New Opportunities for Conceptual Design of Process Systems

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Abstract

In recent years, process development has changed quite significantly in many companies. There is an increased emphasis on tighter project justification through integration of business development with process development. There is an emphasis on reducing the development time and cost, and on reducing investment costs as well as manufacturing costs. At the same time, products and processes are becoming more complex due to increased demand for microstructured products, and for manufacturing systems that combine multiple steps in a single device (process intensification). Moreover, the manufacture of many specialty chemicals and pharmaceuticals involve complex chemistries that provide additional challenges in the early phases of process development. In this paper, we briefly discuss methods for dealing with these challenges, and identify unsolved problems and new areas for process research.

Introduction

Traditionally, process development in the process industries has taken place in an evolutionary way, the main focus being on equipment design and selection of 'best proven practice', rather than on systematic exploration of alternative process configurations. The traditional approach is based mostly on years of experience with existing plants. Although this approach yields useful designs quickly and reliably, it does not promote the use of novel technologies nor does it allow for the comparison of alternative designs. The main danger in the traditional approach is jumping to the "known solution" before the problem is really understood.

A recent major study carried out at the Harvard Business School (Pisano 1997) shows that process innovation, not just product innovation, can be the key to competitive edge. Indeed this is a characteristic of those who have been successful in the commodity chemicals business. Pisano's work reveals that behind the success of many new product introductions lies the development of novel process technologies that provide lower cost, higher quality, and increased flexibility. There is strategic corporate advantage in the integration of process and product development.

These advantages can be captured with a design methodology. This has been recognized since the early 1970's, beginning with the pioneering studies in process synthesis by Rudd, Powers and Siirola. Since that time, a number of design methodologies have emerged, including: *Pinch Technology, Hierarchical Decomposition Methods,* and superstructure optimization-based approaches, such as *Mixed Integer*

Nonlinear Programming. The common feature of all these approaches is that they have been developed to address the conceptual design or process synthesis of flowsheets containing some or all of the following conventional tasks: reaction, separation, mixing, heat exchange, and recycle. These methods are most effective at inventing and designing flowsheets with the conventional serial structure of reaction followed by separation followed by recycle. In recent years new design methods have been developed that are capable of capturing intensified process flowsheets in which some of the tasks are carried out simultaneously, e.g., combining reaction and separation such as in reactive distillation, etc. Although much remains to be done in the conventional arena, the state of the art is nevertheless quite good and systematic methods are now available to solve many design problems of realistic complexity that could not be solved 30 years ago. However, the situation is different when microstructured products are involved.

The process industries are moving from products that are characterized by specifications on product purity towards products that are based on performance and properties (see Cussler and Moggridge). The design of a process to make a microstructured product begins with a definition of the desired properties of the product together with a structure-property-value relation as far as it is known. For example, Villadsen (1997) points out that even a 50 micron glob of material in a skin cream makes the cream feel gritty. When the cream undergoes additional shear during processing to remove the globs, the texture and appearance of the cream is changed, which can have a big impact on its acceptance by customers and hence on its value. Similar considerations apply to many other microstructured liquid products in the health and personal care sector, in foods (sauces and dressings), etc. When solids are involved there are additional considerations, such as the solid-state polymorph, hydrates, and particle shape. For pharmaceutical and other life-science related products it is often necessary to specify whether the active ingredient is a racemic mixture or a particular enantiomorph.

The manufacture of microstructured products often involves *product formulation and microstructure formation* steps which are normally missing from conventional process flowsheets. The set of tasks, therefore, involves some or all of the following: reaction, separation, mixing, heat exchange, product formulation, microstructure formation, and recycle (see Fig. 1). The product formulation, and microstructure formation tasks may occur at one or multiple places in the flowsheet, as indicated in Figure 1. They may also occur simultaneously with conventional tasks. For example, the microstructure formation and texture of ice cream develop simultaneously with cooling, crystallization, and stirring. Microstructure formation is still more art than science, although great strides have been made in this area in recent years. Nevertheless, most design engineers are not equipped to handle these aspects of process design & development in spite of their importance to large sectors of the process industries.

At the current time there is no systematic methodology available in the open literature for the design and synthesis of processes for the production of microstructured products, although some important elements of such a methodology do exist, as noted below. Even though we do not know what this methodology should look like, we do know some of the characteristics it should possess. In process development there are generally many possible process alternatives, so a structured methodology is required to screen and compare them and find the good ones effectively. Good methodologies

provide the reasoning behind the design decisions that have been made and allow for the evaluation of novel technologies. An important feature of a structured approach to

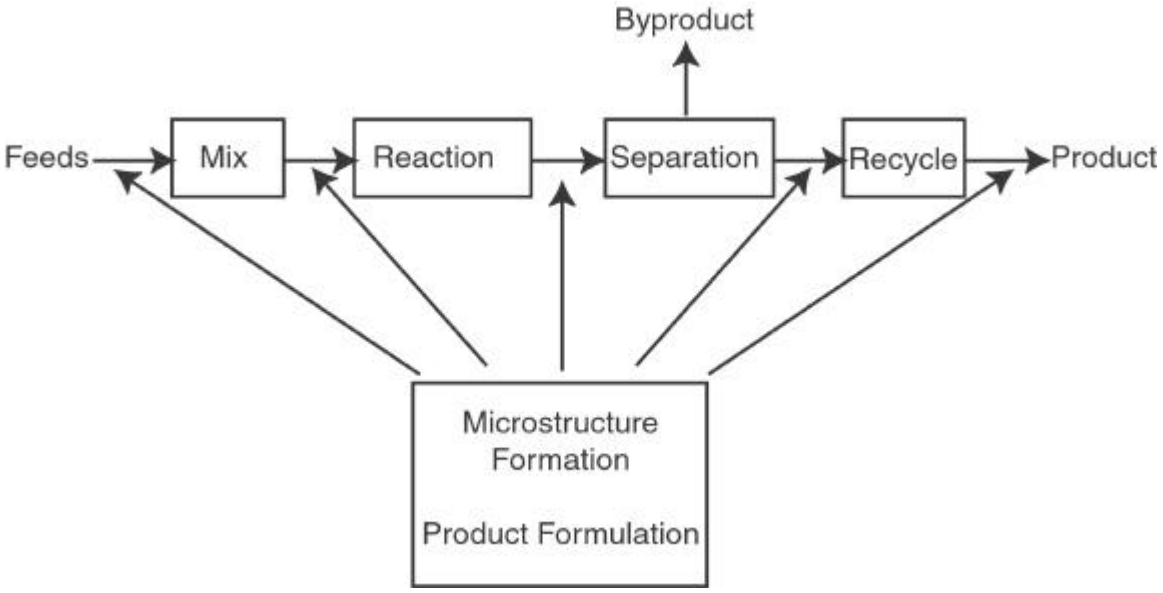

Fig. 1 Tasks for manufacturing microstructured products.

decision making is that it promotes creativity by removing entanglements between the decisions. To capture novel technologies and especially to capture the formation of microstructure, it is important that the methodology links length and time scales and is integrating of disciplines. The methodology must facilitate the invention a process flowsheet based on preliminary estimates of the business opportunity for the product and initial exploratory data and knowledge of the product performance, the product formulation & microstructure, as well as the relevant process chemistry (which may include reaction chemistry, colloid chemistry, crystallography, etc).

One of the guiding principles of conceptual design is that you can't understand the process if you don't understand the chemistry. Another is that the economic performance of an unoptimized flowsheet using the best technology is superior to a highly optimized flowsheet using inferior technology. It has been estimated that for every dollar it costs to correct a problem at the conceptual design stage, it will cost $10 at the flowsheeting stage, $100 at the detailed design stage, $1000 after the plant is built, and over $10,000 to clean up the mess after a failure (Kletz, 1989). Similar guidelines apply in the construction of buildings from the architectural phase to occupancy, as well as in many other areas of engineering.

Product chemistry and formulation have a major impact on the selection of the best process technology. Moreover, the structure of the process flowsheet has a major impact on the key design variables and on the best conditions for performing scientific/formulation experiments. Strong economic performance is the ultimate goal of every project. Therefore, a vital component of successful process development is close cooperation of the business development team with the technical team in all phases of the project, and especially, close integration of process chemists & product formulators with conceptual design engineers.

A successful methodology will be one that can be set-up and implemented rapidly so that the process can be developed simultaneously with the product. This allows for real-time synergies between discovery scientists and engineers that will often lead to a better product *and* a better process. Rapid conceptual engineering also allows for a larger number of alternatives to be considered, thereby increasing the chances of finding the best flowsheet structure before the flowsheet is frozen. The most important benefits of simultaneous product and process development are (1) reduced development time, which leads to faster time to market, and (2) reduced risk.

A successful methodology should, therefore, possess the following characteristics:

(1) It should be based on product performance and value.
(2) It should incorporate the relevant chemistry, including reaction chemistry, colloid chemistry, solid state chemistry, etc.
(3) It should accommodate structure-property-value relations.
(4) Decisions should be based on economics.
(5) It should be quick to set-up and implement.
(6) It should be integrating of disciplines.

Microstructured Liquids

Meeuse et al. (2000) published the first systematic approach to design manufacturing systems for the production of microstructured liquids. Their methodology is divided into Levels based on Douglas's hierarchical decomposition procedure. A brief summary of the approach is:

Level 0: Input Information

The input information is divided into two classes, basis of design, and physical properties. The basis of design consists of process targets and constraints, the desired microstructure, a description of the desired physical chemical transformations and cost data. The physical property information need not all be specified at this level. Data related to finer degree of detail can be given as needed at later levels.

Level 1: Processing Structure

The processing structure is determined, resulting in transformation blocks. All physical chemical transformations which change the chemical composition or microstructure of the product and which occur under the same conditions are grouped together in one block. Therefore, transformations like emulsification, crystallization, and reaction are grouped in separate blocks.

Level 2: Plant Input/Output Structure

It is first determined where each ingredient is added to the process. An Ingredients Table is created, describing the function and the place of each ingerdient in the final microstructure of the product. Overall mass balances are performed, resulting in capacity requirements for the separate processing blocks identified in Level 1. Split ratios of feed distributions, and recycles are also determined at this level.

Level 3: Task Structure

Each block is decomposed into sub-systems, and each sub-system is assigned a particular functional task.

Level 4: Unit Operations

Specific unit operations are selected to perform the tasks identified in Level 3. Characteristic parameters (e.g., shear rate) and targets are set for each unit operation.

Level 5: Equipment Design

Equipment is designed to meet the targets set in Level 4.

Meeuse et al. apply their approach to the production of mayonnaise and dressings where the key microstructure property is the drop size distribution. More recently, Wibowo and Ng (2001) have developed a detailed design procedure for the manufacture of creams and pastes, where again the drop size distribution plays an important role. The drop size distribution is governed by the physical properties of the materials being mixed as well as the mixing equipment used to create shear. A fundamental question is to determine the attainable drop size distribution for any particular set of materials properties, independent of the mixing equipment used. Answers to this question provide targets for the selection of tasks and equipment in the design procedure. Dhingra and Malone (see Dhingra, 2001) have developed some promising ideas and have obtained encouraging results on this problem using concepts from attainable region theory, which was originally developed for reactor design.

Significant progress is being made on the development of design procedures for microstructured liquid products, and we can expect increasing acceptance of these methods in the future.

Products and Processes Involving Organic Crystals

Crystallization is used here as a typical instance of processes that lead to microstructured solids. Manufacturing systems that make products containing solid particles always include structure-forming steps and often formulation steps. For example, the active ingredient in a pharmaceutical process not only needs to be made and structured (e.g., as a crystal), but it must normally be formulated with other ingredients before it can be sold as a product. Currently, no methodology exists for designing processes that include structure-forming steps and formulation steps involving solids. Particle shape, and the structure of the solid-state polymorph play vital roles in these steps. However, polymorphism, and shape manipulation & control are scientifically in their infancy, although some significant progress has been made in the last decade.

The shape of crystals produced by a process often has a major impact on product quality (functionality) as well as processability. Estimating the shape of crystals during the discovery and conceptual design phases of product & process development is of major value in many cases. Molecular modeling is especially well-suited to addressing these types of predictions because of the natural way that microstructure enters the modeling schemes. In crystallization, for example, the molecules are placed on a lattice by defining an asymmetric unit and a set of symmetry operations that act on this unit to create both the unit cell and a periodic array of lattice points. The Bravais-Friedel-Donnay-Harker, and Attachment Energy models are first-order approaches for predicting crystal morphology and shape. They are very effective at estimating the likely faces on a crystal. Their computer implementations are fast and easy to use, and they have proved to be accurate for predicting vapor-grown crystal shapes. These methods also yield

geometric and energetic data that may be useful as input to more detailed kinetic models. The main drawback of these approaches is their inability to account for effects of solvent and other process conditions (i.e., impurities, supersaturation). For example, the experimentally observed shape of succinic acid crystals grown from water is hexagonal plates, whereas the crystals grow as needles out of isopropanol.

The recent approaches of Liu and Bennema (1996), and Winn and Doherty (1998) are the first attempts at using detailed kinetic theory for crystal shape prediction. Figure 2 shows the shape of succinic acid crystals grown from water, and from isopropanol predicted by this new modeling approach. The results are in good agreement with experiment. Both models recognize the significance of interfacial phenomena in crystal shape modeling, and lead the way for future developments, such as new simulation and/or group contribution methods for interfacial free energy prediction. In spite of these successes in predicting the shape of organic materials grown from solution there are still no published methods for the simultaneous prediction of particle size and shape, nor are have any of these prediction schemes been incorporated into a design methodology. This is fertile ground for process research.

In order for the shape prediction models to be of wide applicability they must be improved to cover a broader design space. Some of the key areas for future experimental and modeling research are:

Mixed Solvents: Crystals grown from a mixture of two or more solvents can have different characteristics than

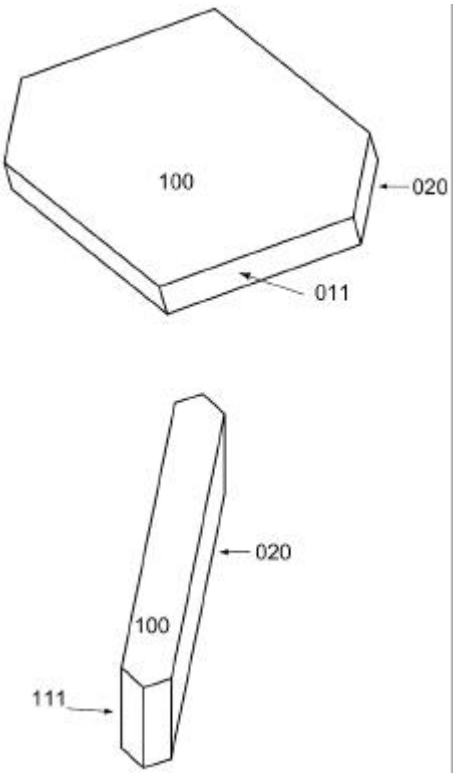

Figure 2. Predicted shape of succinic acid crystals grown from water (top), and isopropanol (bottom).

those grown from any one of the solvents alone. This effect is especially significant if the solute has very different solubility in each solvent. There is great potential for performing modeling studies for mixed solvents.

Hydrogen Bonds & Growth Unit: Identification of the nature of the growth unit that incorporates in the growing crystal faces is an important factor in morphology. Several researchers have discussed pre-condensation in the solution phase to form dimers or other precursors, as well as the need to account for this effect in morphological modeling Hydrogen bonds in the solute and/or solvent molecules play an important role. However, there is still a need for better theories and models for predicting growth units in solution crystallization.

Polymorphs: Polymorphs have always been of interest in crystallization, but they have become a critically important factor in pharmaceutical production and registration because of recent FDA requirements. Different polymorphs have different crystal structures, optical properties, dissolution rates, shapes and interfacial properties. Thus, models of solution-crystal interactions might be able to predict polymorph selection and/or transition. Systematic studies along these lines would be of great practical interest.

Chiral Separations: Single-enantiomer product molecules are a rapidly growing sector of the pharmaceutical industry, and crystallization is one of the key technologies for chiral selection. Crystals of the racemate have different structures than the individual enantiomers. As with polymorphism, interfacial phenomena may influence enantiomeric selectivity, and the challenge is to develop technology, and protocols (aided by modeling) to produce single enantiomer products.

Process Modeling: An important and challenging area for chemical engineering research is to link interfacial models, capable of capturing the above effects, to process models. Such models would allow for novel designs and operating protocols to be developed systematically before they are tested experimentally. This is one of the ways that simultaneous product and process development contributes to faster development times and faster time to market.

Conclusions

In the last two decades there has been an explosion of new methods and models in support of conceptual process design. Most of this activity has focused on classical models for chemical and petrochemical process systems. However, there is tremendous scope for application of new design methodologies for simultaneous product and process development in those sectors of the process industries that make microstructured products. For the most part these methodologies still need to be invented. They are expected to be rooted more firmly in chemistry than the existing methods for chemical process systems, and there will be a growing reliance on molecular models in support of the new design methodologies. The expected benefits of a systematic approach to simultaneous product and process development are reduced development time (faster time to market) and reduced risk.

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