of Chemical Engineers Journal*, Vol.42, No.8, 1996, pp. 2199–2208.
- [5] Lee, J.M., Yoo, C. & Lee, I.B., Fault detection of batch processes using multiway kernel principal component analysis. *Computers and Chemical Engineering*, Vol.28, No.9, 2004, pp. 1837–1847.
- [6] Chen, J. & Liu, K.C., On-line batch process monitoring using dynamic PCA and dynamic PLS models. *Chemical Engineering Science*, Vol.57, No.1, 2002, pp. 63–75.
- Bakshi, B.R., Multiscale PCA with application to multivariate statistical process monitoring. *AIChE Journal*, Vol.44, No.7, 1998, pp. 1596– 1610.
- [8] Wang, D. & Romagnoli, J.A., Robust multiscale principal component analysis with applications to process monitoring. *Journal of Process Control*, Vol.15, No.8, 2005, pp. 869– 882.

- [9] Ränner, S., MacGregor, J.F. & Wold, S., Adaptive batch monitoring using hierarchical PCA. *Chemometrics and Intelligent Laboratory Systems*, Vol.41, No.1, 1998, pp. 73–81.
- [10] Lee, D.S. & Vanrolleghem, P.A., Monitoring of a sequencing batch reactor using adaptive multiblock principal component analysis. *Biotechnology and Bioengineering*, Vol.82, No.4, 2003, pp. 489–497.
- [11] MacGregor, J.F., Jaeckle, C., Kiparissides, C.
 & Koutoudi, M., Process monitoring and diagnosis by multiblock PLS methods. *AIChE Journal*, Vol.40, No.5, 1994, pp. 826-838.
- [12] Kourti, T., Nomikos, P. & MacGregor, J.F., Analysis, monitoring and fault diagnosis of batch processes using multiblock and multiway PLS. *Journal of Process Control*, Vol.5, No.4, 1995, pp. 277–284.
- [13] Yoo, C.K., Lee, J.M., Vanrolleghem, P.A. & Lee, I.B., On-line monitoring of batch processes using multiway independent component analysis. *Chemometrics and Intelligent Laboratory Systems*, Vol.71, No.2, 2004a, pp. 151–163.
- [14] Yoo, C.k., Lee, D.S. & Vanrolleghem, P.A., Application of multiway ICA for on-line process monitoring of a sequencing batch reactor. *Water Research*, Vol.38, No.7, 2004b, pp. 1715-1732
- [15] Tian, X.M., Zhang, X.L., Deng, X.G. & Chen, S., Multiway kernel independent component analysis based on feature samples for batch process monitoring. *Neurocomputing*, Vol.72, No.7-9, 2009, pp. 1584-1596.
- [16] Wang, L. & Shi, H.B., Multivariate statistical process monitoring using an improved independent component analysis. *Chemical Engineering Research and Design*, Vol.88, No.4, 2010, pp. 403-414.
- [17] Albazzaz, H. & Wang, X.Z., Mulitvariate statistical batch process monitoring using dynamic independent component analysis. *Computer Aided Chemical Engineering*, Vol.21, 2006, pp. 1341-1346.
- [18] Stefatos, G. & Hamza, A.B., Dynamic independent component analysis approach for

fault detection and diagnosis. *Expert Systems with Applications*, Vol.37, No.12, 2010, pp. 8606-8617.

- [19] Kano, M., Hasebe, S., Hashimoto, I. & Ohno, H., Evolution of multivariate statistical process control: application of independent component analysis and external analysis. *Computers and Chemical Engineering*, Vol.28, No.6-7, 2004, pp. 1157-1166.
- [20] Xia, C.M. & Howell, J., Isolating multiple sources of plant-wide oscillations via independent component analysis. *Control Engineering Practice*, Vol.13, No.8, 2005, pp. 1027-1035.
- [21] Ge, Z.Q. & Song, Z.H., Online monitoring of nonlinear multiple mode processes based on adaptive local model approach. *Control Engineering Practice*, Vol.16, No.12, 2008, pp. 1427-1437.
- [22] Zhang, Y.W. & Zhang, Y., Complex process monitoring using modified partial least squares method of independent component regression. *Chemometrics and Intelligent Laboratory Systems*, Vol.98, No.2, 2009, pp. 143-148.
- [23] Lee, J.M., Yoo, C.K. & Lee, I.B., Statistical process monitoring with independent component analysis. *Journal of Process Control*, Vol.14, No.5, 2004b, pp. 467-485.
- [24] Back, A.D. & Weigend, A.S., A first application of independent component analysis to extracting structure from stock returns, *International Journal of Neural Systems*, Vol.8, No.4, 1997, pp. 473–484.
- [25] Cardoso, J.F. & Soulomica, A., Blind beam forming for non-Gaussian signals. *IEEExplore-Radar and Signal Processing*, Vol.140, No.6, 1993, pp. 362–370.
- [26] Cheung, Y.M. & Xu, L., Independent component ordering in ICA time series analysis. *Neurocomputing*, Vol.41, No.1-4, 2001, pp. 145–152.
- [27] Box, G.E.P. & Cox, D.R., An analysis of transformations. *Journal of the Royal Statistical Society. Series B*, Vol.26, No.2, 1964, pp. 221-252.

- [28] Comon, P., Independent component analysis, a new concept. *Signal Process*, Vol.36, No.3, 1994, pp. 287–314.
- [29] Hyvärinen, A. & Oja, E., Independent component analysis: algorithms and applications. *Neural Networks*, Vol.13, No.4-5, 2000, pp. 411–430.
- [30] Lee, T., *Independent Component Analysis: Theory and Applications*, Kluwer Academic Publishers, Boston, USA., 1998.
- [31] Hyvärinen, A., Fast and robust fixed-point algorithms for independent component analysis. *IEEE Trans. Neural Networks*, Vol.10, No.3, 1999, pp. 626–634.
- [32] Lee, J.M., Yoo, C.K. & Lee, I.B., Enhanced process monitoring of fed-batch penicillin cultivation using time-varying and multivariate statistical analysis. *Journal of Biotechnology*, Vol.110, No.2, 2004a, pp. 119-136.
- [33] Carroll, R.J. & Ruppert, D., *Transformation* and Weighting in Regression, Chapman & Hall, NewYork, 1998.
- [34] Atkinson, A. & Riani, M., *Robust Diagnostics Regression Analysis*, Springer, NewYork, 2000.
- [35] Westerhuis, J.A., Gurden, S.P. & Smilde, A.K., Generalized contribution plots in multivariate statistical process monitoring. *Chemometrics* and Intelligent Laboratory Systems, Vol.51, No.1, 2000, pp. 95-114.
- [36] Birol, G., Ündey, C. & Cinar, A., A modular simulation package for fed-batch fermentation: penicillin production. *Computers and Chemical Engineering*, Vol.26, No.11, 2002a, pp. 1553-1565.
- [37] Bajpai, R.K. & Reuss, M., A mechanistic model for penicillin production. *Journal of Chemical Technology and Biotechnology*, Vol.30, No.1, 1980, pp. 332-344.
- [38] Birol, G., Ündey, C., Parulekar, S.J. & Cinar, A., A morphologically structured model for penicillin production. *Biotechnology and Bioengineering*, Vol.77, No.5, 2002b, pp. 538-552.