THESES OF THE PhD DISSERTATION

Kinetic modeling for batch process development

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1. INTRODUCTION AND AIM OF THE WORK

Most of the processes in the chemical, pharmaceutical and food industries operate in batch mode. An important feature of batch processes is their inherent flexibility which allows the adaptation to the continuously changing market demands. These process systems generally produce many kinds of products usually in significantly different manufacturing procedures and, at the same time, products are changed and new products are introduced very frequently.

Starting from the results of chemical research the introduction of a new batch process into production requires several development steps. The model-based approach of the development handles the collected information into a unified system of models and this way it reduces significantly the required time and cost.

The research problem is the modelling of the processes taking place in the reaction mixture and the transfer of kinetic information between the development levels. The objectives are:

- The construction of a development-oriented optimum-size model taking into account the objectives of the process development and the limitations of the development infrastructure.
- Development of methods for the identification of the parameters of the kinetic model which can be used with strict constraints on the number of experiments and the analytical measurements.
- The description of the model-based method of process development in an algorithm-wise form and the study of the application on industrial problems.

2. EXPERIMENTAL METHODS AND TOOLS

One of the main research directions at the Department of Process Engineering, Pannon University is the modelling, development and control of batch processes. The results were utilized in several projects with our partners in the pharmaceutical, fine chemical and polymer industries. The subject of the theses is, regarding the development of batch processes, the methods for construction appropriate kinetic models and the study of application methodology of these models. The laboratory and pilot plant tests were conducted at our industrial partners having well-instrumented and automated facilities.

The study of the model-based methods was supported by a goal-oriented simulation tool which was developed in Matlab/Visual Basic environment as a part of the research. This CAPE tool allows the mapping the applied kinetic

models, the identification of their parameters and the application of the models through the development.

3. NEW SCIENTIFIC RESULT

1. The main steps and conditions for obtaining a process development-oriented kinetic model and for compiling the “optimal” model structure considering the development requirements were elaborated.
   - It was found that among the applicable model types the tendency model is the one which can be effectively used in process development, since its structure can be adapted flexibly and gradually according to the requirements of problem solving and the available information.
   - It was determined that in the elaborated tendency model those phases, components and processes which decisively influence the development are to be included according to the needs of problem solving and available information.
   - The most important steps of the simplification of kinetic models were determined. These are the consideration of the active components only, the examination of possible aggregation of processes and the application of a generalized form of the rate equation.
   - It was stated that the model can be further simplified by introducing the application of stochiometrically non-closed reactions,
   - The validity of the above generalized statements was justified by an industrial example.

   Building kinetic models for process development purposes arise several difficulties. A detailed kinetic model may require the treatment of a large number of components and processes as well as it may be necessary the identification of too many parameters compared to the experimental facilities. The reduction of the size and complexity of the model, taking into account the identification of parameters, the appropriate selection of important phases, components and reactions is decisive in the development process. The application of the method, discussed in Chapter 2, can assure obtaining an “optimal-size” development-oriented model.

2. Methods and procedures for identifying the parameters of the tendency model were determined and studied.
   - The main factors for the design of experiments necessary for the parameter identification of kinetic models were determined.

- The basic principles for the decomposition of the identification problems were stated.
- The construction of the appropriate objective function for the identification problem was established using relative errors and the corresponding threshold values.
- The advantageous properties of the identification procedure were proved on an industrial example.

Identification of kinetic parameters used in process development may have high cost and time requirements. The approach, outlined in Chapter 3, including the experimental design aspects, the decomposition of the identification problem and the construction of a suitable objective function, assures that the model parameters can be determined from a relatively small number of experiments and that the reliability of the information sources can be handled.

3. The basic data structures and the meta-algorithms of problem solving were determined and implemented in software form. It was found that the proposed data structures and meta-algorithms as well as their implementation can be effectively used for solving development problems, that is for:
   - the implementation of the developed tendency models,
   - the identification of the kinetic parameters of the model from laboratory, pilot-scale and plant-scale data,
   - the studies and analyses required in process development.

   The application of the methods discussed above requires appropriate software tools. The kinetic simulator and identification package is discussed in details in Chapter 4. This software, compared to the general purpose tools, effectively supports the development activities of process-engineers in the model building, the parameter identification, the process analysis and the recipe development.

4. The steps of the procedure for the systematic application of model-based process development were established. These steps are parts of a closed information chain.
   - The different experimental and measurement levels of the development as well as the method for connecting them together were determined, assuring the possibilities for the transfer or feedback of the kinetic information between the different levels,

- It was found that the method more efficient than the classical scale-up techniques due to the integrated treatment of information.
- The favourable properties of the new method were justified by the results of solving several different process development problems, namely the development of recipes and operational strategies as well as the analysis of process control constraints.

New approaches to process development make the development process more efficient and faster by involving simulation methods and tools. The method described assures the information transfer and feedback from the laboratory-scale to the plant-scale. The simulation methodology discussed in Chapter 5 was applied in solving several pharmaceutical and other chemical industrial development problem; the results of the projects justified the advantages of the method.

4. SCIENTIFIC PUBLICATIONS AND PRESENTATIONS RELATED TO THE THESES

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