1

Integrated Chemical Product-Process Design: CAPE Perspectives

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1.1

Introduction

Chemical process design typically starts with a general problem statement with respect to the chemical product that needs to be produced, its specifications that need to be matched, and the chemicals (raw materials) that may be used to produce it. Based on this information, a series of decisions and calculations are made at various stages of the design process to obtain first a conceptual process design, which is then further developed to obtain a final design, satisfying at the same time, a set of economic and process constraints. The important point to note here is that the identity of the chemical product and its desired qualities are known at the start but the process (flow sheet/operations) and its details are unknown.

Chemical product design typically starts with a problem statement with respect to the desired product qualities, needs and properties. Based on this information, alternatives are generated, which are then tested and evaluated to identify the chemicals and/or their mixtures that satisfy the desired product specifications (qualities, needs and properties). The next step is to select one of the product alternatives and design a process that can manufacture the product. The final step involves the analysis and test of the product and its corresponding process. The important points to note here are that (1) the identity of the chemical product is not known at the start but the desired product specifications are known, and (2) process design can be considered as an internal subproblem of the total product design problem in the sense that once the identity of the chemical product has been established, the process and/or the sequence of operations that can produce it is determined. Note also that after a process that can manufacture the desired chemical product has been found, it may be necessary to evaluate not only the product but also the process in terms of environmental impact, life cycle assessment and/or sustainability.

From the above descriptions of the product and process design problems, it is clear that an integration of the product and process design problems is possible and that such an integration could be beneficial in many ways. For example, in chemical

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product design involving high value products where the reliability of the chemical product is more important than the cost of production, product specifications and process operations are very closely linked. In pharmaceutical products, there is a better chance to achieve success the first time with respect to their manufacture by considering the product-process relations. In the case of bulk chemicals or low-value products, the use of product-process relations may be able to help obtain economically feasible process designs. In all cases, issues related to sustainability and environmental constraints (life cycle assessment) may also be incorporated.

As pointed out by Gani (2004a), integration of the product and process design problems can be achieved by broadening the typical process design problem to include at the beginning, a subproblem related to chemical product identification and to include at the end, subproblems related to product and process evaluation, including, lifecycle and/or sustainability assessments. Once the chemical product identity has been established, Harjo et al. (2004) proposes the use of a product-centric integrated approach for process design. Giovanoglou et al. (2003), Linke and Kokossis (2002) and Hostrup et al. (1999) have developed simultaneous solution strategies for product-process design involving manufacture of bulk chemicals, while Muro-Sune et al. (2004) have highlighted the integration of chemical product identification and its performance evaluation. In all cases, integration is achieved by solving simultaneously some aspects of the individual product and process design problems. Recently, Cordiner (2004) and Hill (2004) have highlighted issues related to product-process design with respect to agrochemical products and structured products, respectively. Issues related to multiscale and chemical supply chain have been highlighted by Grossmann (2004) and Ng (2001).

The objective of this chapter is to provide an overview of some of the important issues with respect to integrated product-process design, to highlight the need for a framework for integrated product-process design by employing computer-aided methods and tools, and to highlight the perspectives, challenges, issues, needs and future directions with respect to CAPE/PSE related research in this area.

1.2
Design Problem Formulations

In principle, many different chemical product-process design problems can be formulated. Some of the most common among these are described in this section together with a brief overview of how they can be solved.

1.2.1
Design of a Molecule or Mixture for a Desired Chemical Product

These design problems are typically formulated as, given the specifications of a desired product, determine the molecular structures of the chemicals that satisfy the desired product specifications, or, determine the mixtures that satisfy the desired product specifications (see Fig. 1.1).

In the case of molecules, techniques known as computer-aided molecular design (CAMD) can be employed, while in the case of mixtures, techniques known as computer aided mixture-blend design (CAM^{b}D) can be employed. More details on CAMD and CAM^{b}D can be found in Achenie et al. (2002) and Gani (2004a,b). These two problems are also typically known as the reverse of property prediction as product specifications defined in terms of properties need to be evaluated and matched to identify the feasible alternatives (molecules and/or mixtures). This can be done in an iterative manner by generating an alternative molecule or mixture and testing (evaluating) its properties through property estimation. This problem (molecule design) is mainly employed in identifying chemicals that are added to the process, such as solvents, refrigerants and lubricants that may be used by the process to manufacture a chemical product. In the case of mixture design, petroleum blends and solvent mixtures are two examples where the product is designed without process constraints.

1.2.1.1
Examples of Solvent Design

Consider the following process-product design problems where solvent design has an important role. The production of an active ingredient in the pharmaceutical industry needs the addition of a new solvent to an existing solvent-solute (reactant) mixture such that solubility is increased, and thereby the conversion is achieved. The new solvent must be totally miscible with the existing solvent (water) and must also be inert to the reactant. First determine all compounds that are totally miscible with water (use either a database or predict water miscibility). Next, screen out those that may react with the solute (this can be checked through the calculation of the chemical equilibrium constant). Next, identify those that will most likely dissolve the solute (this can be checked through the calculation of solubility). For this problem, alcohols, ketones, glycols are likely candidates.

Consider also the following problem: it is necessary to design/select an alternative solvent to remove oleic acid methyl ester, which is a fatty acid used in treatment of textile, rubber and waxes. The alternative solvent must be better than diethyl ether and chloroform in terms of safety and environmental impact while having solubility properties as good as the known solvents. Also, it must be liquid at temperatures between 270 K to 340 K. Searching of a compound that is acyclic (and containing only C, H and O atoms) that has a melting point below 270 K and boiling point above 340 K, has a Hildebrand solubility parameter that is ± 16.95 MPa$^{1/2}$, and an octanol partition coefficient less than 2 generates the following candidates: 2-heptanone, 3-hexanone, methyl isobutyl ketone, isopryl acetate and many more.

Interesting examples of application of CAMD in the agrochemicals, materials and pharmaceutical industries can be found in the edited monograph by Reynolds, Holloway and Cox (1995).

1.2.2
Design of a Process

These design problems are typically formulated, given the identity of a chemical product plus its specifications in terms of purity and amount and the raw materials that should be used, and determine the process (flow sheet, condition of operations, etc.) that can produce the product (see Fig. 1.1).

This is a typical process design problem, which now can be routinely solved (see for example, textbooks on chemical process design) with CAPE methods/tools when the chemical product is a low-value (in terms of price) bulk chemical. The optimal process design for these chemical products is usually obtained through optimization and process/operation integration (heat and mass integration) in terms of minimization of single or multiparametric performance function. For high-value chemical products, however, a more product-centric approach is beneficial, as pointed out by Harjo et al. (2004), Fung and Ng (2003) and Wibowo and Ng (2001).

1.2.2.1
Examples of Product-Centric Process Design

Harjo et al. (2004) have recently developed a systematic method for product-centric process design and illustrated the application of their method through the design of processes for the manufacturing of phytochemical (plant-derived chemical) products. Harjo et al. (2004) provide a general structure of phytochemical manufacturing processes (Fig. 1.2) and provide a list of heuristic rules for constructing flow sheet alternatives (see Appendix).

As examples of application, Harjo et al. (2004) have considered the manufacturing of carnosic acid, which is known to have a powerful antioxidant activity and can be recovered from popular herbs such as rosemary and sage. One of the flow sheet alternatives generated and evaluated by the authors is presented in Fig. 1.3. The solution of the problem required a number of methods and tools, some of which needed to be developed (property and unit operation models) while others needed to be adopted (such as heuristics for flow sheet generation, flow sheet simulation and evaluation, etc.). Since solvents also play an important role in these processes, methods for solvent search are also needed.

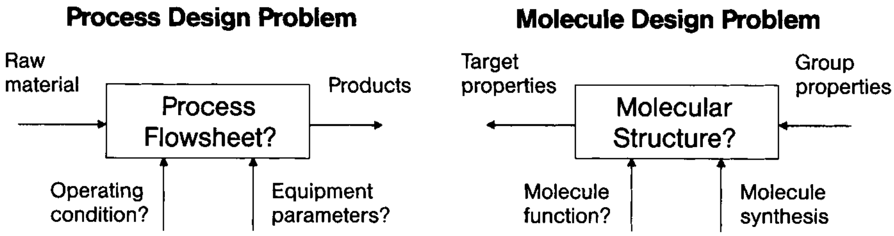

Figure 1.1 Differences between process design and molecule design problems. The question marks indicate what is unknown (needs to be determined) at the start of the design problem solution

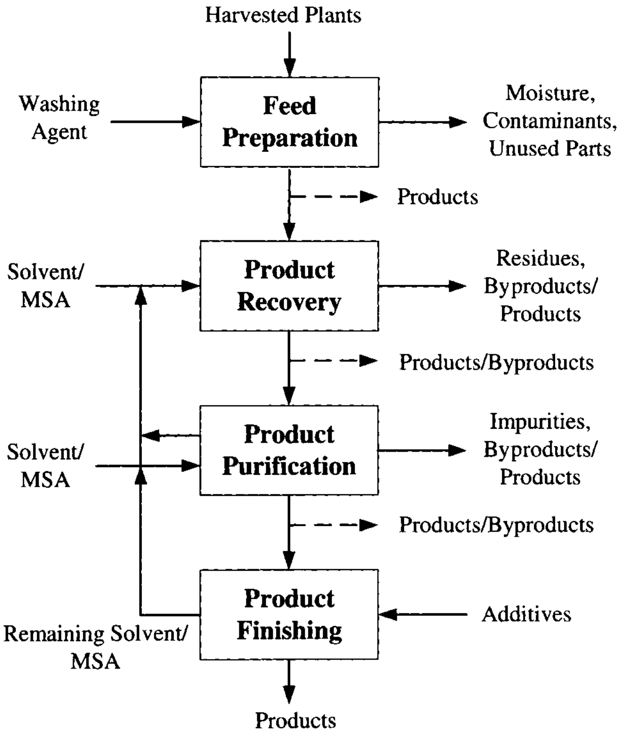

Figure 1.2 The main processing steps for manufacture of phytochemicals (from Harjo et al. 2004, reproduced with permission from IChemE)

1.2.3
Total Design of a New Chemical Product

In these design problems, given, the specifications (qualities, needs and properties) of a desired product, the objective is to identify the chemicals and/or mixtures that satisfy the given product specifications, the raw materials that can be converted to the identified chemicals and a process (flow sheet/operations) that can manufacture them sustainably, while satisfying the economic, environmental and operational constraints.

As illustrated in Fig. 1.4, solution of this problem could be broken down into three subproblems: a chemical product design problem that only identifies the chemicals (typically formulated as a molecule or mixture design problem), a process design part that determines a process that can manufacture the identified chemical or mixture (typically formulated as a process design problem) and a product-process evaluation part (typically formulated as product analysis and/or process analysis problems). In principle, mathematical programming problems can be formulated and solved to simultaneously identify the product and its corresponding optimal sustainable process. The solution of these problems are however not easy, even if the necessary

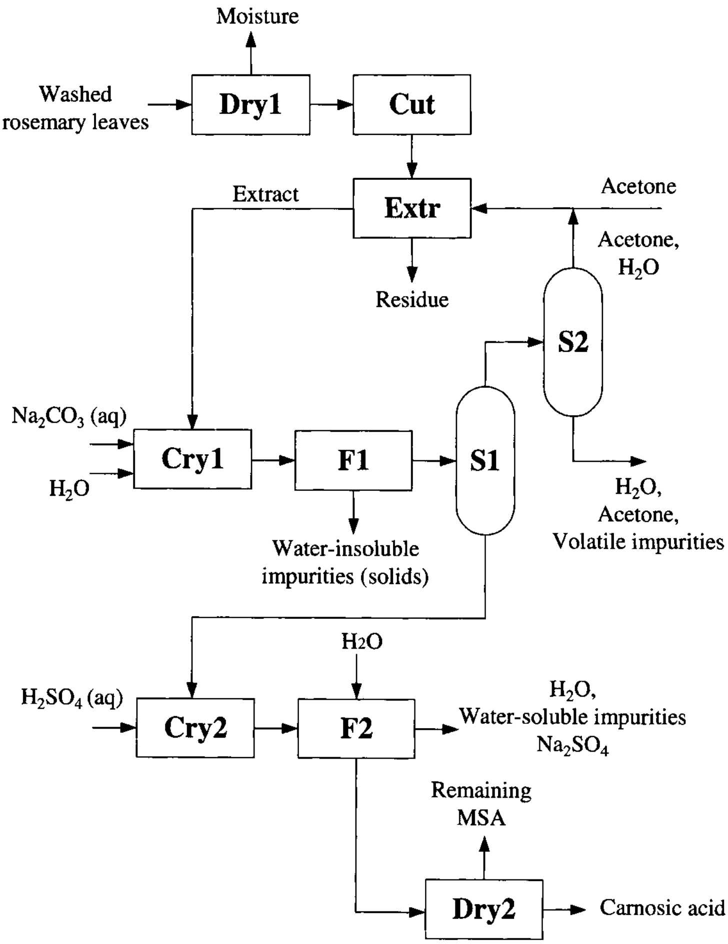

Figure 1.3 Generated process flow sheet for the manufacture of carnosic acid (from Harjo et al. 2004, reproduced with permission from IChemE)

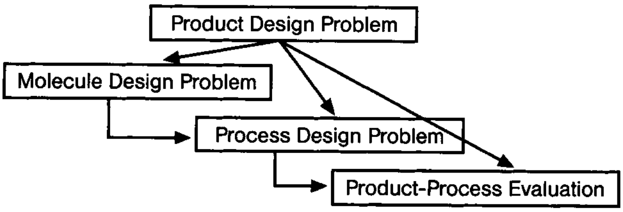

Figure 1.4 Product design problem includes the molecule design and the process design problems

models are available (Gani 2004a). Cordiner (2004) and Hill (2004) also provide examples of problems (formulations and structured products) of this type and the inability of current CAPE methods and tools to handle them.

Numerous examples of new alternatives for the production of known chemical products can be found in the open literature and have been successfully addressed by the CAPE/PSE community. Examples of complete product-process design for new high-value chemical products may not be easy to find because of reasons of confidentiality. Interesting examples of some well known high-value chemical products from the pharmaceutical and specialty chemical industries can however be found, e.g., design and manufacturing of penicillin (Queener and Swartz 1979), and production of intracellular protein from recombinant yeast (Kalk and Langlykke 1985).

1.2.4
Chemical Product Evaluation

In these problems, given a list of feasible candidates, the objective is to identify/select the most appropriate product based on a set of product-performance criteria.

This problem is similar to CAMD or CAM^{b}D except for the step for generation of feasible alternatives. Also, usually the product specifications (quality, needs, and properties) can be subdivided into those that can be used in the generation of feasible alternatives and those that can be used in the evaluation of performance. A typical example is the design of formulated products (also known as formulations) where a solvent (or a solvent mixture) is added to a chemical product to enhance its performance. Here, the feasible alternatives are generated using solvent properties while the final selection is made through the evaluation of the product performance during its application. Consider the following problem formulations:

- Select the optimal solvent mixture and the paint to which it must be added by evaluating the evaporation rate of the solvent when a paint product is applied (Klein et al. 1992).
- Select the pesticide and the surfactants that may be added by evaluating the uptake of the pesticide when solution droplets are sprayed on a plant leaf (Munir 2005).
- Select the active ingredient (AI) or drug/pesticide product and the microcapsule encapsulating it by evaluating the controlled release of the AI (Muro-Sune et al. 2005).
- Select solvent mixtures for crystallization of a drug or active ingredient (Karunanithi et al. 2004).

In all the above design problems, the manufacturing process is not included but instead, the application process is included and evaluated to identify the optimal product.

Consider the following product evaluation problem from the agrochemical industry. A pesticide product consisting of an active ingredient and a surfactant and other additives need to be evaluated in terms of which surfactant can be added to the system to enhance the uptake of the AI into the plant from the water droplets sprayed on the leaf surface. Solution of this problem requires property models that can predict the solubility of the AI in the water plus surfactants mixture, the diffusion of the AI through the leaf and into the plant, the evaporation of the water and many more. A modeling framework able to generate the necessary model for evaluation of the specified problem has been proposed recently by Muro-Sune et al. (2005). Through an integrated set of methods, models, and tools it is possible to not only evaluate the formulated product through its performance (in terms of uptake rate) but also find the best combination of AI, surfactant and plant that provides an improved product.

1.2.5
Chemical Process Evaluation

These problems are formulated typically, given the details of a chemical product and its corresponding process, to perform a process evaluation to improve its sustainability.

To perform such analysis, it is necessary to have a complete design of the process (mass balance, energy balance, condition of operations, stream flows, etc.) as the starting point and new alternatives are considered only if the sustainability indices are improved. Here, the design (process evaluation) problem should also include retrofit design. Uerdignen (2003) and Jensen et al. (2003) provide examples of how such analysis can be incorporated into an integrated approach by exploiting product-process relations. Note that the choice of the product and its specifications, the raw materials, the process fluids (for example, solvents and heating/cooling fluids), the by-products, conditions of operation, etc., affect the sustainability indices.

1.3
Issues and Needs

Three issues and needs with respect to integrated product-process design are considered in this chapter, namely, the issue of models and the understanding of the associated product-process complexities, the issue of integration, and the issue of problem definition.

1.3.1
The Need for Models

According to Charpentier (2003), over fourteen million different molecular compounds have been synthesized and about one hundred thousand can be found on the market. Since however, only a small fraction of these compounds are found in nature, most of them will be deliberately conceived, designed, synthesized and manufactured to meet human needs, to test an idea or to satisfy our quest for knowledge. The issue/need here is the availability of sufficient data to enable a systematic study leading to the development of appropriate mathematical models. This is particularly true in the case of structured products where the key to success could be to first identify the desired end-use properties of a product and then to control product quality by controlling microstructure formation. Another feature among product-process design problems is the question of systems with different scales of time and size.

For integration of product-process design, it is necessary to organize scales and complexity levels in order to understand and describe the events at the nano- and microscales and to better convert molecules into useful products. The relation between length and time scales is very nicely illustrated through Fig. 1.5, which is adapted from Charpentier (2003). Figure 1.6 highlights the relationship between scales (related to the product) and events (phenomena, operation, application, etc., related to the process).

Examples of multiscale modeling for product-process design can be found in structured products and their manufacture, such as polymers by polymerization and solid crystals by crystallization. In polymerization, the nanoscale is used in kinetics, the microscale for mass and energy transport, the mesoscale for particle-particle and particle-wall interactions, the macroscale for global polymerization reactor behaviour, and the megascale for reactor runaway analysis and energy consumption analy-

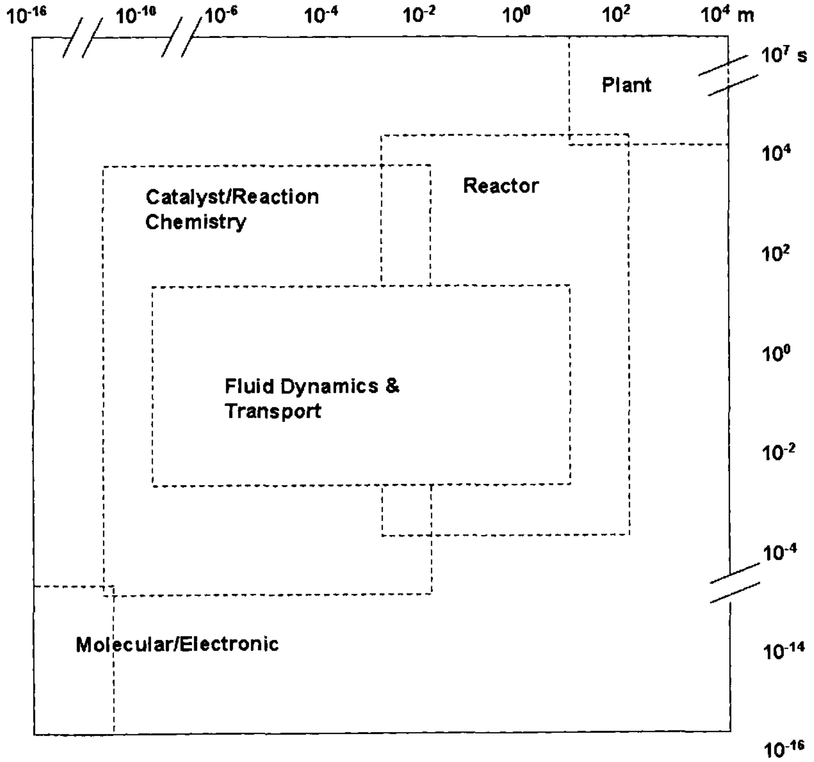

Figure 1.5 Length and time scale covered by multiscale approach

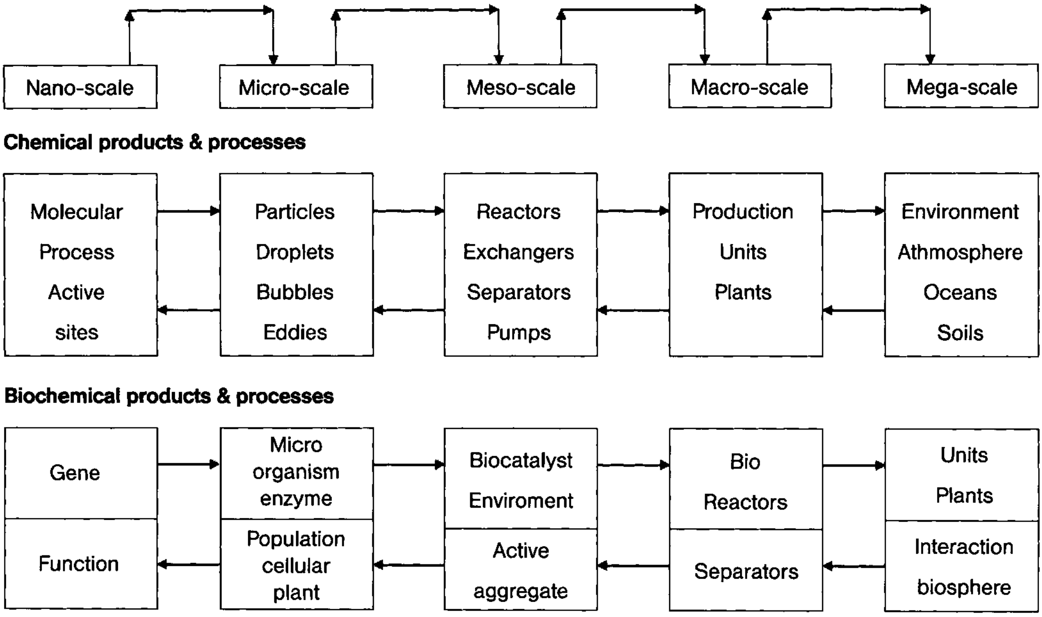

Figure 1.6 Scales and complexity in chemical and biochemical product-process engineering

sis. For a biochemical process, the nanoscale may be used for molecular and genomic processes and metabolic transformations, the microscale is used for enzyme and integrated enzyme systems, the mesoscale is used for the biocatalyst and active aggregates, macroscale and megascales are used for bioreactors, units and plants involving interactions with the biosphere (Charpentier 2003).

1.3.2
The Need for Integration

According to IMTI (2000), integrated product/process development is the concurrent and collaborative process by which products are designed with appropriate consideration for all factors associated with producing the product. To make product right the first time and every time, product and process modeling must support, and be totally integrated with the design function, from requirements capture through prototyping, validation and verification, and translation to manufacture.

Another issue/need is the increasing complexity of new chemical products and their corresponding technologies, which provide opportunities for the CAPE community to develop/employ concurrent, multidisciplinary optimization of products and processes. Through these methods and tools, the necessary collaborative interaction between product designers and manufacturing process designers early in the product realization cycle can be accomplished. Few collaborative (design) tools are available to help turn ideas into marketable products, and those that are available are technology and product-specific. Optimizing a product design to meet a set of requirements or the needs of the different production disciplines remains a manually intensive, iterative process whose success is entirely dependent on the people involved.

1.3.3
Definition of Product Needs

Good understanding of the needs (target properties) of the product is essential to achieve "first product correct", even though it may be difficult to identify the product needs in sufficient details to provide the knowledge needed to design, evaluate and manufacture the product.

1.3.4
Challenges and Opportunities

Based on the above discussion, a number of opportunities have been identified by IMTI (2000), which are summarized below:

Definition of Product-Process Needs (Design Targets)

- Provide knowledge management capability that captures stakeholder requirements in a complete and unambiguous manner.
- Provide modeling and simulation techniques to directly translate product goals to producibility requirements for application to product designs.

Methods/Tools for Product-Process Synthesis/Design

- Provide a first principles understanding of materials and processes to assure that process designs will achieve intended results.
- Provide the capability to automatically create designs from the requirements data and from the characterization of manufacturing processes.
- Provide the capability to automatically build the process plan as the product is being designed, consistent with product attributes, processing capabilities, and enterprise resources.
- Create and extend product feasibility modeling techniques to include financial representations of the product as an integral part of the total product model.

Modeling Systems and Tools

- Provide a standard modeling environment for integration of complex product models using components and designs from multiple sources/disciplines, where any model is completely interoperable and plug compatible with any other model.

Integration

- Provide the capability to create and manipulate product/process models by direct communication with the design workstation, enabling visualization and creation of virtual and real-time prototyped product.
- Provide simulation techniques and supporting processing technologies that enable complex simulations of product performance to run orders of magnitude faster and more cost-effectively than today.
- Provide the capability to simulate and evaluate many design alternatives in parallel to perform fast tradeoff evaluations, including automated background tradeoffs based on enterprise knowledge (i.e., enterprise experience base).
- Provide integrated, plug and play toolset for modeling and simulation of all life cycle factors for generic product types (e.g., mechanical, electrical, chemical).

1.4
Framework for Integrated Approach

The first step to addressing the issues/needs listed above could be to define a framework through which the development of the needed methods and tools and their application in product-process design can be facilitated. Integration is achieved by incorporating the stages/steps of the two (product and process) design problems into one integrated design process through a framework for integration. This framework should be able to cover various product-process design problem formulations, be able to point to the needed stages/steps of the design process, identify the methods and tools needed for each stage/step of the design process and finally, provide efficient data storage and retrieval features. In an integrated system, data storage and retrieval are very important because one of the objectives for integration is to avoid duplication of data generation and storage. The design problems and their connec-

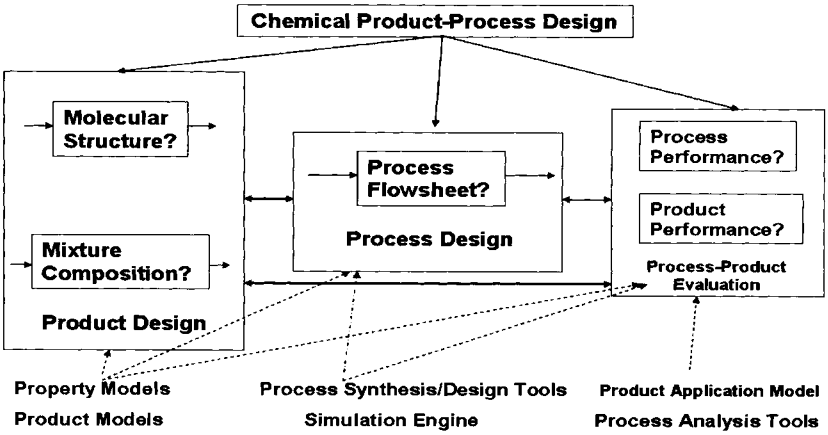

Figure 1.7 Integration of product-process design (see Table 1.1 for data flow details)

tions are illustrated through Fig. 1.3. The various types of design problems described above can be handled by this framework by plugging the necessary methods and tools into it. One of the principal objectives of the integration of product-process design is to enable the designer to make decisions and calculations that affect design issues related to the product as well as the process. The models and the types of models needed in integrated product-process design are also highlighted in Fig. 1.7. In the sections below, the issues of models and data flow and workflow in an integrated system are briefly discussed.

1.4.1
Models

One of the most important issues and needs related to the development of systematic computer-aided solution (design) methodologies are the models. For integrated product-process design, in addition to the traditional process and equipment model, product models and product-process performance models are also needed. A product model characterizes all the attributes of the product while a product-performance model simulates the function of the product during a specific application. Figure 1.8 illustrates the contents and differences among the process, product and product-performance models. Constitutive (phenomena) models usually have a central role in all model types.

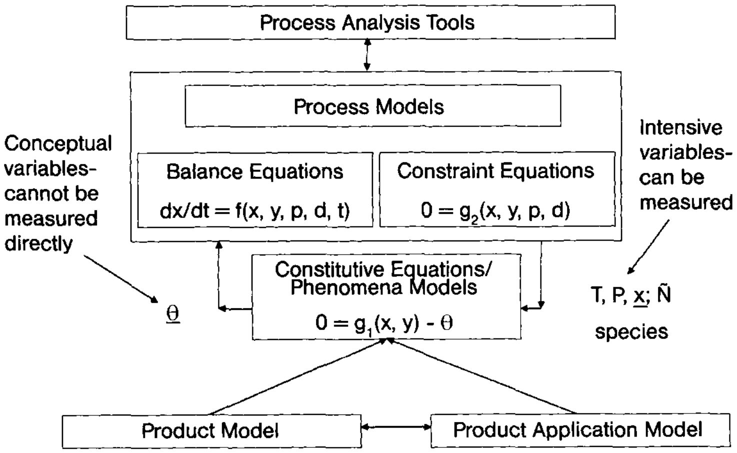

Figure 1.8 Different types of models and their connection to each other

1.4.2
Data Flow and Workflow

The data flow related to the framework for integrated product-process design is highlighted through Table 1.1, where the input data and output data for each design (sub)problem is given.

As highlighted in the problem formulation section, the workflow for various types of design problems is different and needs to be identified. In general terms, however, the following main steps can be considered (note that, as discussed above, some of these steps may be solved simultaneously):

- Define product needs in terms of target (design) properties.
- Generate product (molecule, mixture, formulation, etc.) alternatives.
- Determine if process considerations are important.
  - If yes, define the process design problem and solve it.
  - If no, go directly to the product evaluation (analysis) step.

Table 1.1 Data flow for each design problem

Input data	**Problem type**	**Output data**
Building blocks for molecules, target properties and their upper/lower bounds and/or goal values	Molecular design (CAMD)	Feasible molecular structures and their corresponding properties
List of candidate compounds to be used in the mixture, target properties and their upper/lower bounds and/or goal values at specified conditions of temperature and/or pressure	Mixture design (CAMbD)	List of feasible mixtures (compounds and their compositions) and their corresponding properties
Desired process specifications (input streams, product specifications, process constraints, etc.)	Process design/synthesis (PD)	Process flow sheet (list of operations, equipments, their sequence and their design parameters)
Desired separation process specifications (input streams, product specifications, process constraints, etc.) and desired (target) solvent properties	Process solvent design	Process flow sheet (list of operations, equipments, their sequence and their design parameters) plus list of candidate solvents
Details of the molecular or formulated product (molecular structure or list of molecules and their composition and their state) and their expected function	Product evaluation	Performance criteria
Details of the process flow sheet and the process (design) specifications	Process evaluation	Performance criteria, sustainability metrics

Table 1.2 List of methods/algorithms and tools/software that may be used for each problem (design) type

Problem type	Method/Algorithm	Tools/Software
Molecular and mixture design (CAMD)	Molecular structure generation Property prediction and database Screening and/or optimization	ProCAMD
Process design/synthesis (PD)	Process synthesis/design Process simulation/optimization Process analysis	ICAS (PDS, ICAS-sim, PA)
Process solvent design	CAMD methods/tools Process synthesis/design Process simulation/optimization Process analysis	ICAS (ProPred, ProCAMD, PDS, ICAS-sim, PA)
Product evaluation	Property prediction and database Product-performance evaluation model Model equation solver	ICAS (ProPred, ICAS-utility, MoT)
Process evaluation	Process synthesis/design Process simulation/optimization Process analysis	ICAS (ICAS-sim, ICAS-utility; MoT, PA)

- Analyze the process in terms of a defined set of performance criteria.
- Analyze the product in terms of a defined set of performance criteria.

In Table 1.2, the methods/algorithms and their corresponding tools/software are listed. Under tools/software, only tools developed by the author and coworkers have been listed (see the tools and tutorial pages at www.capec.kt.dtu.dk/Software/).

Examples of application of the tools listed above are not given in this chapter but can be found in several of the referenced papers.

1.4.3

Simultaneous Molecular and Flow Sheet Design

Design of chemical products is often described as the design of molecules and their mixtures with desired (target) properties and specific performance, as drugs, pesticides, solvents or food products. Molecules likely to match the target properties and performance are identified, usually in experiment-based trial and error solution approaches. In product-centric process design, it is necessary to match a set of target performance criteria for the process, usually through process simulation. For process design, alternative process flow sheets can be generated through simulation-based synthesis/design methods, where simulation is mainly used to evaluate and test alternatives. Systematic methods for generation of process alternatives are either rule-based or mathematical optimization-based.

Group contribution methods, which provide the basis for molecule and mixture design, can also be applied in process design. That is, in the same way functional groups are defined to represent molecules and to estimate their properties, process groups are also defined to represent process flow sheets and to estimate their operational properties. Therefore, if a table of process groups representing a wide range of operations can be established, the technique of CAMD can be adapted to computer-

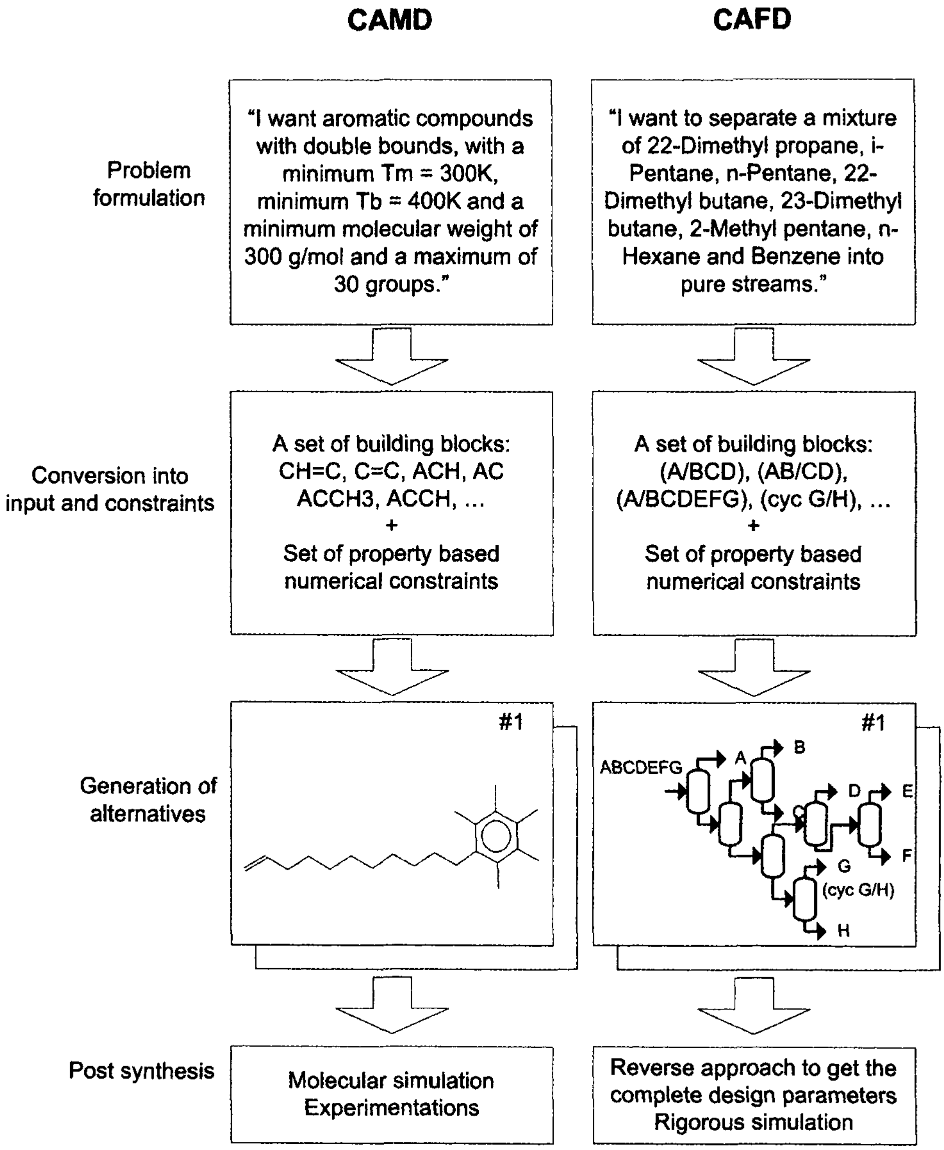

Figure 1.9 Common framework overview (from d'Anterroches et al. 2005, reproduced with permission from IChemE)

aided flow sheet design (CAFD), so that CAMD and CAFD can both be used for modeling, synthesis and design. Also, since CAMD can generate and evaluate thousands of molecules within few seconds of computer time, CAFD would also be able to generate numerous process alternatives without any loss of accuracy or application range. d'Anterroches et al. (2005) has developed a group contribution-based method for simultaneous molecular and mixture design. Figure 1.9 illustrates the features of a common framework for CAMD and CAFD.

1.5
Conclusion

As pointed out by Cordiner (2004), Hill (2004), and the referenced papers by Ng, even though the primary economic driver for a successful chemical product is speed to market, this does not mean that process design is not strategically important to these products. The important questions to ask (to list a few) pertain to the chemical product, how they will be manufactured, how sensitive is product quality related to cost and production, where they will be used or applied, how their performance will be evaluated and, how long a period will they be sustainable? Obviously, the answers to these questions would be different for different products and consequently, the methods and tools to be used during problem solution will also be different. Many opportunities exist for the CAPE/PSE community to develop systematic model-based solution approaches that can be applied to a wide range of products and their corresponding processes. It is the study through these model-based solution approaches that will point out under what conditions the process or operational issues become important in the development, manufacture and use of a chemical product. Successful development of model-based approaches will be able to reduce the time to market for one type of products, reduce the cost of production for another type of product, reduce the time and cost to evaluate another type of product. The models, however, need to be developed through a systematic data collection and analysis effort, before any model-based integrated product-process tools of wide application range can be developed. Finally, it should be noted that to find the magic chemical product, these computer-aided model-based tools will need to be part of a multidisciplinary effort where experimental verification will have an important role and the methods/tools could be used to design the experiments.

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Appendix

Heuristics for constructing flow sheet alternatives (from Harjo et al. 2004, reproduced with permission from IChemE).

Feed Preparation

1. Consider reducing the size of the plant material to 2–5 mm to obtain good performance in industrial scale S-L extraction.
2. Consider using particle size bigger than 0.25 mm in S-L extraction to avoid clogging of the filter.
3. If the plant material is hard and abrasive, consider using size reduction by ball mill, fluid jet mill, or hammer mill.
4. If the plant material is soft and tough or fibrous and woody, consider using size reduction by cutting mill, disk mill, or hammer mill.
5. If the plant material is brittle or crystalline, consider using size reduction by fluid jet mill, hammer mill, or roller crusher.
6. If the plant material is tough, fibrous, and very heat-sensitive, consider using cryogenic size reduction by cutting mill, disk mill, fluid jet mill, or hammer mill.
7. Consider reducing the moisture content of harvested plants to about 10% for a safe storage.

Product Recovery

8. Consider using disk press for mechanical pressing of fibrous materials.
9. Consider using immersion type S-L extraction equipment if the target compounds are in low concentrations, strongly bound, and/or slowly diffusing.
10. Consider using percolation type S-L extraction equipment if the target compounds are in high concentrations, loosely bound, or slightly soluble in the solvent.

Product Purification

11. Whenever possible, consider using the same MSA as in the product recovery step.
12. For heat-sensitive materials, consider separations using L-L extraction, chromatography, or crystallization.
13. Consider using adsorption to separate natural pigments.
14. Consider using chromatography and/or crystallization for the separation of chiral molecules or when multiple single-compound products are desired.
15. Consider using pH swing crystallization for separation of compounds with acidic or basic groups.
16 Consider using large polarity differences between the mobile and stationary phases in reversed-phase chromatography to achieve high selectivity.
17. When handling liquid systems with little density difference, easily emulsified, or short contacting time is required, consider using centrifugal L-L extractors and separators.
18. When handling liquid systems containing suspended solids, easily emulsified, or large capacity, consider using reciprocating-plate L-L extractor columns.

19. When handling liquid systems with high viscosity or large capacity, consider using mixer-settler L-L extractors.
20. If the material has a very steep solubility curve (e.g., very sensitive to temperature), consider using cooling-type crystallizers.
21. If the material has a normal or moderate solubility curve, consider using evaporative-cooling, surface-cooling, or isothermal-evaporative crystallizer.
22. For batch and relatively low capacity processes, or feed with viscous solutions, consider using either plate-and-frame filter presses or leaf filters.
23. For continuous and large capacity processes, consider using either continuous rotary-vacuum-drum filter or continuous rotary-disk filter.

Product Finishing

24. If the feed to be dried is in liquid, suspension, or slurry solution forms, consider using either drum or spray dryers.
25. If the wet granular solids are to be dried, consider using either rotary or tray dryers.
26. Use freeze-drying only for heat-sensitive materials which may not be heated in the ordinary drying or when the loss of flavor and aroma must strictly be avoided.