Chemometrics and Intelligent Laboratory Systems 116 (2012) 67–77

Contents lists available at SciVerse ScienceDirect

Chemometrics and Intelligent Laboratory Systems

journal homepage: www.elsevier.com/locate/chemolab

Combining fundamental knowledge and latent variable techniques to transfer process monitoring models between plants

Emanuele Tomba [a], Pierantonio Facco [a], Fabrizio Bezzo [a], Salvador García-Muñoz [b], Massimiliano Barolo [a,*]

[a] CAPE-Lab — Computer-Aided Process Engineering Laboratory, Dipartimento di Ingegneria Industriale, Università di Padova, via Marzolo 9, 35131 Padova PD, Italy
[b] Pfizer Worldwide R&D, 445 Eastern Point Road, Groton, CT 06340, USA

ARTICLE INFO

Article history:
Received 31 January 2012
Received in revised form 16 April 2012
Accepted 27 April 2012
Available online 7 May 2012

Keywords:
Model transfer
Process monitoring
JY-PLS
Quality-by-design
PAT
Scale-up
Design space

ABSTRACT

In this paper we explore the issue of the transfer of process monitoring models between different plants that exploit the same manufacturing process to manufacture the same product. Given a source plant A and a target plant B, the objective is to use the data available from plant A to monitor the operation of plant B, until a sufficient amount of data entirely representative of the operation in plant B is collected to allow building a process monitoring model based on these data only.

Two different model transfer methodologies are proposed, which depend on the nature of the measured process variables (namely, on whether they are common between the two plants or not). Both the proposed approaches combine fundamental engineering knowledge on the system (derived from mass or energy balances) with latent variable modeling techniques (namely, principal component analysis and joint-Y partial least-squares regression). Both approaches are based on adaptive algorithms, which make them practical for online use, and are tested on a benchmark problem related to the scale-up of the monitoring model for an industrial spray-drying process. Results show that both proposed procedures provide robust and prompt fault detection, even when very few data are available from plant B.

1. Introduction

When the manufacturing of a product with assigned quality specifications is transferred from a source plant A to a target plant B, it would be highly desirable to have a reliable monitoring system available for plant B as quickly as possible, in order to detect incipient faults and possibly to diagnose them since the beginning of the operation in plant B. Multivariate statistical process control techniques have been applied successfully in several industrial applications for online process monitoring and fault detection [1–3]. In order to build a reliable process monitoring model, these techniques require that data representing the common cause variability (CCV) to which the process is subject be available.

In production transfer activities (e.g. plant scale-up), experiments in the target plant B are limited to those needed to define the normal process conditions of the operation, and process data are therefore usually insufficient to build a monitoring model for this plant based on multivariate statistical techniques. Experimental campaigns designed to produce CCV data in plant B are carried out very rarely, especially if the cost of raw materials is high or the product manufacturing is subject to a rigid regulatory environment (as in the case of the food and pharmaceutical industries, for example). At the same time, if the product has already been manufactured in plant A, several operating data are usually available from this plant, and a set of normal operating conditions (NOC; [4]) may have been identified that guarantee that the product quality meet the specifications with acceptable variability.

It would be therefore useful to transfer the knowledge already available for plant A in order to monitor the manufacturing process in plant B until a sufficient amount of data is collected in this plant to design a process monitoring model entirely based on the plant B data. In this paper, a possible strategy to solve this problem (which we refer to as a process monitoring model transfer or simply *model transfer* problem) is presented.

The problem of transferring models or standardizing data between different sources has been treated in spectroscopy to transfer calibration models from one instrument to another one of the same type [5]. However, model transfer approaches developed for these models are not suitable for the transfer of process monitoring systems, since they rely on the correspondence between samples measured in different instruments, which is hard or even impossible to find when samples come from different plants. Methodologies for transferring a model to a new process have been recently proposed by Lu and coworkers [6,7]. Although these procedures are effective, they basically refer to the transfer of predictive models rather than to the transfer of monitoring models, and therefore are not appropriate for the problem under investigation.

* Corresponding author. Tel.: +39 049 827 5473; fax: +39 049 827 5461.
E-mail address: max.barolo@unipd.it (M. Barolo).

0169-7439/$ – see front matter © 2012 Elsevier B.V. All rights reserved.
doi:10.1016/j.chemolab.2012.04.016

Jaeckle and MacGregor [8,9] tackled the *product transfer* problem, and proposed a methodology based on latent variable models (LVMs) to transfer products between different manufacturing plants. This problem was further investigated by García-Muñoz et al. [10], who proposed a new modeling technique, called joint-Y partial least-squares (JY-PLS) regression, to model the correlation between the operating conditions in different plants through the latent space generated by the quality of the manufactured products. The effectiveness of this method has been tested industrially in different applications, for product scale-up [11] and data standardization purposes [12]. However, the product transfer problem considered in all the above studies is fundamentally different from the model transfer problem considered in the present work.

A reliable procedure to transfer monitoring models between plants needs to account for different issues intersecting with each other. Firstly, one should consider the type of information initially available, namely if process data only or process data as well as fundamental process knowledge (for example, in the form of conservation laws) shall be used. The appropriate model transfer approach also depends on the source of the available process data (plant A data only, or plant A data as well as plant B data), and on the type of process variables that are used to design the monitoring model (only variables with similar physical meaning whose measurements are available in both plants, i.e., common variables, or common variables as well as other measured variables). Depending on the combination of the issues mentioned above, different scenarios may arise, as illustrated in Fig. 1. For each scenario, a solution strategy based on LV modeling for the model transfer issue can be devised. In this paper, we address the problem by combining the use of process data with fundamental engineering knowledge about the process; this corresponds to the paths indicated by the solid lines in Fig. 1. Other model transfer approaches, corresponding to the dashed line paths in Fig. 1, will be presented elsewhere [13].

The benefits deriving from the use of fundamental process knowledge with data-based models have been reported in several studies [14–16], where fundamental knowledge from first-principles models is combined with data-based models with the aim of providing good model interpretation and good data fit at the same time.

In the model transfer approaches proposed in this paper, the monitoring model is built using LV modeling concepts only. To transfer information between the plants, a way to relate the operations in different plants is needed. To this purpose, fundamental knowledge is used in terms of conservation laws to identify physically-relevant combinations of variables that can be considered independent of the plant. This procedure is typical of scale-up exercises, when plant A is a lab- or pilot-scale unit, whereas plant B is a production unit [17]. Since the new identified variables account for the physical phenomena occurring in both the source and target plants, they can be used to match similar states of the plants and to support the transfer.

Two alternative model transfer approaches are proposed (Scenario 1 and Scenario 2 in Fig. 1), depending on whether only common or both common as well as other measured variables are used to carry out the monitoring model transfer. The effectiveness of the proposed approaches is evaluated on a case study concerning the transfer of the monitoring model for a pharmaceutical spray-drying process between two industrial plants that differ in the production scale.

2. Process, plants and datasets

The process considered in this study is a pharmaceutical spray-drying process. Spray-drying is widely used in the pharmaceutical industry, not only for the preparation of solid amorphous dispersions, but also for excipient manufacturing, biotherapeutic particle engineering, drying of crystalline active pharmaceutical ingredients and encapsulation [18]. A schematic of the process is shown in Fig. 2. [19,20].

Two geometrically-similar plants of different sizes are considered, namely a pilot-scale unit (plant A) and a production-scale unit (plant B). The goal is to use the process data available from plant A and fundamental knowledge to design a process monitoring model for plant B, until enough CCV data are collected in plant B to design a monitoring model based entirely on these data.

The available plant A data are assembled in matrix $\mathbf{X}^{A}$ $[N^{A}\times V^{A}]$, which includes $N^{A}=15{,}031$ CCV samples of $V^{A}=16$ variables. The entire dataset available for plant B is denoted by matrix $\mathbf{X}^{B}$ $[N^{B}\times V^{B}]$, which includes $N^{B}=4224$ CCV samples on $V^{B}=10$ variables. However, to evaluate the performance of the proposed model transfer approaches when only a limited number of plant B samples is available, only the first W samples of $\mathbf{X}^{B}$ are assumed to be available initially (e.g. because plant B was just started up). These samples are organized in matrix $\mathbf{X}_{W}^{B}$ $[W\times V^{B}]$.

In Table 1 the process variables measured in each plant are listed. Note that the process variables measured in plant A are not the same as the ones in plant B, although there are 9 measured variables that are common in the two plants. These common variables are indicated with the same coded name and by symbol * in Table 1.

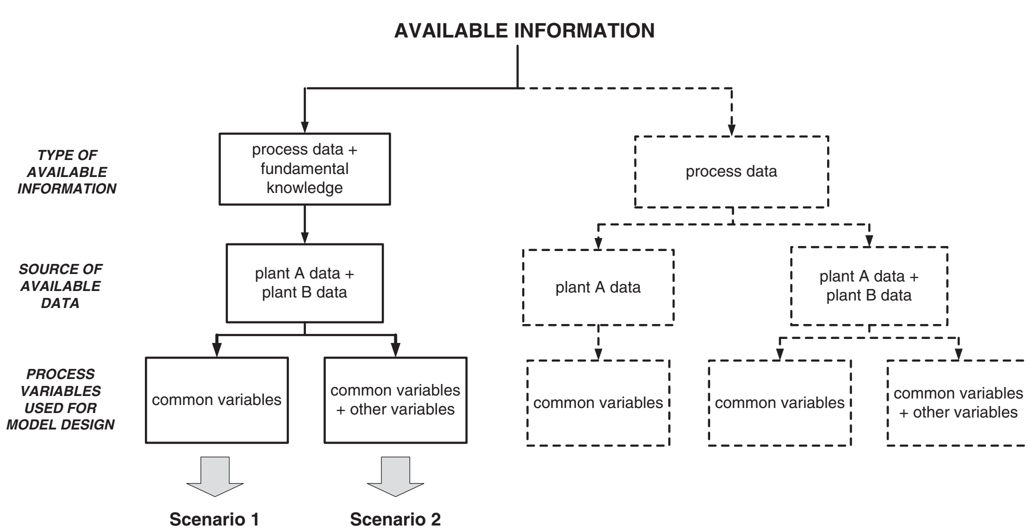

Fig. 1. Framework for the development of latent variable approaches to the transfer of process monitoring models between different plants. The path indicated by dashed lines is not discussed in this paper.