CAPEC-PROCESS Research Report 2012

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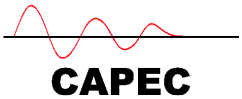
CAPEC-PROCESS Industrial Consortium Research Report – 2012

Rafiqul Gani & John M. Woodley

June 2012



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Preface

This report provides an overview of our research activities and achievements for the period June 2011 to June 2012. An overview of the active research projects is provided in terms of PhD-projects, post-doctoral and other research projects. A brief overview of the CAPEC-PROCESS software is also included in this report.

While CAPEC and PROCESS remain as independent centers, research results from both of the two centers are made available to the member companies of the consortium. In this way, the consortium members get access to a larger number of MSc- and PhD-projects as well as post-docs than before.

During the last 12-months, a number of PhD-projects have been successfully completed, while an equal number of new projects have been started. More specifically, within CAPEC: Carlos Axel Diaz-Tovar (PEC11-23) and Martina Heitzig (PEC12-24); within PROCESS: Yuan Xu, Bodil Voss and Mads Orla Albæk; and jointly within CAPEC-PROCESS: Alicia Roman-Martinez (PEC11-24); and PROCESS-CAPEC: Linfeng Yuan (PEC11-45); Wenjing Fu (PEC11-46); Philip Lutze (PEC12-22), Albert Emil Cervera Padrell (PEC12-23) and Paloma Santacoloma have all successfully defended their PhD-theses. At the same time, new PhD-students (Hemalata Ramesh, Marie Andersson, Laura Snip, Jason Price, Deenesh K. Babi, Hande Bozkurt, Larissa P Cunico, Peam Cheali and Marina Fedorova) have started their PhD-projects at CAPEC and PROCESS centers while 1 new post-doctoral project was also started (Albert Cervera-Padrell).

Collaborations with our member companies continue to help us to apply our research results to interesting industrial problems, to get valuable feedback on our methods & tools and to plan our future projects. Collaborations with our friends from academia help us to develop more comprehensive CAPE/PSE methodologies and techniques. We appreciate these collaborations and we thank our industrial and academic partners for their valuable contributions. During the last 12-months, we have started projects with AstraZeneca, Syngenta and Alfa-Laval from our consortium members, and, Univ of Lorraine (France), Chulalongkorn Univ-PPC (Thailand), PROSPECT-UTM (Malaysia), Univ of Kansas (USA), Univ of West Virginia (USA) and Auburn Univ (USA) from academia.

We would like to acknowledge the financial support in the form of membership fees from our member companies. We would like to welcome Pfizer Inc (USA) and Janssen Pharmaceutika N V (Belgium) as new consortium members. For funding of PhD and post-doctoral research projects we would like to thank the Danish funding agencies FTP, EFP and ATV and the EC-research programs under FP7. Also, we would like to thank the governments of Malaysia, Brasil and Mexico for sending students with PhD/MSc-scholarships.

Finally, we take this opportunity to thank all co-workers of CAPEC and PROCESS for their hard work and dedication. The research results highlighted in this report are their achievements. This is the 15th year since CAPEC and the industrial consortium was established. At PROCESS Ulrich Kruhne was promoted to Senior Researcher and Mrs. Gitte Nielsen joined as a secretary.

For more information about the CAPEC-PROCESS consortium, please contact Mrs Eva Mikkelsen (eva@kt.dtu.dk), or Mrs. Gitte Nielsen (gnie@kt.dtu.dk).

Rafiqul Gani & John M. Woodley 1 June 2012

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1. Introduction

1.1 The CAPEC Center

Research at CAPEC is organized in terms of six research programs (see Fig 1.1). At the inner most level (research programs A, B), the topics are related to fundamental research while at the outer most level (E), the topics are related to applied research. In the intermediate levels (C, D), systematic model-based algorithms, methods and tools are developed by employing the results from the inner levels for use in applied research in the outer level. Since all research programs need numerical tools and databases, research program F supplies this need to all levels. The main theme of the research at CAPEC is to manage the complexity in the systematic analysis and solution of a wide range of product-process engineering problems from various industrial sectors.

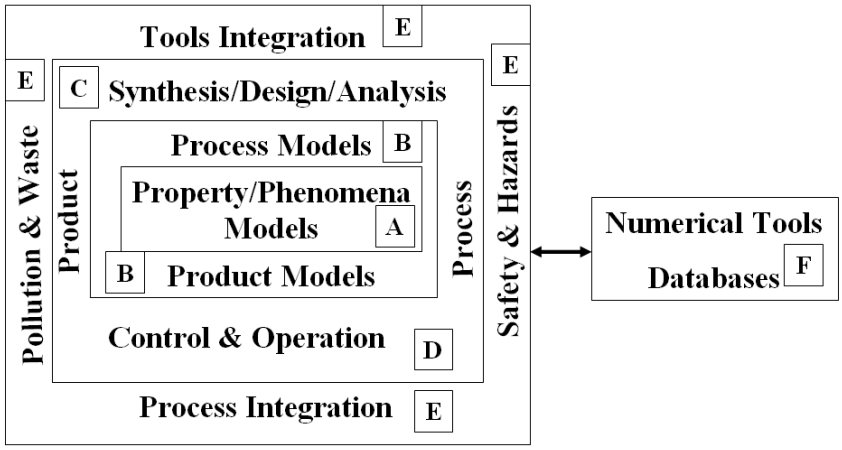


Figure 1.1: Organization of research in CAPEC in terms of research programs

The six research programs are briefly described below:

- *Research Program A – Property and Phenomena Modelling*: deals with theoretical studies of properties (pure component and mixture) of chemical systems and phenomena such as permeability through membranes, reaction kinetics and mass transfer through diffusion. A library of group contribution based models for a wide range of properties of organic chemicals is one of the highlights of program A.
- *Research Program B – Process-Product Modelling and Simulation*: deals with the development of models and model-based simulation systems for prediction of the behaviour and performance of a wide range of chemical and biochemical processes (operating in batch, fed-batch and continuous modes) and a wide range of chemicals based products. A computer-aided modelling system for efficient model development and a collection of process-product models of various types, forms and scales are some of the highlights of program B.
- *Research Program C - Synthesis, Design & Analysis*: deals with the development and use of systematic algorithms, methods and tools for synthesis, design and analysis of chemical and biochemical processes and chemicals based products. Techniques such as computer aided molecular and/or mixture design (CAMD), and, process flowsheet design (CAFD) using the reverse approach are some of the highlights of program C.

- *Research Program D - Process Control, Operation & Monitoring*: deals with the development of use of systematic algorithms, methods and tools for process control, operation and monitoring, including process analytical technologies. Techniques for tuning of controller parameters in model predictive control and methods for design of PAT systems are some of the highlights of program D.
- *Research Program E - Process and Tools Integration*: deals with on-line (process) and off-line (tools) integration as well as safety & hazards, sustainability analysis, and integration of process design-control, process-product design and process-process. Integrated software such as ICAS, virtual process-product design lab, SustainPro and their associated methodologies are some of the highlights of program E.
- *Research Program F - Database and Numerical methods*: since the CAPEC-PROCESS software needs to be self-sufficient in all respects for use by the industrial consortium companies, CAPEC also maintains a library of numerical methods and databases (properties of chemicals and solvents, reaction synthesis, membranes, and analysis equipments). The other research programs benefit from this in terms of data for modelling and improved simulation strategies.

Based on the above, the research objectives of CAPEC is summarized as:

> *Develop computer-aided systems for efficient and reliable process simulation; for systematic synthesis, design and analysis of sustainable chemical products and their manufacturing processes; for robust control, operation and monitoring of processes from principally chemical, petrochemical, pharmaceutical and biochemical industries. The computer-aided systems are to be developed based on fundamental and/or data-based modelling studies that incorporate correlation and estimation of thermo-physical and phase equilibrium properties as well as modelling the underlying principles / behaviour of the process-product. That is, by managing the complexity in a systematic and efficient manner.*

CAPEC's research is focused - while the application horizon is wide (oil and gas, petrochemical, chemical and specialty chemical, pharmaceutical, food and bio industrial sectors) the focus is on the use of a systems approach. CAPEC's strengths in terms of its research focus - pioneering work in certain research areas (such as modelling; methods for synthesis, design and analysis of process as well as products; process and tools integration), industrial collaboration (dissemination of research results through the industrial consortium as well as collaboration with academia), and contacts (ability to influence developments within chemical engineering and CAPE/PSE). More specifically, CAPEC's contribution in the areas of thermodynamic property modelling for process-product design; computer-aided molecular-mixture design for consumer product development; targeted reverse approach for process intensification and integration; systematic computer-aided methods and tools for modelling, design, analysis and control are well known within the CAPE/PSE community.

Through the industrial consortium, CAPEC co-workers have the unique opportunity to get quick and useful feedback on their developed models, methods and tools as well as insights to the current and future needs of the various industrial sectors represented by the consortium members.

The dissemination of the research results of CAPEC is carried out in terms of:

- *Computational Tools*. Predictive models for reliable property estimation for a wide range of chemicals; generic mathematical models for process operation, product performance; computer-aided tools for product-process synthesis & design, etc., are used by leading industries and close to 50 universities from all over the world.
- *Technology*: Developed systematic methodologies for process-product synthesis, design, analysis and control (& operation), simulation strategies, solvent selection (& design), pollution prevention, sustainable process-product alternatives, etc., are routinely used to solve industrial problems and in education.
- *Application*: Industrial case studies, tutorial case studies, technology transfer studies and consulting.

CAPEC is involved in the following large collaborative projects in Denmark and in Europe:

The activities shown in Table 1.1 highlight the scope and significance of the research results available to the CAPEC-PROCESS industrial consortium members in terms of the industries where the developed methods and tools are applicable.

Table 1.1: Scope and significance of CAPEC research results shown in terms of industries where they can be applied (1: Includes also oil & gas industries; 2: includes also specialty chemicals; * Solving problems in process modelling, simulation, design, analysis and control)

CAPEC Research Programs	Application of Research Results in terms of Industry					
	Petro-chemicals[1]	Chem-icals[2]	Pharma-ceutical	Agro-chemical	Bio & Food	Aroma
Models & modelling tools						
Synthesis, design analysis & evaluation						
Control, operation & Monitoring						
Process & tools Integration						
Databases & Numerical Methods						

Well developed methods & tools available*	Available methods & tools can easily be adapted if not directly applicable*	Available methods & tools applicable to only a small number of problems*	Needs development*	Work done during 2011-2012
				More focus given in these areas

Some of the challenges for the future are to use our methods and tools to find alternative routes for the production of important chemical products in the petrochemical and chemical sectors using renewable resources; to retrofit or adapt the current processes for changes to bio-based feed materials; to identify new block/platform chemicals, and, to incorporate in all problem solutions the issues related to energy, water, environment and green chemistry.

- MultiMod project: This is a EC-funded Marie Curie ITN project in the area of multi-diemensional modeling. Together with Alfa Laval, CAPEC has received funding for three PhD-scholarships. The project started in 2009 and ends in 2013. The objective here is to train researchers in the area of modelling.
- OPTICO project: This is a EC-funded research project in the area of modelling and process intensification. CAPEC has received funding equivalent to 48 man-months of funding for researchers. The project started in January 2012 and ends in January 2015. The objective of the project is to develop model based methods and tools in the area of process intensification.
- QNRF: This is a project funded by the Qatar National Priority Research Program. The objective is the design of synthetic fuels and value added chemicals derived from natural gas via combined experimental and process integration methodology. The project officially starts around September of 2012 and ends in 2015 with the Texas A&M University at Qatar, the Texas A&M University at College Station (Texas) and CAPEC as partners.
- EcoDesign MBR: The Danish Council for Strategic Research has founded the EcoDesign MBR Centre in the period from 2010-2016 together with companies and universities. As project partner, CAPEC received funding for 1 PhD and 1 postdoctoral researcher in the area of developing membrane bioreactor(MBR) based technology for wastewater treatment. CAPEC will be developing process modeling to support technology development including design, optimization, operation and control as well as model-based tool for bioprocess scale-up to full-scale applications.
- SWI: Storm- and Wastewater Informatics "SWI" is a strategic Danish Research Project funded for the period of 2008-2012 with an overall aim to close the knowledge gaps within prediction and control of current and future conditions in integrated urban wastewater systems. CAPEC received funding for 1 postdoc. As part of this project, CAPEC also received an industrial PhD funding from FTP the period 2011 – 2014. The project will develop optimizing control for integrated sewer and wastewater treatment plant systems.
- IEA-IETS: This is an EUDP funded project to support Danish participation in IEA-IETS for the period 2011-2013. This is about particiapting in International Energy Agency (IEA) implementing agreement on industrial energy related technologies and systems (IETS). CAPEC has received funding to coordinate a task group on Energy efficient separation systems.

1.2 The PROCESS Center

The Center for Process Engineering and Technology is focused on the development of new and innovative production processes for industry. PROCESS works at the interface of a number of disciplines, including chemical engineering, biotechnology, process engineering and chemistry. The objective is to provide the necessary infrastructure and support to evaluate and implement the next generation of processes in the chemical, bio-based and pharmaceutical sectors in particular. All research is carried out in close collaboration with

industry and work is carried out at three levels, namely: laboratory scale experimental process evaluation; model based evaluation of process technology and pilot-scale process validation. Two demonstration units operate in the pilot facilities (both for immobilized and soluble enzyme reactions at 10-20L scale). Using the results from work at the three levels enables new technology and processes to be evaluated both experimentally and also from the perspective of implementation, including eceonomic and environmental evaluation. The research is divided into 6 research area:

Main research areas:

1. Micro processes – the development of miniaturised unit operations and processes, both to collect data rapidly and in parallel of use for modelling and also to develop process screening tools.

2. Continuous processes – the development of new continuous or semi-continuous processes form batch. New concepts are developed including the creation of gereic process plant.

3. Biocatalytic processes – the development of enzymes (and whole-cell) based processes where high selectivity and mild conditiopns are required. The focus is especially on multi-enzymatic and chemo-enzymatic processes. Downstream processing and product recovery are integrated in all processes.

4. Process intensification and intensified unit operation – development of integrated unit operations (e.g. ISPR) and methods and tools for assessing new operations and processes operating at an intensified level.

5. Process Analytical Technologies (PAT) – development of monitoring and control techniques to allow on-line adjustment of process parameters such that product quality can be maintained. Particular focus is on the phramacutical industry (where the FDA drive such changes).

6. Scale translation – development of techniques for predicting scale-up and scale-down of processes and we as experimental validation.

The PROCESS Center is involved in the following large collaborative projects in Denmark and in Europe:

- Sustainable Biodiesel is a project established in 2008 with the Danish National Advanced Technology Foundation, DTU Management, Novozymes A/S, Aarhus University and Emmelev A/S. It is focused on developing a new enzymatic route to biodiesel.
- Towards Robust Fermentation Processes by Targeting Population Heterogeneity at Microscale is a project established in 2009 with the Danish Council for Strategic Research, DTU Systems Biology, DTU Fotonik, Department of Biology (University of Copenhagen), Department of Biotechnology, Chemistry and Environmental Engineering (Aalborg University), Crystal Fibre A/S, Fermenco ApS and Foss A/S. It is focused on characterization and control of the heterogeneity of a population of microorganisms in a fermentation.

- In the pharmaceutical sector several projects (BIONEXGEN, ENG-BIO, AMBIOCAS and BIOTRANS) sustain the development of the next generation of enzyme based methods for the synthesis of optically pure molecules. These EC-funded projects are with many industrial and academic partners. The Center is also involved in a 5-year project with Lundbeck aiming at moving from batch towards continuous production, Specifically on the development of microbioreactors, PROCESS has initiated a project of the Free Research Council – Technology and Production Sciences (FTP) (Novel greener and lean processes using integrated microfactories).
- A new FP7 project (BIOINTENSE) is in the negotiation phase to start in mid 2012 focused on microscale approached to the rapid development of biocatalytic processes. PROCESS are the project coordinators.
- PROCESS has joined the SANITAS project, an EC-funded project (ITN) with focus on the development of the next generation of modelling and simulation tools for performance evaluation of wastewater treatment plants.

The vision of the Center for Process Engineering and Technology is to provide the necessary support to enable the next-generation of processes to be implemented in industry. In this way the new developments in biotechnology, catalysis and separation science alongside process engineering can be translated into industrial practice. New processes with reduced waste, high efficiency and based on all the principles of sustainability can be developed which will help develop the European industrial sector in the production of chemicals, bio-based materials and chemicals, as well as pharmaceuticals.

1.3 CAPEC-PROCESS Activities

While maintaining their unique center activities, it has been decided to join forces on a set of research topics of mutual interest within the pharmaceutical, agrochemical and bio & food industrial sectors. The interaction between the CAPEC and PROCESS centers at the level of the industrial consortium is illustrated through Figure 1.2. For the industrial consortium, the CAPEC-PROCESS collaboration should result in increased data-knowledge on chemicals based products and their processes, design of the product-process, control-monitoring of the product-process, and, development of more sustainable and "greener" products-processes. The two centers tackle these problems from two different approaches: CAPEC employs a model-based systems approach that also leads to computer-aided tools, while, PROCESS employs a systematic experiment/data based process understanding to perform the necessary process analysis and evaluation. The CAPEC-PROCESS collaboration therefore is able to generate methods and tools that are not only able to provide new innovative product-process designs but can also provide fundamental understanding, analysis and evaluation of the design problem. This is essential for future implementation of these processes in industry.

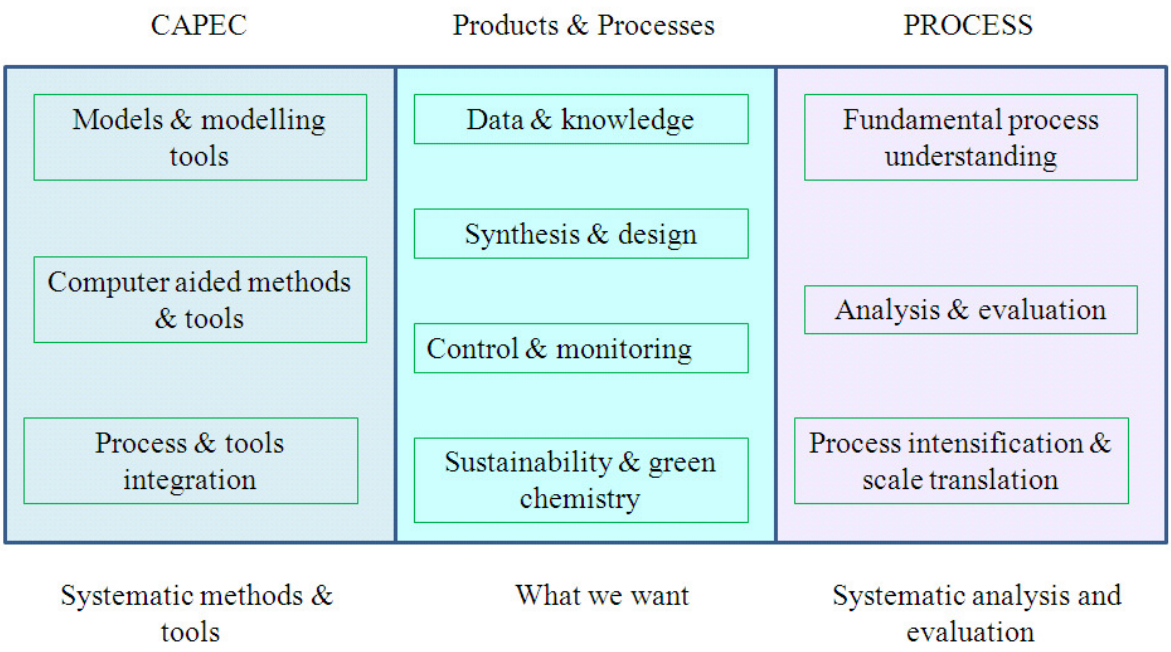


Figure 1.2: Collaboration between CAPEC and PROCESS centers

1.4 Research Highlight

One research project from each center is highlighted below. From CAPEC, its project on computer aided solvent selection and design is highlighted. From PROCESS its project on microtechnology is highlighted. In both these projects, there are collaborations and use of each others results.

CAPEC: Generic solvent selection methods and tool

Solvents are widely used in a number of applications, for example, as separation agents, reaction mediums, cleaning agents and product carriers. The use of solvents may be classified as either required for processing (separation, reaction, cleaning) and/or as part of a chemical-based product (cosmetic products, delivery devices). While there are some solvent selection databases and special software for very specific applications, a comprehensive database and/or framework for the general solvent selection/design problem is lacking. Also, in many instances, solvents are selected from a list mainly by experience (previous experience or expert knowledge) and/or experiment based trial and error. Therefore, a systematic generic approach to solvent selection and design for all types of solvent use is highly desirable, even though it provides some challenges in terms of database management, inclusion of expert knowledge, model-based solvent design and integration of the various methods and tools within a generic framework. Such a systematic approach should ideally be model/data-based, encouraging innovation, and focused on experiment-based verification only as the last step before solvent application. An important additional aspect in solvent selection and design is the consideration of environmental impact, which is a crucial factor in the disposal (or waste) of industrial solvents. That is, the solvent selection and design framework must also incorporate the “Green Chemistry Principles”.

Within CAPEC, a generic computer-aided solvent selection and design framework is being developed (see Figure 1.3). The framework should integrate different methods and tools needed to manage the complexity and solve a wide range of solvent related problems in an efficient, flexible and robust manner. In particular, new models for solubility predictions, multi-level property estimation as well as molecular and solvent blend design, solvents database, and, solution of a wide range of problems from industry should be possible.

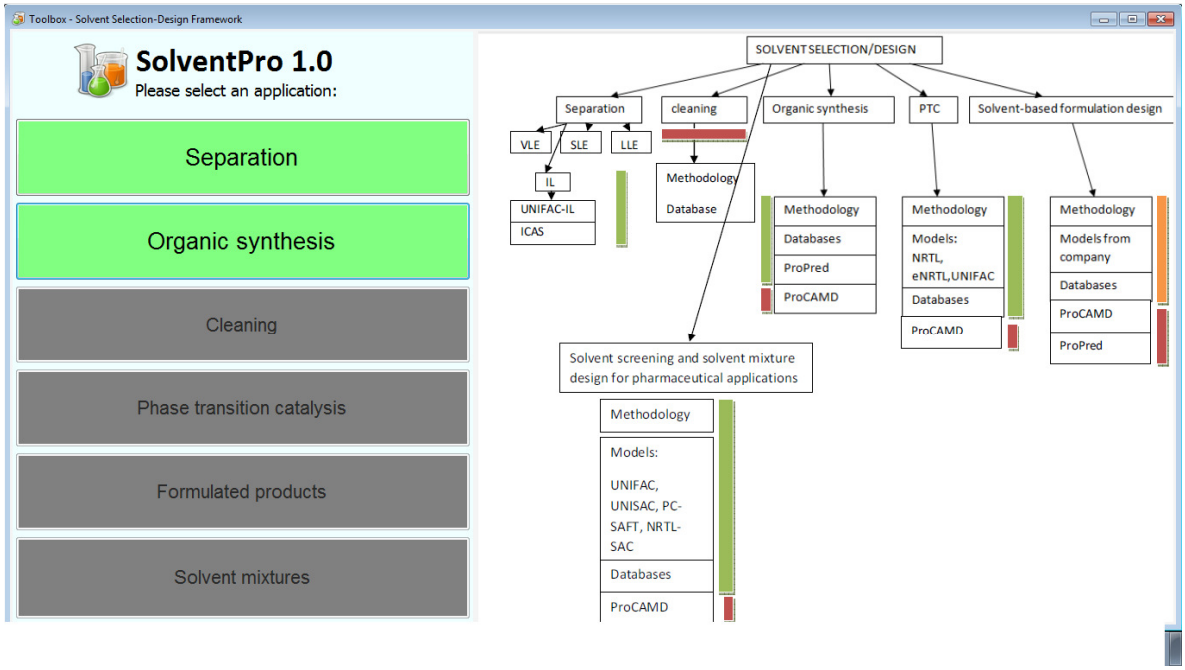


Figure 1.3: A generic computer-aided solvent selection and design framework

The first prototype, SolventPro, based on the computer-aided solvent selection and design framework (see Fig 1.3) is now available for the consortium member companies. It guides users through problem specific templates for various solvent related problems such as, solvents for organic synthesis (including complex reaction systems), solvent-based separations (separations involving vapour-liquid, liquid-liquid and/or solid-liquid equilibrium systems), solvents for phase transfer catalysis (PTC) reactions, solvents for pharmaceutical industry (API solubility), solvents in formulations (as part of cosmetic and other solvent based formulations), and as cleaning agents. The template helps the user by pointing to the essential and desirable steps for different solvent selection and design problems. Experts may, however, use the general interface and create their own template for the types of solvent related problems they usually solve. Among the different tools integrated into SolventPro, there is a solvents database, which currently contains information about more than 1000 organic solvents and their properties, including environmental and transportation properties, and, there are also about 1000 ionic liquids (IL), which may be considered as potential solvents for extraction-based separation processes. The database contains an efficient search engine to find the solvents (organic or IL) and a corresponding method for computer aided molecular-mixture design. Property models library include state of the art group contribution^{plus} based models for pure component as well as mixture property predictions. These predictive models allow the selection and/or design of innovative solvent based processes and/or products. Another feature of the model library is the availability of models needed for solvent performance analysis/verification. For example, models for calculating the driving force diagrams

needed for solvent-based separations; saturation diagrams for solid solubility; controlled release predictions for product delivery; and many more.

PROCESS: Mastering process intensification across scales with help of microtechnology and computational fluid dynamics

Microtechnology has attractd increasing attention over the last years within many research areas. Chemical Engineers are also discovering more and more the opportunities that miniaturized systems offer and therefore it is expected that microtechnology will soon find its way from academia to industry. Microtechnology is based on Microsystems that,

i) use minitue amounts of precious reactants,
ii) have favorable kinetic characteristics,
iii) have superior heat transfer abilities, which allow quasi adiabatic reactions,
iv) allow the performance of physically difficult experiements, which cannot be established in normal scaled experiments.

One issue in microfluidic applications is that it should be possible to calculate the fluid dynamic conditions, for example, with the help of computational fluid dynamic methods and the prediction accuracy of such numerical simulations should be of high quality under laminar flow conditions. In this way, the mathematical complexity of the model formulation is reduced to the solution of the Navier Stokes equation and no turbulence models need to be considered. In Fig 1.4 typical laminar flow conditions are presented in a simulation (a) and an experimental setup (b).

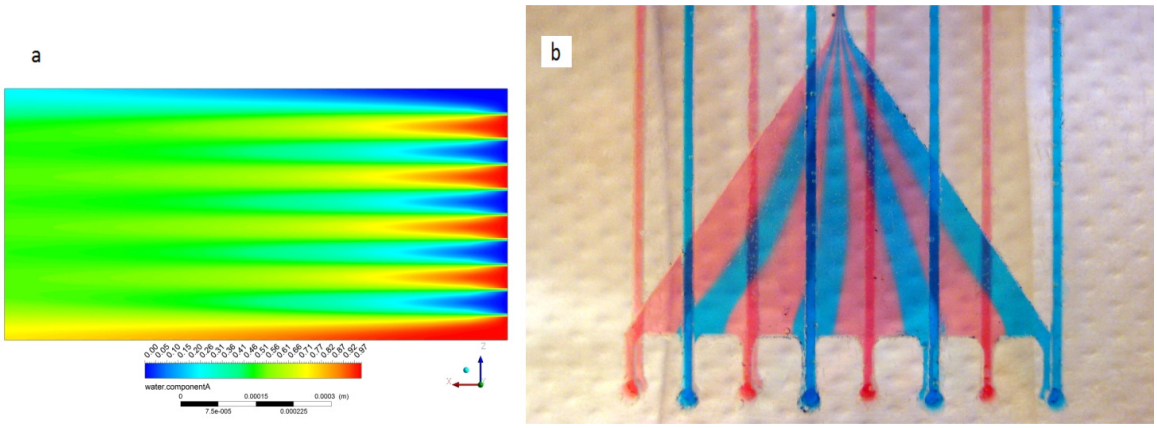


Figure 1.4: (a) CFD simulation of diffusion based mixing in interdigitated microchannels; (b) experimental realisation of the inlet region of a miniaturized reactor

Within PROCESS, the ojective is to develop microtechnology based processes, which use the advantage of micro scaled fluid dynamic properties and their influence on chemical, biochemical and physical interactions. A special emphasis is the integration of different unit operations into a single step process, avoiding such the accumulation of inefficiencies of serial performed processes.

The use of CFD methods coupled with, for example, structured models furhtermore help to predict the process intensification performance across the scales and are placed at the heart of the CAPEC-PROCESS research activities. These activities are acompanied by the use of

modern rapid prototyping fabrication methods as presented in Fig 1.5. In this figure a 3D printer located at the PROCESS laboratories is presented along with a sketched and printed flow cell that is supposed to be used in a NIR spectroscopy setup.

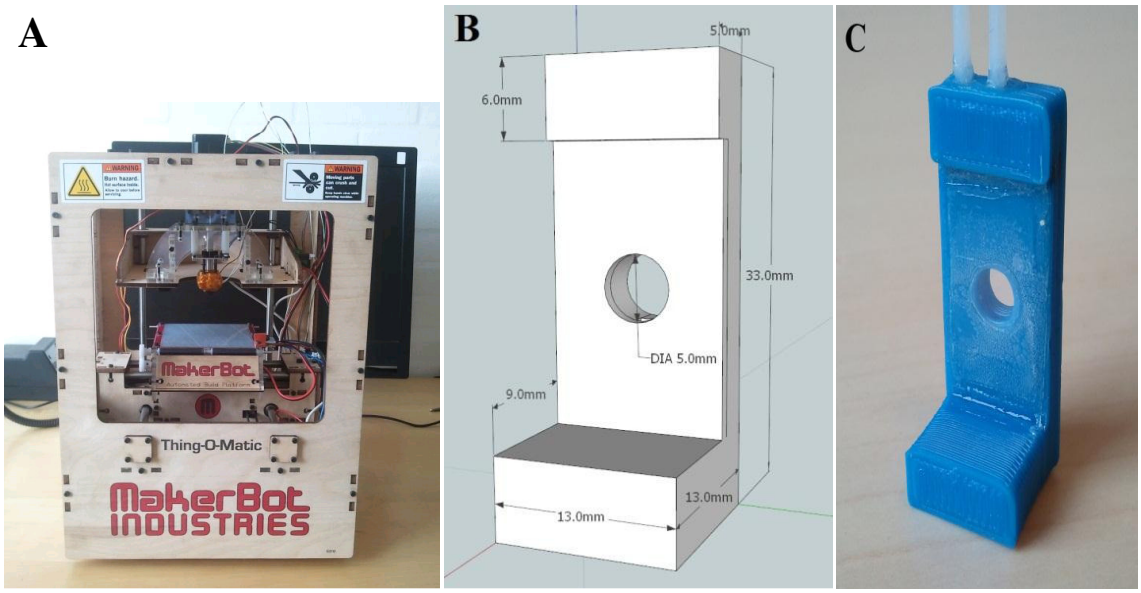


Figure 1.5: A Fused Deposition Modelling 3D printer, B sketch of a NIR flow cell, C Printed NIR flow cell

2. Organization of Activities

The organization of educational and research activities within CAPEC and PROCESS are conducted by the faculty members of the two centers together with the researchers and students associated with them. Figure 2.1 highlights these activities, where it can be noted that the research results coming out of the six research programs of CAPEC-PROCESS are disseminated in education and industry.

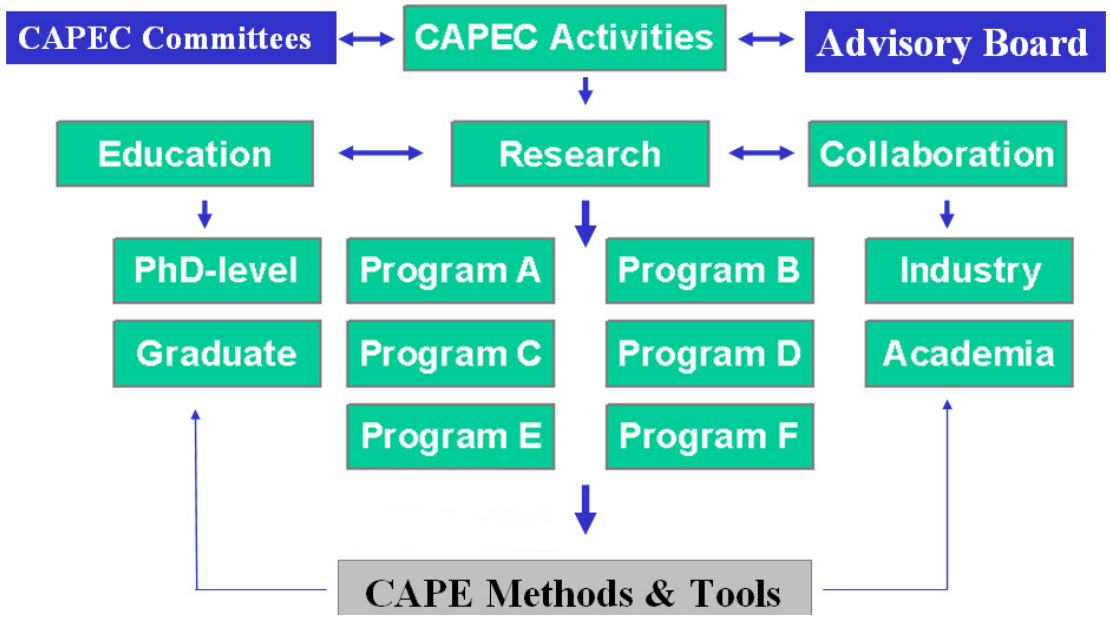


Figure 2.1: Organization of educational and research activities within CAPEC.

2.1 Permanent Members

CAPEC	
 **Assistant Professor Jakob K Huusom (JKH)**	The primary research area is process operation and control. Specific activities are related to: • First principle modelling and simulation of dynamical systems related to the chemical and biochemical industry. • Parameter estimation in dynamical systems. • Chemical and biochemical plant monitoring and operation. • Plant wide control. • Optimal control and state estimation. • Modelling and estimation for process control. • Tuning and maintenance of control implementations. Current projects are related to applications within: Diabatic distillation; automotive flue gas cleaning; and enzymatic production of biodiesel. ***Research Areas (CAPEC):*** *B, D, E*

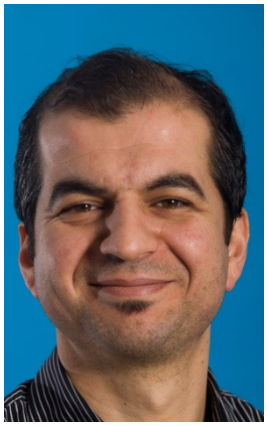
Associate Professor Jens Abildskov (JA)

Research focuses on development and analysis of correlations and predictive models for thermodynamic properties of fluids for chemical process design. Relationships are sought between molecular structure and thermodynamic properties for simple descriptions of thermodynamic properties. For densities and activities of strongly non-ideal fluids this is offered by statistical mechanical methods based on molecular correlation functions and their connections to fluctuation properties. Examples of applications are

- thermodynamic modeling and microscale simulation for properties relevant to biocatalysis
- mixed solvents (liquids and ionic liquids) with dissolved gases, enzymes and pharmaceuticals

Exploration is also being made of process energy requirements, to determine the efficiencies of diabatic distillation processes. Reverse engineering is employed in a set of contexts.
Collaborations (outside DK) involve researchers in the U.S., the Netherlands and Germany.

Research Areas (CAPEC): *A, B, F*



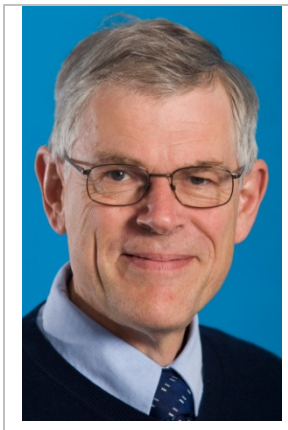
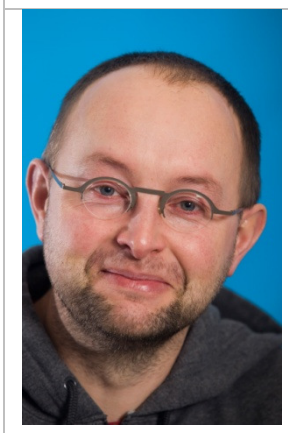
Associate Professor Gürkan Sin (GSI)

The research, in general, focus on development of systematic methods and tools for understanding, design, operation and control (bio)chemical processes and aims at providing rationale basis for better informed decision-making in engineering applications to achieve energy efficient and sustainable chemical & biochemical industry. Current research aims at moving the current design paradigm to predictive and probabilistic-based approaches and includes:

- Model-based product - process design; model-based technology evaluation, process synthesis & process retrofitting, risk-based design ; robust decision making under uncertainty
- Dynamics and process control; Integrated process design and control; plantwide control; model-based control and operability analysis
- Process modelling; model identification; model analysis; numerical methods; systems approach
- Uncertainty analysis; Sensitivity analysis; Monte-Carlo simulations; Bayesian Inference; Variance decomposition
- Process monitoring, safety and risk assessment

Applications in chemical, biochemical (biotechnology, fermentation technology, etc), pharmaceutical, food and water industries.

Research areas (CAPEC): *B, C, D, E*

 **Reader Karsten Clement (KHC)**	KHC is the Director of BSc Study Program (Chemistry & Chemical Engineering). His research interests lie in process modelling and process control and operation. ***Research areas:*** *B, D*
 **Professor Rafiqul Gani (RaG)**	RaG is Director and Co-founder of CAPEC. His research areas of interest covers modelling (properties, process & product); molecular-mixture (product) design; process synthesis, design & analysis; process-tools integration (PAT, sustainable design, intensification, design-control); and, development of computer-aided systems. Some of the currently active research topics are listed below: • Modelling (chemical products, processes and their operations; performance of products; properties of chemical systems) • Synthesis, design and analysis of chemical products and their sustainable processes (CAMD and CAFD) • Development of methods for sustainable process design; for process intensification; for integration of design-control; for model-based product quality control • Development of integrated computer-aided systems (ICAS, PAT, SustainPro, Databases) Applications in petrochemical, chemical, specialty chemical, agrochemical, food and pharmaceutical industries ***Research Areas (CAPEC):*** *A, B, C, D, E, F*
PROCESS	
	KVG's research covers process modelling; process design/analysis; process control, monitoring & operation; and, process integration-intensification. KVG is a faculty member of the PROCESS center. Currently active research topics are listed below. • Process modelling, applied to fermentation, biocatalysis, wastewater treatment, food production, pharmaceutical production, biorefineries; focus on the use of systems of ODEs, but increasingly also population balance models (PDEs) and CFD. • Parameter estimation and model analysis (*e.g.*, sensitivity and uncertainty analysis), *i.e.*, linking process models to plant data • Design of new reactor systems, including microbioreactors for

Associate Professor Krist V Gernaey (KVG)	enzymatic reactions and fermentation + systems for continuous production of pharmaceuticals • Design of PAT systems + biorefineries • On-line monitoring of fermentation processes + continuous organic synthesis, Process Analytical Technology (pharmaceutical production) • Benchmarking of control strategies for wastewater treatment plants ***Research Areas (PROCESS):*** *1-6*
 **Professor John Woodley (JW)**	JW is the head of the PROCESS center and his main research interests lie in the following topics: • Next generation processes (integration of biocatalysis with heterogeneous and homogeneous catalysis; processes based on renewable; green chemistry; pharmaceutical processes; and, biorefineries). • Methodology (process intensification; reactor design; evaluation methodologies) Applications in chemical, biochemical (e.g. biotechnology, fermentation technology, etc), pharmaceutical, food industries. ***Research areas (PROCESS):*** *1-6*
Senior Researchers	
 **Ulrich Krühne (ULKR)** Started: 01-03-2011 Finish: 01-03-2013	***Micro process development in chemical engineering*** ULKR is coordinating the research-development of microtechnology, has gained significant importance in chemical engineering. Topics of research interest: • Micro scaled fluid dynamic properties and their influence on chemical, biochemical and physical interactions • Integration of different unit operations into a single step process • Avoid the accumulation of inefficiencies of serial performed processes The starting point of the research will be a FTP project with the title *Novel greener and lean processes using integrated microfactories*. The project aims to demonstrate that fermentation and biocatalysis can be integrated. Project supervisors: JW, KVG

CAPEC-PROCESS Secretaries	
 **Eva Mikkelsen (EVA)**	Eva is the administrative secretary for the CAPEC and PROCESS centers and the CAPEC-PROCESS consortium. Eva also serves as the secretary for the editorial office of the Computers and Chemical Engineering journal office.
 **Gitte Nielsen (GNIE)**	Gitte started on 16 April 2012 as an additional administrative secretary for the CAPEC and PROCESS centers and the CAPEC-PROCESS consortium.

3. Research Projects

3.1 List of current research projects

Research at CAPEC & PROCESS are conducted through research projects at various levels: post-doctoral, PhD, MSc, BSc and visitor-collaboration projects. Table 3.1 provides a list of the currently active projects.

Table 3.1 Currently active research projects at all levels

CAPEC Post-Doc	Project Title	Supervisors	Start	End	Funding
Chiara Piccolo	Prediction of phase equilibria involving phase transfer catalysis	RaG	04-2010	01-2012	Syngenta
Miguel Mauricio Iglesias	Model based scale up of bioprocesses	GSI	10-2010	9-2012	H.C. Ørsted postdoc position /DSF EcoDesign project
Sascha Sansonetti	The rational selection of lipids for pharmaceutical formulations	RaG	3-2011	2-2012	Astra Zeneca

PROCESS Post-Doc	Project Title	Supervisors	Start	End	Funding
Pär Tuvfesson	Biocatalytic processes	JW	5-2010	5-2013	Ambiocas
Mathias Nordblad	Process design and evaluation for enzymatic biodiesel production	JW	12-2008	11-2012	Højteknologifonden (HTF)/Novozymes
Ulrika Türnvall	Development of the next generation biocatalysts for industrial production of chemicals	JW	1-2011	1-2013	Ambiocas/Bionexgen
Ulrich Krühne	Novel greener and lean processes using integrated microfactories	KVG	3-2011	5-2011	FTP
Paloma A. Santacoloma	Multi-enzymatic processes	JW	2-2012	7-2012	Bionexgen
Albert Cervera-Padrell	Modelling of heterogeneous populations of microorganisms	KVG	12-2011	8-2012	Strategic Research Council (DSF)

CAPEC PhD Student	Project Title	Supervisors	Start	End	Funding
Azizul Azri Bin Mustaffa	Development and analysis of Group-Contribution^{plus} models for property prediction of organic chemical systems	RaG/GK	4-2009	3-2012	Malaysia

Amol Hukkerikar	Model based integrated process-product design – retrofitting and optimisation	GSI/RaG Bent Sarup	6-2010	5-2013	Alfa Laval MultiMod
Alberto Quaglia	Incremental refinement of process design	GSI/RaG/ Bent Sarup	6-2010	5-2013	MultiMod/Alfa Laval
Igor Mitrofanov	A methodology for systematic design and selection of green solvents for increased yield in organic reactions	RaG/GSI	11-2010	10-2013	MultiMod
Michele Mattei	Systematic methodology for design of emulsion based chemical products	RaG/GK	8-2011	7-2014	DTU
Ane H. Mollerup	Optimizing control of the integrated urban wastewater system	GSI	8-2011	7-2014	Københavns Energi/FTP Industrial PhD
Larissa Peixoto Cunico	Modelling of phase equilibria and related properties of mixtures involving lipids	RaG/Roberta Cerriani/Bent Sarup	2-2012	1-2015	Alfa Laval
Marina Fedorova	Systematic Methods and Tools for Computer Aided Modeling	RaG/GSI	4-2012	3-2015	EU FP7 OPTICO project

CAPEC-PROCESS PhD Student	**Project Title**	**Supervisors**	**Start**	**End**	**Funding**
Noor Asma Fazli Bin Abdul Samad	Control of Process Operations and Monitoring of Product Qualities Through Hybrid Multi-Scale Model-Based Analysis	RaG/GSI/ KVG	1-2009	12-2011	Malaysia
Naweed Al-Haque	Modelling controlled release of substrate and removal of product in biocatalysis	JW/RaG/PT	11-2009	10-1012	DTU/AMBIOCAS
Nor Alafiza Yunus	Tailor-made design of chemical products: Bio-fuels and other blended products	RaG/JW/ KVG	7-2010	7-2013	Malaysia
Anna Katrine Vangsgaard	Modeling and Control of Novel Membrane Processes for Autotrophic Nitrogen Removal	GSI/ KVG/ BFS	9-2010	8-2013	DSF EcoDesignMBR
Kresten Troelstrup Meisler	Multi-dimensional population balance models of crystallization processes	RaG/KVG/ NVS	3-2011	2-2014	DTU
Deenesh Babi	Phenomena based process intensification	RaG/JW	8-2011	7-2014	DTU
Jason Price	Operation and Control of enzymatic biodiesel production	JW/JKH	9-2011	8-2013	DTU
Hande Bozkurt	Computer aided framework for synthesis, design and retrofit of water networks in processing	GSI/KVG	12-2011	12-2014	DTU

	industries				
Peam Cheali	Integrated framework for synthesis and design of multi-product biorefinery networks	GSI/RaG/KVG	5-2012	4-2015	EU FP7 OPTICO project

PROCESS PhD Student	Project Title	Supervisor	Start	End	Funding
Rita Lencastre Fernandes	Population balance models and computational fluid dynamics: a model framework to describe heterogeneity in fermentors	KVG/AJ/IN	11-2009	10-2012	DTU/KT FøSu
Joana de Lima Ramos	Guiding biocatalytic process improvements using engineering evaluation tools	JW/PT	3-2010	2-2013	Biotrains (Marie Curie ITN, Grant agreement no.: 238531)
Aleksandar Mitic	Operational aspects of continuous pharmaceutical production	KVG/KDJ	11-2010	11-2013	DTU/Lundbeck/MP2T
Vijaya Krishna Bodla	Integrated Microfactories for enzyme production	KVG/JW/ULKR	3-2011	2-2014	FTP

External PhD-Students	Project Title	Supervisor	Start	End	Funding
Klaus Reinholdt Nyhuus Hansen	New Product Introduction for the Pharmaceutical Industry	MG/RaG	9-2009	8-2012	DTU Management
Lida Simasatitkul	From Biomass to Fatty Alcohol via Bio-Diesel: Optimal Process Design	A Arpornwichanop /RaG	1-3-2011	1-11-2011	Chulalongkorn University, Thailand
Muhammad Zaman	Process Simulations Oriented Solvent Design for Carbon Dioxide Capture	RaG	1-2012	7-2012	KAIST, Korea
Muhammad Rizwan	Optimal Design of Biorefineries	RaG	6-2012	12-2012	KAIST, Korea
MSc-project Students	**Project Title**	**Supervisor**	**Start**	**End**	**Funding**
Guofeng Zhou	Model based monitoring and control of the SCR process for diesel engines (30 ECTS)	JKH	1-2012	6-2012	
Elena Ballesteros Fernández	Separation of azeotropic mixtures (30 ECTS)	RaG/GSI	2-2012	6-2012	Erasmus
Fabrício Rodrigues	Advances in Process Systems Engineering	RaG/DKB	2-2012	1-2013	Federal University of Uberlândia, Brazil
Alessandra Pennati	Synthesis of Water Networks (35 ECTS)	RaG/GSI/ AQ	1-2012	6-2012	Erasmus
Thomas Bisgaard	Dynamic effects of diabatisation in distillation columns (30 ECTS)	JA/JKH	2-2012	6-2012	

Jan Erik Nielsen	Diabatic distillation (30 ECTS)	JA/JKH	1-2012	6-2012	
Borja Valverde Perez	Control and operation of novel autotrophic nitrogen removal systems (45 ECTS)	GSI/MMI	9-2011	5-2012	Erasmus

3.2 CAPEC-PROCESS research programs versus co-workers

Table 3.2a provides an overview of the research programs and the CAPEC personnel involved with them

Research Programs	**CAPEC coworkers & research activities**				
	Faculty[1]	**Post-Docs**[2]	**PhD-students**[2]	**MSc-students**[3]	**Others**[4]
A: Property & Phenomena Modelling	**JA**; RaG	(*ChP*; *SSA*)	AZM; NOY; AMH; *LACU; MICU*	S. Kalakul; (*S. Piyarak*)	*B D Christian*; Q Chen
B: Product & Process Modelling	**RaG**; GSI; JA; JKH	(*ChP*); MMI	NAS; AMH; NOY; AQ; AKV*;* KreTM*;JAPR; HBoz; MFad; PChe*		*L Simasatitkul; M Zaman*
C: Synthesis, Design & Analysis	**GSI**; RaG	MMI; (*SSA*)	AZM; NOY; IGM, AQ; KreTM*; MICU; DKBabi; HBoz; PChe*	J E Nielsen; E Ballesteros; F. Rodriguez	*L Simasatitkul*; Q Chen, *B D Christian*
D: Control, Operation & Monitoring	**JKH**; GSI; RaG; (KHC)		NAS; KreTM; *JAPR*	G Zhou, T Bisgaard, B V Perez	*M Zaman*
E: Process & Tools Integration	**GSI**; RaG; JKH		AMH; AQ; KreTM; IGM; AKV; KRNH; *DKBabi;HBoz; MFad PChe*	F. Rodriguez; A Penatti; S. Kalakul; S. Mangnimit; (*P Nidhinandana*)	*M Rizwan*
F: Databases & Numerical Methods	**JA**; RaG		AMH; IGM; MICU; LACU	S. Kalakul	*B D Christian*; Q Chen
Currently active	**4**	**1**	**18**	**8**	**4**

1: Research area coordinators are indicated in bold; 2: New PhD-students who have started are indicated in italic; post-docs who have finshed are marked in italic-parenthesis 3: MSc-students who have finished are indicated by italic-parenthesis; 4: Here, visiting students (PhD, MSc, BSc) are listed, PhD-students are listed in italics. All other names indicate current coworkers at CAPEC-PROCESS.

Table 3.2b provides an overview of the research programs and the PROCESS personnel involved with them
Only those attending the Annual meeting have been included

Research Programs	**CAPEC coworkers & research activities**				
	Faculty[1]	**Post-Docs[2]**	**PhD-students[2]**	**MSc-students[3]**	**Others[4]**
1: Micro reactors	KVG; JW	ULKR	AM; VKB		
2: Continuous processes	KVG; JW	ULKR; PT; MAN; UT; ACP	AM; JP; VKB		
3: Biocatalytic processes	KVG; JW	PT; MAN; UT; PSA	NAH; JLR; VKB; JP		
4: Process intensification & intensified unit operations	KVG;JW	PT; MAN; UT	NAH; JLR; VKB; JP		
5: PAT	KVG; JW	ULKR; ACP	AM		
6: Scale translation	KVG; JW	PT; MAN; UT; ACP	RLF		
Currently active (at the annual meeting)	**2**	**6**	**6**		

1: Research area coordinators are indicated in bold; 2: New PhD-students who have started are indicated in italic, names in italic-parenthesis indicate coworkers who will soon stop; 3: MSc-students who have finished are indicated by italic-parenthesis; 4: External (or visiting) PhD-students who have returned to their home university are indicated by italic-parenthesis. All other names indicate current coworkers at PROCESS.

3.3 Post-Doctoral Research Project Overview

Miguel Mauricio Iglesias (MMI)

CAPEC
Supervisors: GSI
Start: 01-01-2012; End: 30-09-2012

Model-based scale-up of bioprocesses

Scale-up is an important step in the development and commercialization of new process technologies in many industries, for production of chemicals such enzymes, antibiotics or materials such as bioplastics. Moving a fermentation process from a lab-scale to a commercial/ production scale remains still challenging due to a number of factors that affects biological response of cells to changing conditions from cultivation. Scale-up problems may arise then due to inadequate interphase mass transfer, heat removal and non-uniform temperature and concentration gradients in the reactor. As a result, many large-scale fermentation processes give a lower yield than achieved in the laboratory.
This project conducted as part of DSF funded EcoDesign aims at developing a framework for scale-up of bioreactors based on data and information translated into quantitative knowledge using models. The framework allows using multiobjective scale-up principles and various degree of models, from first-principles to empirical (e.g. response surface type models based on experimental data) to hybrid models.

Research area: B, D

Mathias Nordblad (MAN)

PROCESS
Supervisors: JW
Start: 01-12-2008; End: 31-11-2012

Process design and evaluation for enzymatic biodiesel production

Biodiesel is one of the more established renewable fuel alternatives. It is traditionally produced using alkaline catalysis, which comes with certain limitations.
The use of enzymatic catalysis promises several advantages over traditional production method, including higher yields, compatibility with a wider range of oil feedstocks and a safer process. Additionally, the mild reaction conditions also reduce the need for product purification and increase the value of the by-product glycerol. However, the process requires development and optimization to meet criteria for performance and operating costs.
The focus of this project is the reaction and process design for enzymatic biodiesel production, based on evaluation of the performance of individual unit operations and overall process economics. The project is part of, and supported by, a larger collaboration looking into catalyst and reactor performance in enzyme-catalyzed biodiesel reactions, as well as system thermodynamics and sustainability issues.

Collaborators: Emmelev; Novozymes; Aarhus University; DTU Management

Albert Emili Cervera Padrell (ACP)  **PROCESS** Supervisors: KVG	***Heterogeneous microbial populations: modeling distributions of protein production rate and plasmid copy numbers in E. coli*** Often the production of heterologous proteins in bacterial hosts relies on the expression of multi-copy plasmids. The productivity is, in these cases, closely correlated to plasmid stability. Although a selective marker (e.g. antibiotic) is typically present allowing for the selection of plasmid-bearing cells, the distributions of plasmid copy numbers within the population vary. This reflects a trade-off between the protein production and the growth rate. This project aims at exploring modeling techniques to further understand the dynamics of cellular distributed properties under different growth conditions. The production of green fluorescence protein (GFP) in *E. coli* is used as case study. Starting from an unstructured kinetic model describing the growth of *E. coli*, and increasing the model complexity, steps will be taken towards the development of a population balance model (PBM). This PBM should describe the distribution of protein (and production rates) for cells presenting different plasmid copy numbers, under varying substrate availability. Tools such as parameter estimation routines, numerical solvers for ordinary differential equations, and discretization techniques for partial differential equations will be explored in the formulation, implementation and solution of the mentioned models.
Chiara Piccolo (ChP)  **CAPEC** Supervisors: RaG, P Piccione (Syngenta) Start: 01-04-2010; End: 31-03-2012	***Prediction of phase equilibria involving phase transfer catalysis*** Phase transfer catalysis (PTC) has the potential to stand out as an attractive alternative to conventional processes for the synthesize of special organic chemicals, from two immiscible reactants, that normally will not contact each other: in PTC systems a phase transfer catalyst acts as a shuttle between a polar phase that contains the salt reactants and a non-polar phase that contains the organic reactants. Many factors affect PTC processes, for example, choice of the organic phase, choice of the catalyst, presence of extra ionic species, temperature, stirring rate. The aim of this project is to enable semi-quantitative and quantitative estimations of phase equilibria involving PTC and, ultimately, to develop a systematic methodology to select the best system features and operating conditions for a given synthesis *Research area: A; B; C*
Sascha Sansonetti (SSA)	***The rational selection of lipids for pharmaceutical formulation*** Lipidic dose forms are applicable to both the early and late stages of product development in the pharmaceutical industry. They are most frequently used to formulate Active Pharmaceutical Ingredients (API's) with inherently poor

 **CAPEC** Supervisor: RaG, P Crafts (AZ) Start: 01-03-2011; End: 29-02-2012	aqueous solubility. They can also be used to avoid a solid dose form and the solid state issues that often blight this category. The aim of the project is to develop a software tool to predict the thermodynamic solubility of drug molecules in high molecular weight liquids *Research area: A, C*
Pär Tufvesson (PT)  **PROCESS**	***Biocatalytic production of chiral amines using transaminases*** Project Description: Biocatalytic transamination is being established as key tool for the production of chiral amine pharmaceuticals and precursors due to its excellent enantioselectivity as well as green credentials. Recent examples demonstrate the potential for developing economically competitive processes using a combination of modern biotechnological tools for improving the biocatalyst alongside using process engineering and integrated separation techniques for improving productivities. However, many challenges remain in order for the technology to be more widely applicable, such as technologies for obtaining high yields and productivities when the equilibrium of the desired reaction is unfavorable. The current project adresses these process challenges and develop strategies to overcome them, and aim to understand these and their applicability based on fundamental principles. *Research area: Process evaluation, Biocatalysis*
Ulrika Törnvall (ULRT)	***Development of the next generation biocatalysts for industrial production of chemicals*** A major hurdle for a widespread implementation of biocatalysis in industry is the lack of appropriate process technology, especially in fields where extra demands are

PROCESS
Supervisor: JW
Start: 10-01-2011; End: 09-01-2013

placed on the process, such as oxidation reactions. In this project, oxidation reactions catalyzed by oxidases and/or Baeyer-Villiger monooxygenases will be used as model reactions to develop a standardized methodology, a "process discovery platform", which will guide researchers in the establishment of cost-efficient and environmentally friendly industrial bioprocesses.
In the first instance, scale-down laboratory reactors and processes will be used to assess new configurations and modes of operation. In the latter stages of the project, pilot-plant trials will serve as an assessment and a demonstration of the new process technology on selected targets. After collection of kinetic, stability and thermodynamic data, these will be used for process modelling from a technical and economic perspective. In order to evaluate also the environmental benefits, simplified life cycle assessments of the developed technologies will be performed.
Collaborators: UCL-London, Slovak Univ of Tech, CLEA Technologies B.V., LentiKat´s a.s.

Paloma Andrade Santacoloma (PSA)

PROCESS

Supervisors: JW, KVG, GSI
Start: 01-11-2008; End: 31-10-2011

Multi-enzyme process modelling

Nowadays multi-enzyme processes are seen as an alternative to assist in the synthesis of complex compounds of industrial interest. In general, a multi-enzyme in-pot process is characterized by the mixture of enzymes that catalyze several reactions in a single pot. Therefore, the individual enzyme contributes with its specific action driving thus a given transformation to the subsequent one until the desired product is obtain. In this manner, purification steps of intermediate products may be eliminated. Consequently, it potentially leads to considerable process improvements like increases in the process yield and reduction in downstream processing and operating costs.
Reliable mathematical models of such multi-catalytic schemes can improve the potential benefit of this technology. In that manner, the best outcome of the process can be obtained on the basis of a thorough understanding of what modifications in the system are required to optimize the use of enzymes. In order to do this evaluation effectively, a methodological framework is developed for the mathematical modeling of these processes, integrated with a computer-aided methodology which enable the analysis of models, simulations, parameter estimation, sensitivity analysis, multi-objective criteria evaluation and the like. The idea is to use the models to find either promising configurations for experimental validation, or, evaluate and analyze an existing process under different conditions by simulation, to identify opportunities for improvement.

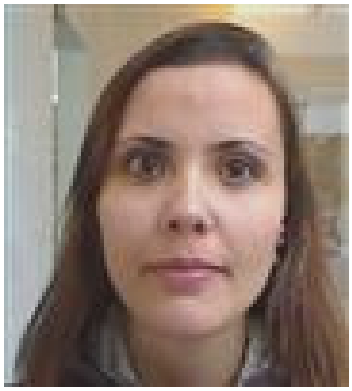
Research area: Process technology and units operations

3.4 PhD-Research Project Overview

Naweed Al-Haque (NAH)  **PROCESS-CAPEC**	***Modelling of controlled substrate supply using solid sorbents in biocatalysis*** With the development of biocatalysts, greener technologies have become more accessible to industry. The obvious advantage of this technology is selectivity which is necessary to obtain a high yield of a specific product. The other advantages of operating in benign operating conditions make it an alternative worth investigating. However In bioprocesses, especially in bioconversions, the substrate and the product may inhibit or damage the biological catalyst or interfere with other components in the reaction medium above a critical concentration. This limitation can be overcome with methods such as *in-situ* product removal (ISPR) and *in-situ* substrate supply (ISSS) using solid sorbents. This project will focus on the latter issue and in particular for the development of this novel substrate release technique with controlled diffusing rate of the substrate in the reaction medium using a solid resin(s). Supervisors: JW; PT; RaG Start: 1-11-2009; End: 14-11-2012 *Research area: Biocatalysis, controlled substrate supply, resins, ISPR, mathematical modelling*
Vijaya Krishna Bodla (ViKB)  **PROCESS**	***Integrated microfactories for enzyme production*** This project aims to demonstrate that fermentation and biocatalysis can be integrated into a novel leaner and greener process. The hypothesis is to construct and operate integrated microscale reactors using transaminase model system (adapted to specific microorganism and the biocatalytic reaction) in an intensified and more efficient process also for scaling-up. It is the intention to use an integrated microfactory to quickly and effectively screen for different process conditions. The proposed microfactory has a number of features that are advantageous for large-scale production with respect to improved economy of the proposed process: (1) the method for preparing the catalyst is considerably cheaper as no intermediary purification steps are needed; (2) the system process intensity is inherently enhanced through the continuous operation; (3) large hydrophobic substrates would be easily accessible since the cell membranes are lysed. Supervisors: KVG,ULKR,JW Start: 01-03-2011; End: 28-02-2014 *Research area: Microreactors; Biocatalysis*

Hande Bozkurt (HBOZ)  **CAPEC-PROCESS**	***Computer-aided framework for synthesis, design and retrofit of future wastewater treatment systems*** Currently, the WWTP layout designs are mainly based on expert decisions and experiences. This approach takes the values like environmental issues, water reuse, by-product recovery and public impacts into account and identifies the alternatives based on experience, similar solutions and brainstorming to come up with the most viable WWTP systems. However, with increased complexity of the technologies and stricter limit values for effluents; making the most feasible decision with this approach became harder. What is proposed in this paper is therefore, a new approach based on mathematical programming to manage the complexity of the problem and generate/identify novel and optimal WWTP layouts for specific wastewater feed domestic as well as industrial nature. The tool will be developed to formulate the design problem as an MINLP and by using the database of wastewater treatment technologies; it will generate many alternatives and evaluate at their optimality. Since the tool will cover both environmental and sustainability metrics, it will be a powerful decision making agent for WWTP layout design. Supervisors: GSI, KVG Start: 16-12-2011; End: 16-01-2015 *Research area: B,C, E*
Peam Cheali (PCHE)  **CAPEC-PROCESS**	**Integrated framework for synthesis and design of multi-product biorefinery networks** In this PhD project, a framework for synthesis and design of integrated-intensified chemical and biochemical processes is to be developed. The framework will focus on biorefinery network design and synthesis in addition to a systematic approach which is used to manage the complexity and solving simultaneously both the business and the engineering dimension of the problem. This approach allows generation and comparison of a large number of alternatives at their optimal point, in order to identify the optimal raw material, multi-product portfolio and process technology selection for the different cases defined by market scenario, their sustainability metrics and risk of investment under market uncertainties. More specifically, the framework will include the following features: library of models and database for the assessment of process performance, generation and analysis of processing technology alternatives and intensification options, computer-aided synthesis and design of processing paths in networks, MINLP, assessment and comparison of the candidates at their optimality. Case studies of biorefinery network are considered focusing on production of biochemicals, biofuels and optimal blends of mixtures with fossil fuels will be used to highlight the novel features. Supervisors: GSI, RaG,KVG Start: 01-05-2012; End: 31-05-2015 *Research area: B, C, E.*

Larissa P Cunico (LACU)



CAPEC

Modelling of phase equilibria and related properties of mixtures involving lipids

The objective of this project is to perform a systematic numerical analysis to determine the needs of phase equilibria and related properties in the production of edible oils, biodiesel and other oleochemicals. The available data in literature will be analyzed for consistency and then used to develop/adopt the most appropriate models, for example, group-contribution combined with atom connectivity based models. For systems that are not in literature, some experimental work will be conducted in UNICAMP – Department of Chemical Engineering in Brazil, where the necessary facilities exist. These developed predictive models will be used to determine the sensitivity of design variables with respect to uncertainties in the predicted properties. The application of the developed properties models will be illustrated through case studies involving different lipid compound processing steps. Then, the obtained results will be implemented in process simulation software and will be applied on industrial cases from Alfa Laval Copenhagen A/S as one of the means to validate the models.

Supervisors: RaG, Prof R. Cerriani, Dr. B Sarup
Start: 1-3-2012; End: 28-2-2015
Research areas: A, F

Marina Fedorova (MFAD)

CAPEC

Systematic methods and tools for computer aided modelling

Models play an important role of increasing importance in design and analysis of chemicals/bio-chemicals based products and the processes that manufacture them because of the increasing use of computer-aided methods and tools. The advantage of using these model-based methods and tools is that they have the potential to reduce the number of experiments, which can be expensive and time consuming. As the required models may be complex and require multiple time and/or lengths scales, their development and application for product-process design is not trivial. Therefore, the modelling framework can contribute by reducing the time and resources needed for model development and application, thereby reducing the overall time and cost for product-process development
The objective of this project is to develop methods and tools that will allow systematic development of models and their solution using a modelling framework, which consists of a model generation tool, a model analysis-solution tool and templates for solving different modelling problems. Through a number of modelling case studies, the novel features of the modelling framework will be illustrated.

Supervisors: RaG, GSI
Start: 1-4-2012; End: 31-3-2015
Research areas: B, E, F

Rita Lencastre Fernandes (RLF)

PROCESS

Population balance models and computational fluid dynamics: a model framework to describe heterogeneity in fermentors

The project focuses on the development of models that can predict the growth and behaviour of heterogeneous microbial populations. Experimental data is used to formulate Matlab based models that can predict changes in the microbial distributed properties (e.g. single cell protein content, growth and productivity) due to varying environmental conditions in the fermentor. In a later stage, the population model will be integrated with a fluid dynamics model for a stirred reactor, allowing for predicting process behavior under different environmental conditions. The project is partly funded by the Danish Council for Strategic Research in the frame of the project "Towards robust fermentation processes by targeting population heterogeneity at microscale", and developed in tight collaboration with the ERA-NET Industry Biotechnology project "Targeting population heterogeneity at microscale for robust fermentation processes".

Supervisors: KVG, AJ, Ingmar Nopens (Ghent Univ)
Started: 01-11-2009; Finish: 07-12-2012
Research area: Process-product modelling/design

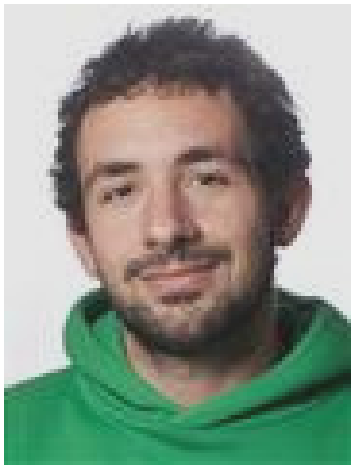
Amol S Hukkerikar (AMH)

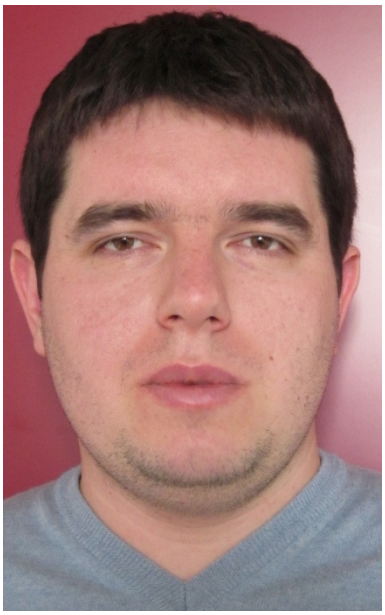
CAPEC

Model based integrated process-product design - retrofitting and optimisation

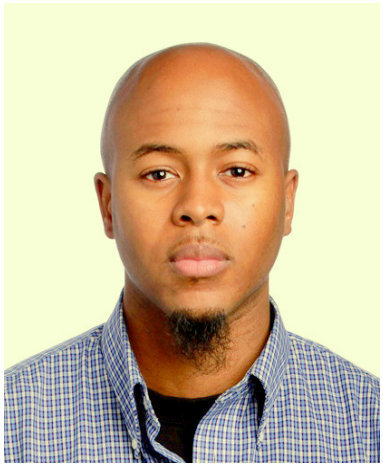
The main objective of this project is to develop a systematic framework for model based design and optimisation of the principal unit operations involved in edible oil/bio-fuel industry and apply the developed methodology for improvement in the performance of existing installations for edible oil/bio-fuel processes. Although the oleo-chemical industry is mature and based on well established processes, the complex systems that lipids compounds form, and the lack of accurate unit operation models have limited a wide application of computer aided methods and tools for process synthesis, modeling and simulation within this industry. In consequence, the first part of this project will be the development of unit operations model library consisting of a collection of new and adopted models that are not available in existing process simulation tools. The second part of the work will focus on application of developed models for optimisation of existing processes with respect to performance indicators such as minimum operational cost, product yield improvement and sustainability index.

Supervisors: RaG, GSI, Bent Sarup (Alfa Laval).
Started: 01-07-2010; Finish: 30-06-2013
Research area: A, B, C, E

Deenesh K. Babi (DKBabi)  **CAPEC-PROCESS**	***Development of a phenomena based approachfor process intensification*** Process intensification (PI) is a means by which process industries can achieve a more efficient and sustainable chemical process through the improvement of for example energy efficiency and waste generation. The objective of this project is the further development of the phenomena based process synthesis and design methodology and extension of its application to entire processes together with the development of a computer framework and computer-aided tool for application of the methodology. The algorithm is part of a larger PI framework which is being developed as collaboration between the laboratory of Fluid Separations (FVT), TU-Dortmund and CAPEC, DTU. This framework will allow the intensification of processes through the combination of an experimental and model-based approach. Supervisors: RaG, JW Start: 1/8-2012; End: 30-7-2015 *Research areas: B, C, E*
Michele Mattei (MICU)  **CAPEC**	***Development of a systematic methodology for emulsion based chemical product design*** The goal of chemical product design is to find a product that exhibits a set of desirable or specified behavior. A chemical product design problem can be summarized as follows: given a set of desired (target) properties, establish a list of chemical formulations satisfying these targets and then choose from them the most appropriate candidate to be verified experimentally. The chemical product of interest can be a single chemical or a mixture/blend; a formulated product is a mixture that contains different chemicals, active ingredients as well as additive. The objective of this project is to develop a systematic methodology for the design of emulsified chemical products. The methodology will employ a model-based product synthesis/design stage and a model-experiment based further refinement and/or validation stage. The success of any model-based methodology depends on the availability of reliable and predictive models. The project therefore will also develop, where necessary, the required property prediction models for emulsions. Design of consumer products will be considered as suitable case studies. Supervisors: RaG, GK Start: 1/8-2012; End: 30-7-2015 *Research areas: A, C, F*
Kresten T. Meisler (kretm)	***Multi-dimensional population balance models of crystallization processes*** The project aims at describing the complex phenomena occurring during a crystallization operation in multiple dimensions. The phenomena include nucleation, growth,

 **CAPEC-PROCESS**	breakage and agglomeration and a population balance model is based on the phenomena allowing calculation of the multi-dimensional crystal size distribution (CSD). The translation of measured data for monitoring of crystallization operations is used for model parameters and the full model with parameters is used for analysis of the crystallization process through simulation within a framework describing the balance equations. With the simulations different operational policies and process options are explored through generation of the CSD for the systems. An operational policy for the desired crystal size distribution for a given crystallization process is designed. Supervisors: RaG, KVG, NvS Start: 01-03-2011; End: 28-02-2014 *Research area: B, C, D*
Aleksandar Mitic (ASMI)  **PROCESS**	***Operational aspects of continuous pharmaceutical production*** Most pharmaceutical productions are based on batch and semi-batch processes and involves many problems, such as long reaction sequences, non-uniform conditions inside vessels, implementation of PAT applications. Continuous manufacturing might offer a solution to those problems. Therefore, the main focus of this PhD project is to develop efficient continuous production of zuclopenthixol, a product of H. Lundbeck A/S. A grignard reaction, hydrolysis and a dehydration reaction should all work in continuous mode with high selectivity in order to avoid intermediate crystallization steps. Simplifications and improvements of the liquid-liquid separation, as well as acceleration of the slow hydroamination reaction are additional challenges. Potential use of micro-scale equipment, such as microreactors and L-L microseparators will be tested. Also, on-line monitoring and control of the established continuous process will be studied. Applications of NIR spectroscopy will be tested. Supervisors: KVG, Kim Dam-Johansen (CHEC) Start: 15-11-2010; End: 14-11-2013 *Research area: continuous pharmaceutical production, PAT, microreactor technology*
Igor Mitrofanov (IGM)	***A methodology for systematic design and selection of green solvents for increased yield in organic reactions*** Methodology for selection and design of single organic reactions has previously been developed at CAPEC (Gani et al, Computers and Chemical Engineering, 2005, 2008). This methodology is based on a rule-based algorithm. However, the methodology is applicable only to organic chemicals that are

 **CAPEC**	inert within the reaction system. The next step is extending the application range of current methodology to multi-stage reactions (because, for example, pharmaceutical reactions are normally multi-step), more complex reaction systems, known solvent substitution problems as well as reaction promotion. Supervisors: RaG; GSI, JA Start: 01-11-2010; End: 31-10-2013 *Research area: C, E, F*
Ane H Mollerup  **CAPEC**	***Optimizing control of the integrated urban wastewater system*** Since the EU Water Framework directive came into force in 2000, wastewater systems (sewer system and wastewater treatment plants) in Europe have been put under pressure to reduce the number of combined sewer overflows (CSOs) from the system to protect the aquatic environment. The aim of this project is to formulate the problem of design and analysis of the regulatory level from a process control perspective and to develop a methodological approach to find the optimal solution. The project aims at developing a methodology for determining the best control structure and technique for an integrated system of both sewer system and wastewater plants, when optimizing towards defined objectives, e.g. minimizing flooding, overflow from the sewer system, bypass from the WWTP, electrical consumption, etc.One of the issues to be examined is the robustness of the control structure with respect to actuator failure and uncertainty on measurements.Also the optimization of the system is addressed. With the introduction of better climate models and radar predictions of the precipitation it might be possible to introduce a supervisory control layer with Real Time Optimization (RTO). Supervisors: GSI, Peter S Mikkelsen, Dines Thornberg Start: 1-8- 2011; End: 1-8-2014 *Research area: B, D*
Azizul Azri Mustafa (AZM)	***Development and analysis of GC^{Plus} models for property prediction of organic chemical Systems*** Accurate, reliable and efficient prediction of properties is very

 **CAPEC**	important in chemical process-product design. However, due to the increased complexity of the molecular structures of chemicals, their wider applications, and demands for greater accuracy, extension and analysis of the current prediction methods as well as development of new models are necessary. Therefore, the combination of group-contribution (GC) and atom connectivity (CI) (the GC^{Plus} approach) that is able to extend the application range of the host property model has been developed and extended to predict the UNIFAC GC-model parameters (see PEC09-17). The objectives of this PhD-project is to analyze the performance of the GC^{Plus} approach in VLE and SLE calculations and based on it, to extend and further develop the GC^{Plus} approach for other versions of the UNIFAC models and to apply the models for chemical process synthesis and design. Supervisors: RaG, GK Start: 01-04-2009; End: 31-09-2012 *Research area: A, B, C*
Jason Price (JAPR)  **CAPEC-PROCESS**	***Operation and Control of Enzymatic Biodiesel Production*** This work explores the control of biodiesel production via an enzymatic catalyst. Currently enzymatic catalysts are not in widespread use for commercial-scale biodiesel production. This is mainly due to non-optimized process designs. Furthermore is it unclear what process variables need to be monitored and controlled to ensure optimal economics. Critical to the project is to develop a control methodology to optimize the productivity of biodiesel production. The implementation of a control system to handle changes in the feed composition and the correct dosing of alcohol can potentially lead to very large energy savings and at the same time provide a more consistent product quality. However given most conversion and quality analyses of biodiesel are commonly done by chromatographic methods, suitable measurement techniques will need to be investigated to obtain real-time information on the states of the system. The main deliverable is a steady state and dynamic simulation model of the process including a strategy for monitoring and process control. This model and the proposed strategies will be validated experimentally on the department's pilot facilities. Supervisors: JW, JKH, MAN Start: 01-09-2011; End: 01-10-2014 *Research area: B, D*
Alberto Quaglia (AQ)	***Incremental refinement of process design*** Process Simulation is not common in the food and biofuels industries, mainly due to the complexity of thermodynamics and transport properties of the species involved.

 **CAPEC**	This project aims to introduce a paradigm shift in product-process design through the application of CAPE/PSE tools in these industries. The research will focus on the use of validated models in the early stages of product-process design in order to eliminate redundant alternative process routes. The objective will be to identify the most promising process route so that the more time consuming and costly steps (computational as well as experimental) can be reduced. To achieve this objective, a systematic framework for Computer-Aided Flowsheet Synthesis and Design (CAFD) will be developed and evaluated in collaboration with Alfa Laval. A particular emphasize will be given to deal with uncertainties in data and models. Supervisors: GSI, RaG, Bent Sarup (Alfa Laval) Start: 01-06-2010; End: 31-05-2013 *Research area: B, C, E*
Joana de Lima Ramos (JLR)  **PROCESS**	***Guiding biocatalytic process improvements using engineering evaluation tools*** Biocatalysis is an emerging area of technology and to date few reports have documented the economics or environmental profile of such processes During the development of a biocatalytic process and in particular during its scale-up, there are several required considerations. Two of the most important are the economic and environmental profile. The present project is focused on the development of engineering tools in order to assist a fast and accurate economic and environmental analysis. When applied to a given process these have a decisive role in helping to identify bottlenecks in process development, and to justify where to put effort and resources. Further, to exemplify the methodology, guidelines for the successful biocatalytic production of chiral amines using transaminases will be identified through process economic and environmental assessment. The outcome of the present research will establish new tools and knowledge useful in biocatalysis and (bio-) process development. Supervisors: JW, PT Start: 01-03-2010; End: 01-03-2013 *Collaborations: Evonik, DSM, Lonza*
Noor Asma Fazli Bin Abdul Samad (NAS)	***Control of process operations and monitoring of product qualities through hybrid multi-scale model-based analysis*** A generic multi-dimensional model-based framework of batch crystallization processes has been developed covering a wide range of crystallization models and operational scenarios. In order to control and monitor the crystallization operations and to ensure that the desired crystal size distribution (CSD) is achieved, an appropriate Process Analytical Technology (PAT) system (= set of appropriate monitoring tools + actuators) needs

 **CAPEC-PROCESS**	to be designed as well. Therefore the use of the generic model is illustrated through the ICAS-PAT software for design of process monitoring and control systems. ICAS-PAT consists of a model library and a knowledge base that allows the user to design/validate PAT systems through a systematic computer-aided framework. The generic crystallizer model has been implemented in the ICAS-PAT model library. The application of the model-based framework has been tested through a batch cooling crystallization process case studies (potassium dichromate, paracetamol, sucrose etc.) where the objective is to obtain a desired CSD. Supervisors: RaG, KVG, GSI Start: 15-01-2009; End: 31-12-2011 *Research area: B, C, D*
Anna Katrine Vangsgaard (AKV)  **CAPEC-PROCESS**	***Validation of structured model for autotrophic nitrogen removal in high strength wastewater*** Autotrophic nitrogen removal is a relatively new and emerging technology for treatment of sidestream wastewaters with high nitrogen concentrations, such as sludge digestion liquor or landfill leachate. It is therefore of great importance that a better understanding of the process dynamics is established. In this project, a model to be used for design of experiments will be developed according to a structured modeling framework. The aim of this project is to develop a detailed metabolic model for the selected bacterial groups, performing autotrophic nitrogen conversion, and integrate that into complete ecosystems models, which describe how the major microbial groups interact. This insight will be used to design experiments in which relevant operational conditions will be identified and tested. The relevant conditions are under which the nitrogen removal process is optimized through the development of selection principles, for a targeted removal or enhancement of specific microbial groups. The final objective is to obtain a validated model which can be used for process prediction and thus determination of optimal operational conditions. Supervisors: GSI, KVG, Barth F. Smets Started: 01-09-2010; Finish: 31-08-2013 *Research area: B, E*
Nor Alafiza Yunus (NOY)	***Tailor-made design of chemical products: Bio-fuel and other blended products*** This study proposes a methodology for tailor-made design of chemical products more specifically bio-fuels and other blended products. This project emphasize on product blends because most of the chemical based products are mixed of several chemicals. A single chemical is not always able to meet all the product specifications. Therefore, a mixture/blend of chemicals is likely to improve and enhance the product qualities. Identifying mixture of appropriately identified compounds that

CAPEC-PROCESS

satisfied product attributes is the main goal of this study. In order to achieve the objectives, four key tasks are needed. Firstly, the general chemical blending problem is formulated. Then, the property models are identified to estimate the pure and mixture properties. The unavailable property models are being developed by using experimental data and appropriate modeling tools. Next, the chemical mixture/blend algorithm is developed in order to find the best mixture/blend using suitable solution strategy. Finally, the developed mixture/blend algorithm is applied to case studies and validated with experimental data.

Supervisors: RAG, JW, KVG
Start: 01-06-2010; End: 01-05-2013
Research area: A, B, C

3.4 External PhD-students (projects)

Klaus Reinholdt Nyhuus Hansen (KRNH)

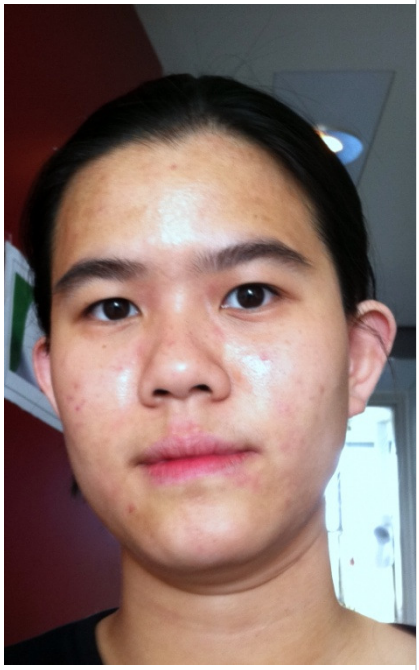
DTU Management - CAPEC

New product introduction for the pharmaceutical industry

It is well known, that the pharmaceutical industry is struggling with increasing cost and length of R&D projects. Earnings of a drug drop drastically after patent expiration. Thus, the industry spends much effort on reducing Time-to-Market. However, a suitable methodology for planning operations immediately prior to launch is especially lacking.
Due to strict cleaning requirements, production setups are very long. Production volumes are thus large and intermittent and the entire supply chain becomes rigid and inflexible. Besides forecast uncertainty, which is difficult for new products, other risks and uncertainties from carrying out reimbursement negotiations with authorities in each market e.g. reimbursement levels and product price can also disrupt the execution of a market launch.
In this project a MILP-based methodology for planning operations before and during market launch is developed, which fits into the S&OP structure of pharmaceutical companies while considering risks and uncertainties. The methodology should be connected to the existing methodologies; pipeline planning, capacity planning and production planning.

Supervisors: Renzo Akkerman (DTU-MAN); Martin Grunow; RaG
Start: 01-09-2009; End: 31-08-2012
Research area: D, E

Lida Simasatitkul (LDSI)



Chulalongkorn-CAPEC

From biomass to fatty alcohol via bio-diesel: Optimal process design

The objective of this project is to develop a systematic step by step methodology to obtain flexible process flowsheets for biodiesel and related products from different bio-sources. The methodology will generate different flowsheet alternatives, analyze them through process simulation and evaluate them based on operational issues, economics, and supply chain as well as sustainability measures to deteremine the best process design. The systematic methodology will be applied to a case study to determine the optimal process design to produce a combination of at least two products: bio-diesel and/or fatty alcohol from at least two different biosources: palm oil and waste cooking palm oil. The process flowsheet should be flexible to allow the processing steps required for both the products using both the raw material sources. The process design should be flexible so that changing prices/supply of raw materials as well as prices/demand of products can be handled. That is, the process flowsheet should be able to handle the changing operating conditions for the raw material to product processing routes.

Collaboration with Chulalongkorn University, Bangkok, Thailand (Prof A Arpornwichanop)
Research areas: B, C, E

Muhammad Zaman

KAIST-CAPEC

Carbon dioxide capture from power plants: Performance and control studies

Carbon dioxide is responsible for 60 percent of the global warming caused by greenhouse gases (GHGs). According to the International Energy Agency's roadmap, 20 percent of the total CO_2 emissions should be removed by CCS by year 2050. Hence the capture of CO_2 from power plants, mainly form coal based power generation is much significant for greenhouse gas reduction. The overall objective of this project is to perform comparative performance study for different solvents and alternative configurations of the carbon capture process, and to perform dynamic simulations for the selected process to resolve control issues. For the base case, mature solvent monoethanolamine (MEA) will be used. For process simulation and analysis, commercial simulators with user-added modules will be used. The project will try to identify suitable solvent replacements; identify the most important design-control parameters; develop dynamic models for the CO2 capture process; identify novel integration opportunities to make the process more sustainable than the existing base case designs.

Collaboration with KAIST, Korea (Prof Jay H. Lee)
Research areas: B; D, E

4. CAPEC Software

Development of CAPEC software is closely related to the CAPEC research projects. Since a majority of CAPEC research projects deal with the use of computers to solve process/product engineering problems, the theories and algorithms developed in the research projects are validated through these computer programs. Among these, the computer programs that have a general appeal with respect to their application and do not have any restrictions imposed by a consortium member company, are collected and distributed as part of the CAPEC software. CAPEC software is not a commercial software and are distributed exclusively only to the CAPEC industrial consortium member companies. A special version is distributed at a nominal price for educational purposes.

The objective of the CAPEC software is to promote the use of computer aided methods and tools developed by CAPEC in the solution of current and future process/product engineering problems. The CAPEC software consists of the following:

- Integrated Computer Aided System – ICAS
- EXCEL based macros (ProPred, CAPECDB Manager)
- UNIFAC-Utility (group definitions, VLE database, etc.)
- Special Software (ICAS-PAT, SustainPro, *v*PPD-*Lab*, ECON, LCSoft)
- PC-SAFT software package
- SMSWIN – A tool for properties and phase equilibrium calculations, especially suitable for solid-liquid systems (compliments with the features in ICAS)

4.1 Integrated Computer Aided System – ICAS 15.0

ICAS combines computer-aided tools for modelling, simulation (including property prediction), synthesis/design, control and analysis into a single integrated system. These tools are present in ICAS as toolboxes. During the solution of a problem, the user may move from one toolbox to another to solve problems requiring more than one tool. For example, in process synthesis, one option is to define the feed stream, then analyse the mixture (analysis and utility toolbox), then generate a flowsheet (synthesis toolbox), then optimise the flowsheet (design toolbox), and finally verify the design (analysis toolbox). From any toolbox it is possible to invoke the simulation engine to perform steady state and/or dynamic simulation for batch and/or continuous process operations. From the synthesis toolbox, it is possible to invoke the solvent design tool (in design toolbox) if a solvent is needed for a specific separation task. There is also a utility toolbox, which determines properties, phase diagrams, etc., which can be used by the other toolboxes or by the user to analyze the behaviour of the specified system. “ICAS documentations” provides information on installation of ICAS, tutorials at basic and advanced levels and other useful information such as a list of dll-files copied during installation and new features of the latest version of ICAS. Figure 4.1 highlights the idea of integration and the advantages that can be obtained through this integration.

In ICAS 15.0, new features have been added to the following tools: ProPred (pure component property prediction), MoT (modelling toolbox), ProCamd (computer aided molecular design), and the CAPEC-database. A new tool, SolventPro, has been added to ICAS. The EXCEL based macros (ProPred and CAPECDB manager) have been updated

with new features and corresponding manuals. The CAPECDB manager also includes an azeotropic data collection and analysis feature. In addition, three special software (EXCEL based): Sustain-Pro, ICAS-PAT, ECON and the Virtual PPD-lab (*v*PPDL) have been revised and improved. Each of these software, use a number of ICAS tools and models generated through MoT. For a list of ICAS tools, see ICAS Documentation or the ICAS poster. A number of new properties for organic chemicals as well as polymer repeat units have been added to ProPred. ProCAMD, ProPred, Database have been integrated through SolventPro.

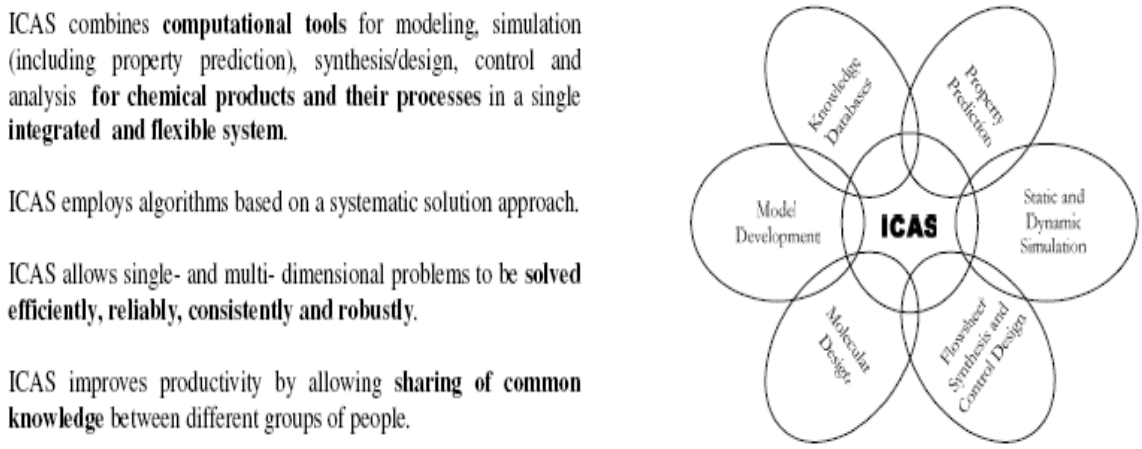


Figure 4.1: The idea of integration within ICAS

In general, ICAS 15.0 has become a much more robust and reliable version of ICAS with a wider application range. New additions to ICAS are also highlighted in the corresponding ICAS-tools manuals. New versions of manuals for the following tools in ICAS are also available - ProPred, MoT, ProCamd and SolventPro. After installation of ICAS, users will find a number of worked out examples given in the "examples" and "tutorials" directories. Figure 4.2 highlights the new features in ICAS 15.0 while Fig. 4.3 highlights the work-flow in the implementation of a model (starting from transferring the published model equations to MoT and ending with a COM-object that can be executed from different external software).

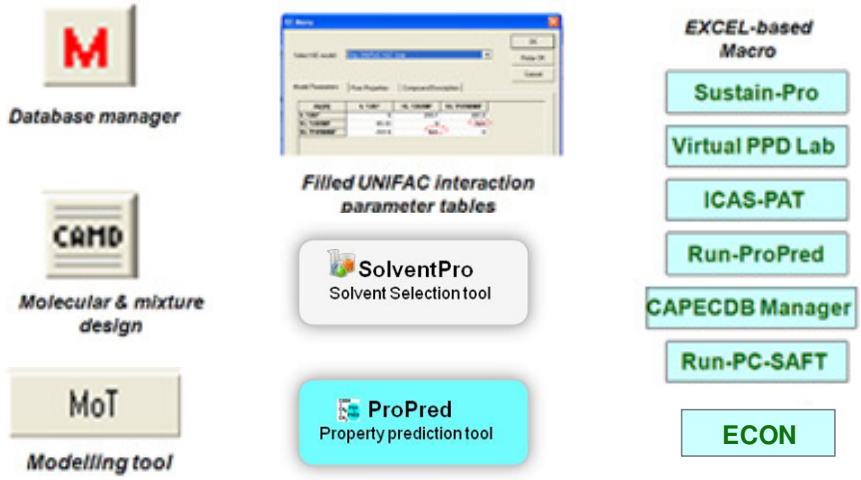


Figure 4.2: Highlight of new features in ICAS 15.0

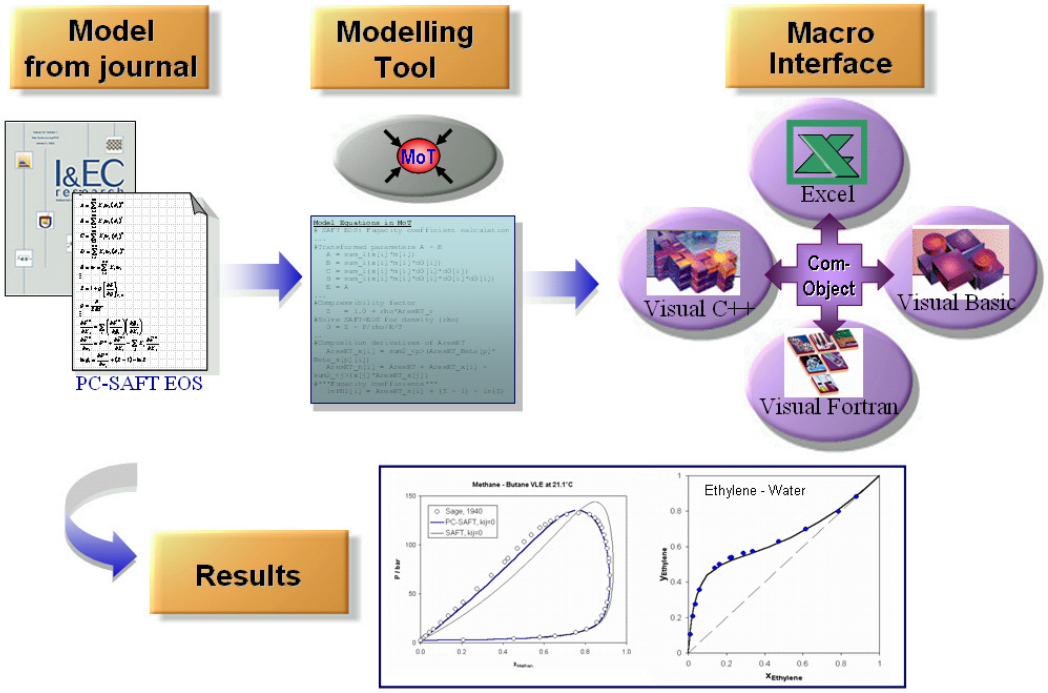


Figure 4.3: COM-object generation through MoT and use in external software

In ICAS 15.0, MoT has new features (see the MoT new features document); ProCamd and ProPred have had bug-fixes; a new solvents database has been added to the CAPECDB (EXCEL version); and SustainPro and the *v*PPD-lab has new versions.

In ICAS 15.0, Propred 4.3 has a number of new additions and updates. These new features includes estimation of 10 environment-related properties (LC50,GWP, …) of organic compounds using MG method with uncertainty estimates, estimation of lipids properties including single and temperature dependent properties by MG method, an extended internal database (with more than 23000 molecules), revised and improved property estimation, estimation of new properties such as liquid thermal conductivity, user friendly navigation features, quantification of prediction uncertainties (95% CI). Last but not least, it is now possible to run PC-SAFT from Propred for estimation of temperature-dependent properties (see Figure 4.4)

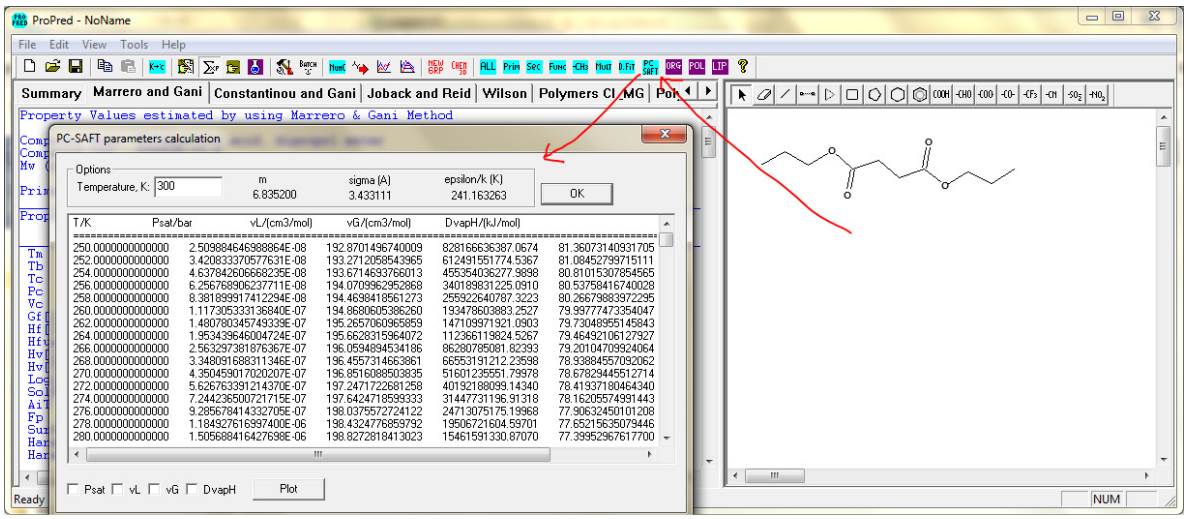


Figure 4.4 Running PC-SAFT from Propred 4.3

4.2 EXCEL based macros (ProPred, CAPECDB Manager)

Two EXCEL based software has been developed to further facilitate the use of ICAS-ProPred and the CAPEC-database. EXCEL-ProPred, the user opens the EXCEL macro and then performs different property calculations through ProPred. Here, the EXCEL spreadsheets become the working area and ProPred is the property calculator.

In the CAPECDB Manager, the EXCEL macro helps the user in the search for data available in the CAPEC database. A new feature to this database is the availability of azeotropic data. A solvents database consisting of information on approximately 1400 solvents has been added.

4.3 UNIFAC-Utility

KT-UNIFAC-utility is a program that helps the user to check the consistency of UNIFAC groups, their parameter values and the representation of the molecules with the UNIFAC groups. For a specified mixture, the program determines the UNIFAC group information and passes the relevant data to ICAS for use in TML and other tools.

4.4 Special ICAS-based software (ICAS-PAT, SustainPro, vPPD-lab)

4.4.1 ICAS-PAT

ICAS-PAT is an EXCEL based software that designs and/or analyzes a process monitoring system, given the process information. It has a built-in knowledge base of information about process operations, the variables that need to be measured, the variables that need to be monitored and the equipments that could be used. It also has a library of models that may be needed to supplement the data available for the process under investigation. The library models are run through ICAS-MoT. The EXCEL macro guides the user through an established work-flow based on the systematic methodology developed by Singh et al. (see PEC08-05). A manual and several solved case studies are available. Figure 4.5a highlights the main features of ICAS-PAT.

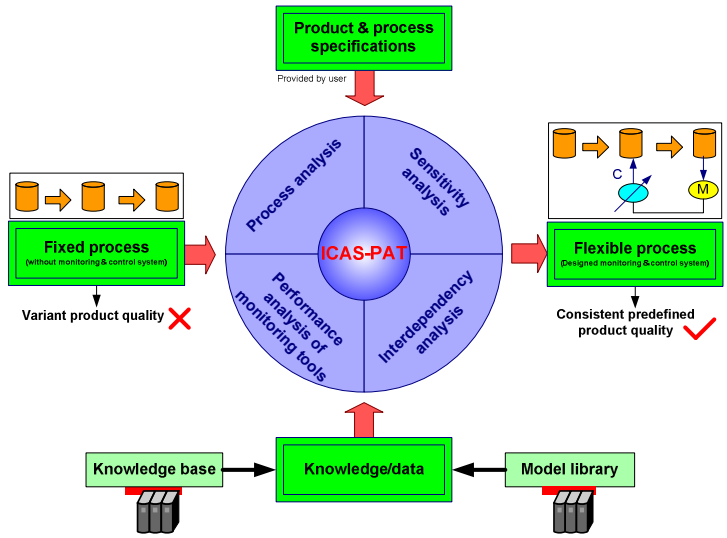


Figure 4.5a: Overview of the main features of ICAS-PAT.

4.4.2 SustainPro

SustainPro is an EXCEL based software, which provides options for retrofit analysis and performance analysis of a given process. A new version is now available with more automated steps. The objective is to perform sustainable process design through SustainPro.

As highlighted in Fig 4.5b, the inputs to *SustainPro* are the mass and the energy balance data that can be collected either from the plant or from process simulations. To perform the retrofit analysis, *SustainPro* also requires as input, several cost related data (the prices for utilities, the prices for chemicals, etc.). *SustainPro* is able to read the mass and the energy balance from an EXCEL file generated by a commercial simulator. The EXCEL interface guides the user through the steps of the work-flow (solution steps). After applying all the steps *SustainPro* gives as output for the retrofit analysis, a new design alternative suggestion for improving the process being investigated. When the software is used for performance analysis, the output provides the calculated values of the sustainability metrics and the safety indices. As it can be seen from Fig 4.5b, the two options can be combined, which means that they complement each other. After applying the retrofit analysis, the performance analysis is performed and compared with the base case design.

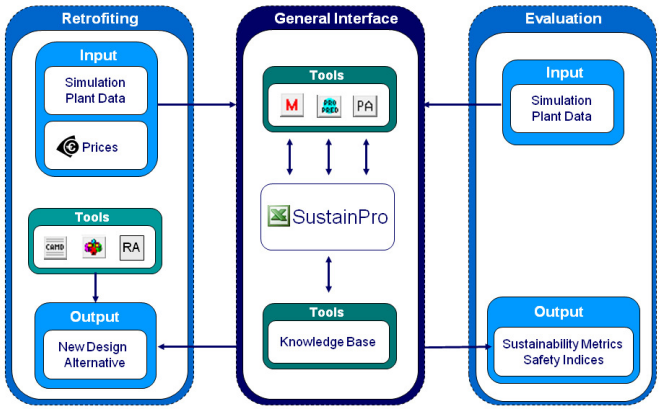


Figure 4.5b: Overview of the main features of SustainPro

4.4.3 Virtual Product-Process Design Lab

The idea behind the virtual product-process design lab is the following: instead of doing the experiments needed to search for a product and its process to manufacture it, the engineer/scientist performs *virtual* experiments, through the *v*PPD-lab software. The software therefore contains a large knowledge base of data (of chemicals, of solvents, of plants, of microcapsule devices, etc.); a large collection of models (models for property prediction, models for controlled release, models for mixing, etc.); of design algorithms (methods for formulation design, methods for molecule design, methods for polymer design, methods for process flowsheet synthesis, etc); other tools (property prediction software; model generation software; equipment design software; design of experiments software, etc.). All of the above are organized through a framework for efficient management of the complexity. Figure 4.4c gives an overview of the main features of the

*v*PPD-lab software, which has been used in the design and evaluation of the controlled release of a drug active ingredient (codeine) through a polymeric microcapsule. In the first step the problem is defined (identity of the active ingredient; the desired controlled release parameters, etc., are given in the "documentation" box of *v*PPD-lab). In the second step the selection of the application source (codeine released into the body), the primary properties of solvent and the polymer (needed by the controlled release model) is made (if the user is unable to provide this information, methods for solvent design and polymer design are used to generate a list of candidates to select from). In the next step the selection and calculation of the functional properties needed to evaluate the controlled release design is made (if models are not available, the modelling software helps to generate new models). In the next steps, the product performance model is used to predict the product behaviour. If the desired (target) performance is matched, then the last step of verifying the product performance through experiments is performed. If the target is not matched, it is possible to repeat from any of the earlier steps with a new design alternative. An option for formulation design together with the associated databases has been added.

Important issues to note from this example are that multi-scale models have been used, data and knowledge from different disciplines have been used and, design/evaluation problem has been effectively used by solving a collection of sub-problems according to a pre-determined sequence. The final step (not shown) would be to select a few of the alternatives and perform the necessary experiments to validate the selection. Therefore, the experiments are done not to design the product but to verify the product. This approach has the potential to save time and money in bringing a chemical based product to the market. Obviously, the accuracy and range of application of the *v*PPD-lab software depends on the available data and models in the software.

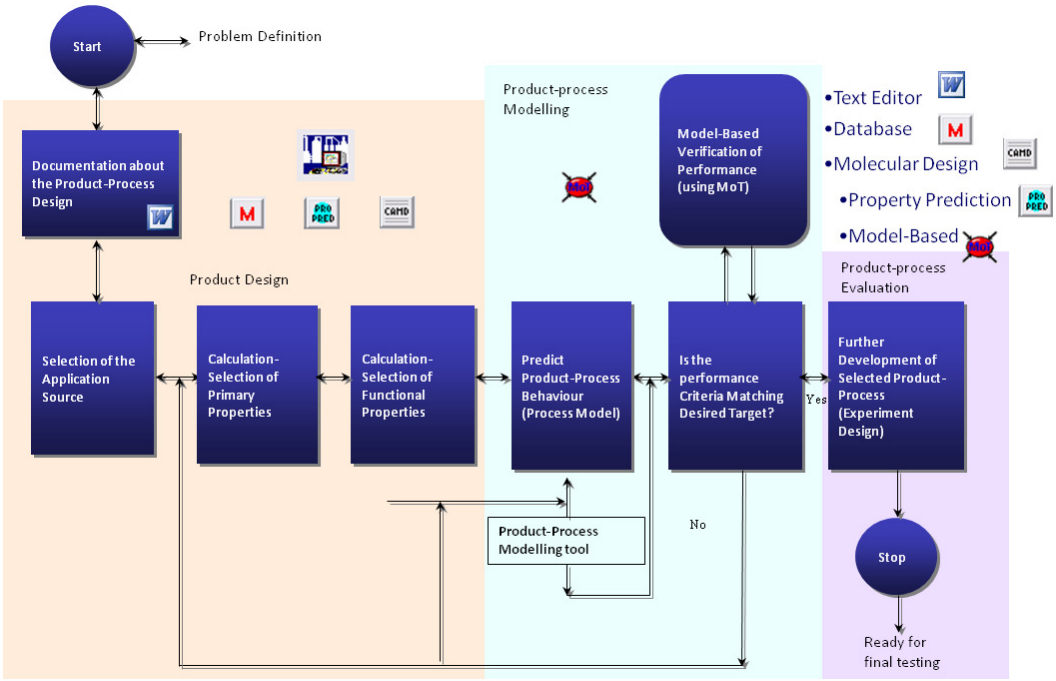


Figure 4.4c: The virtual product-process design lab

4.5 PC-SAFT Software Package

This software performs multicomponent phase equilibrium calculations at given temperature with the PC-SAFT equation of state.

• The user firstly provides some information about the molecules involved in the mixture and gives the molar fraction of each of them. The temperature of the mixture is also required. Molecules may be chosen from an extended databank of nearly 1000 compounds (including some polymers) or may be created from GC^+ methods.
• Once the mixture completely described, the user chooses between two kinds of calculations:

[1] *bubble point calculation:* The mixture is assumed to be a saturated liquid. The software calculates the bubble pressure and the composition of the vapour phase in equilibrium (a single bubble in this case).

[2] *dew point calculation:* The mixture is assumed to be a saturated vapour. The software calculates the dew pressure and the composition of the liquid phase in equilibrium (a single droplet in this case).

A new option has been made available in Propred 4.3 to run PC-SAFT for the calculation of the temperature dependent properties of pure components.

4.6 SMSWIN

SMSWIN is a software package that Syngenta has given to CAPEC for maintenance, further development and integration with ICAS. SMSWIN has a database of compounds and their properties, a collection of property models for phase equilibrium calculations, which are especially suitable for solution properties involving solids. Currently, ProPred and the KT-UNIFAC model have been integrated with SMSWIN.

A new version of SMSWIN is available. The following changes are made in the new version: (i) the default units are now °C and Bara (750mmHg) for all the plots, and (ii) the search is now correctly returning the same number of results when doing
a list by property or a property search (duplicates ar removed)

5. Research highlights (2010-2012)

The research highlights are discussed below in terms of new developments (results from completed PhD-projects) as well as publications record.

5.1 Summary of completed PhD research projects

5.1.1 Bodil Voss, 2011, "Value-added Chemicals from Biomass by Heterogeneous Catalysis", Ph.D. thesis (PROCESS)

In the contemporary debate on resource utilisation, biomass has been discussed as an alternative carbon source to fossil reserves in order to reduce the emission of CO2 to the atmosphere. The replacement or supplement of oil based transportation fuels through biomass based conversions has already been implemented. The subject on chemical production has received less attention.
This thesis describes and evaluates the quest for an alternative conversion route, based on a biomass feedstock and employing a heterogeneous catalyst capable of converting the feedstock, to a value-added chemical. The project work to fulfil the above object has been conducted with a multi-disciplinary approach ranging from fundamental catalyst research, through experiments, characterisation and process evaluation to market analysis.
The motivation herein is sought in the assets of sustainable resource utilization obtained for such a process and the hypothesis that process feasibility in comparison with the conventional synthesis gas based technologies may further be attainable, taking advantage of the conservation of chemical C-C bonds in biomass based feedstocks. With ethanol as one example of a biomass based feedstock, having retained one C-C bond originating from the biomass precursor, the aspects of utilizing heterogeneous catalysis for its conversion to value added chemicals is investigated. Through a simple analysis of known, but not industrialised catalytic routes, the direct conversion of ethanol to acetic acid product is identified to show good perspectives.
The nesting of a useful catalyst and an effective process is crucial to the potential of the overall process innovation. In a pre-screening study a group of Cu based catalysts active in the conversion have been identified. Considering the freedom to operate, the prospects of process development are further identified through process calculations based on the experimental evidence attained, theory and the process elements described in literature (primarily patent-related). The protection of the process inventions made in relation to this is sought through the filing of three patent applications. The most important contributions of this thesis are reflected in the eventual conclusion that an ethanol to acetic acid process and a related catalyst, both subject to further development, are identified.
The understanding of the catalytic behaviour of down-selected catalysts, Cu spinel (CuAl2O4) and Cu/SiO2, is furthered through characterisation as well as activity, selectivity and stability studies in appropriately developed experimental set-ups. Through numerous characterisation analyses (XAFS, XRPD, SEM, TEM, TPR, carbon analysis etc.) the rapid deactivation of the Cu spinel catalyst may be concluded to be attributed to the formation of high molecular carbonaceous compounds covering the catalytic surface, being catalysed by acidic alumina sites present during and after catalyst activation. This theory explains several phenomena observed for this catalyst. The Cu/SiO2 catalyst, having an inert support, shows far higher robustness to process variations, but immediately exhibits a too low activity from an industrial angle. Several means of improving its activity are elucidated. For example an activity dependence on the Cu crystal size is indicated by the comparison of the activity and XRPD analyses obtained for crushed and whole catalyst

pellets. Empirical kinetic models, in good agreement with the experimental data obtained for the Cu/SiO2 catalyst, are developed in order to support the establishment of an improved economic evaluation of the investigated process. Extrapolation of the derived model to the industrial pressure regime indicates a satisfactory activity. The Cu/SiO2 catalyst is further able to withstand partly oxidative dehydrogenation conditions, allowing for immense process improvements. Finally, the ethanol to acetic acid process is put into a broader context, by reviewing the methods used in this work, the market influence on its fate, the conclusions and improvements listed. Eventually, with an outlook on some alternative process possibilities, my recommendations given under the consideration of the initial project objective.
The results of the thesis, taking one example of biomass conversion, show that the utilisation of biomass in the production of chemicals by heterogeneous catalysis is promising from a technical point of view. But risks of market price excursions dominated by fossil based chemicals further set a criterion of a solid economic margin. Therefore, under market considerations other alternatives are to be investigated.
In addition to the technical conclusions it appears that a multi-disciplinary approach to process innovation is advantageous.

5.1.2 *Carlos Axel Díaz-Tovar, 2011, "Computer-Aided Modeling of Lipid Processing Technology", Ph.D. thesis (PEC11-23)- CAPEC*

Vegetable oils and fats have an important role in human nutrition andin the chemical industry since they are a source of energy, fat-soluble viatimins, and now also in the production of renewable sources energy. Nowadays as the consumer preferences for natural products and healthier foods increase along with gorowing interest in biofuels, the oleochemical industry faces in the upcoming years major challenges in terms of design and development of better products and more sustaibale processes to make them.
Computer-aided methods and tools for process synthesis, modeling and simulation are widely used for design, analysis, and optimization of processes in the chemical and petrochemical industries. These computer-aided tools have helped the chemical industry to evolve beyond commodities towards specialty chemicals and "comsumer oriented chemicals based products". Unfortunately this is not the case for the edible oil and biodiesel industries. The oleochemical industry lags behind the chemical industry in terms of Thermophysical property modeling and development of computational tools suitable for the design/analysis, and optimization of lipid-related processes.
The aim of this work has been to develop systematic computer-aided methods (property models) and tools (database) related to the prediction of the necessary physical properties suitable for design and analysis of processes emploiying lipid technologies. The methods and tools include: the development of a lipid-database (CAPEC_Lipids_Database) of collected experimental data from the open literature, data from industry, and, generated data from validated predictive property models; as well as the development of a databse user-interface and an external version of this database, for use in commercial process simulators, for fast adoption-analysis of property prediction models and for fast development of process models not available in process simulators.
This was achieved by first identifying and classifying the lipd compounds found in the edible oil and biodiesel industries. Then creating a list of the thermophysical properties needed for model-based design and analysis of edible oil and biodiesel processes. Next, collection of the available experimental data from different sources for the indentified compounds. Finally, selecting and adopting the appropriate models to predict the necessary

properties, to fill-out the lipd-database and to make it suitable for application with other computer-aided tools (such as commercial process simulators).
The developed computer-aided methods (property models) and tools (CAPEC_Lipids_Database) have been linked to the proposed methodology for the design/analysis of lipid-related processes. In this PhD thesis the analysis, in terms of their design variables and their impact in the process behavior, of three lipid-related processes has been performed: the solvent recovery section of the extratction of crude soybean oil, the deodorization of palm oil, and the deacidification of soybean oil.

5.1.3 *Alicia Román-Martínez, 2011, "A model-based framework for design of intensified enzyme-based processes", Ph.D. thesis (PEC11-24) - CAPEC*

This thesis presents a generic and systematic model-based framework to design intensified enzyme-based processes. The development of the presented methodology was motivated by the needs of the bio-based industry for a more systematic approach to achieve intensification in its production plants without an excessive investment in experimental resources. Process intensification has recently gained a lot of attention since it is a holistic approach to design safer, cleaner, smaller, cheaper and more efficient processes. This dissertation proposes a methodological approach to achieve intensification in enzyme-based processes which have found significant application in the pharmaceutical, food, and renewable fuels sector. The framework uses model-based strategies for (bio)-chemical process design and optimization, including the use of a superstructure to generate all potential reaction(s)-separation(s) options according to a desired performance criterion and a generic mathematical model represented by the superstructure to derive the specific models corresponding to a specific process option. In principle, three methods of intensification of a bioprocess are considered in this thesis: 1. enzymatic one-pot synthesis, where, for example, the combination of two enzymatic reactions in one single reactor is examined; 2. chemo-enzymatic one pot synthesis, where, for example, one enzymatic reaction and one alkaline catalytic reaction occur simultaneously in a single reactor; and 3. *in-situ* product recovery/removal (ISPR), where, for example, a separation step is integrated with the reaction step.
Often, enzyme-based processes have limited productivity and yield, which may be due to the unfavorable reaction equilibrium, product inhibition to the enzyme and/or product degradation. Additionally, downstream processing for enzyme-based processes is difficult and a way to simplify it is by reducing the reaction and separation steps by for example, combining the reaction and separation in a single processing step. The implementation of intensification methods usually involves experiment-based investigation which causes limitations in the search space of process options leading to a high risk of implementing sub-optimal processes. Therefore, applying the framework presented in this thesis, all possible process options can be considered, and using a hierarchical decomposition approach for optimization, the search space is reduced to locate the candidate process options, giving an optimal design where further experimental efforts can be focused on.
The application of a generic and systematic model-based framework is illustrated through a case study involving the production of an important intermediate pharmaceutical: *N*-acetyl-D-neuraminic acid (Neu5Ac). A second case study is added and deals with the enzymatic production of biodiesel.

5.1.4 Linfeng Yuan, 2011, "Membrane Assisted Enzyme Fractionation", Ph.D. thesis (PEC11-45) – PROCESS-CAPEC

Purification of proteins is an increasingly important process for the biotechnology industry. Separation of the desired high value protein from other proteins produced by the cell is usually attempted using a combination of different chromatographic techniques. These techniques separate mixtures of proteins on the basis of their charge, degree of hydrophobicity, affinity or size. Adequate purity is often not achieved unless several purification steps are combined thereby increasing cost and reducing product yield. Conventional fractionation of proteins using ultrafiltration membranes is limited to the variation in size of the proteins and a reasonable separation factor can be observed only when the size difference is in the order of 10 or more. This is partly caused by concentration polarization and membrane fouling which hinders an effective separation of the proteins. Application of an electric field across the porous membrane has been demonstrated to be an effective way to reduce concentration polarization and membrane fouling. In addition, this technique can also be used to separate the proteins based on difference in charge, which to some extent overcome the limitations of size difference.
In this thesis, separations using crossflow elecro-membrane filtration (EMF) of amino acids, bovine serum albumin (BSA) and industrial enzymes from Novozymes were performed. The main objective of this study was to investigate the technological feasibility of EMF in the application of industrial enzyme fractionation, such as removal of a side activity from the main enzyme activity.
As a proof-of-concept, amino acids were used as model solution to test the feasibility of EMF in the application of amphoteric molecule separation. A single amino acid was used to illustrate the effect of an electric field on the transport of a charged amino acid; the mass transport can be enhanced or decreased enormously when an electric field is applied in the same direction with convective transport or opposite to the direction of convective transport. Water splitting caused by limiting current density situation was observed at polarity +UF- (anode at ultrafiltration membrane side) due to the depletion of ions in the permeate compartment. By applying the electric field in UF filtration, it was possible to uncouple the transport between the charged Glutamic acid (Glu) and neutral Leucine (Leu) due to the fact that mass transport of Glu was enormously decreased because of electrophoretic force and that of Leu was not affected. The separation performance can be tuned by choosing different combinations of current density and TMP. The highest selectivity value (Leu separation from Glu) was achieved at nearly 90 in the condition of 60 A/m2 current density and TMP 0.3bar. The effect of electric field was also investigated and verified with EMF filtration of BSA solution. EMF filtration of BSA both with ultrafitration (UF) membrane and more open microfiltration (MF) membrane was studied and compared with normal UF and MF filtration in terms of flux and transmission. It was found that the flux and BSA transmission can be well manipulated and predicted based on the knowledge of solution pH and the polarity of electric field. However, the membrane-protein and protein-protein interactions caused by electrostatic interactions have to be taken into account and should be considered for optimization purpose.
Finally the separation experiments with a binary mixture of Lipase (LP) and Phospholipase (PLA) were performed. Results have shown that separation of LP (side activity) from PLA (main activity) which is not possible to achieve with normal MF has been successfully performed with EMF filtration using MF membrane. The highest selectivity value (LP separation from PLA) of around 5 was obtained when operating with EMF. The effects of feed concentration, solution pH, property of porous membrane TMP and electric field strength have been investigated in the EMF experiments. It has been found that the separation performance in terms of selectivity and Lipase purity in permeate was dependent on the feed concentration, solution pH and membrane properties. The effects of increasing electric field strength and TMP on the separation performance were very small in the investigated range. The mass transport of each enzyme can be well explained by the Extended-Nernst-Planck equation. Better separation

was observed at lower feed concentration, higher solution pH in the investigated range and with a polysulfone (PS) MF membrane. It can be concluded that EMF has been successfully demonstrated for the separation of enzymes which normal pressure-driven membrane process could not achieve. However, in order to achieve better separation a holistic optimization procedure is needed for future work.

5.1.5 *Wenjing Fu, 2012, "Process Design and Evaluation for Chemicals Based on Renewable Resources", Ph.D. thesis (PEC11-46) PROCESS-CAPEC*

One of the key steps in process design is choosing between alternative technologies, especially for processes producing bulk and commodity chemicals. Recently, driven by the increasing oil prices and diminishing reserves, the production of bulk and commodity chemicals from renewable feedstocks has gained considerable interest. Renewable feedstocks usually cannot be converted into fuels and chemicals with existing process facilities due to the molecular functionality and variety of the most common renewable feedstock (biomass). Therefore new types of catalytic methods as well as new types of processes for converting renewable feedstocks to bulk and commodity chemicals are required. In the future, it seems increasingly likely that a combination of biocatalysts (in the form of enzymes) as well as chemical catalysts will be needed in the production of bulk chemicals from renewable feedstocks. In addition, another characteristic of chemicals based on renewable feedstocks is that many alternative technologies and possible routes exist, resulting in many possible process flowsheets. The challenge for process engineers is then to choose between possible process routes and alternative technologies as well as to match different catalyst conditions. These kinds of problems are crucial, especially at the early stages of process development, when information is limited.
This thesis describes a methodological framework for dealing with the challenges and giving direction to research in the process development of chemicals based on renewable feedstocks. As an example, this thesis especially focuses on applying the methodology in process design and evaluation of the synthesis of 5-hydroxymethylfurfural (HMF) from the renewable feedstock glucose/fructose. The selected example is part of the chemoenzymatic process design of the synthesis 2,5-furandicarboxylic acid (FDA) from glucose.
By using the selected case study, the complexity and challenges for the process engineer to choose between different alternative routes and technologies as well as to combine two different kinds of catalysis (enzymatic catalysis and chemical catalysis) were illustrated.
Different process routes for the synthesis of HMF from fructose in the literature have been analyzed and evaluated. Using an aqueous route for HMF production is not economically feasible due to the low reaction yield. Using an anhydrous solvent for HMF synthesis is associated with high energy consumption and difficulties with solvent recycle in a large-scale production. The synthesis of HMF from fructose using a biphasic route is found to be promising, cost effective and give a better chance to be integrated with chemo-enzymatic cascades for producing FDA from glucose.
A process flowsheet using chemo-enzymatic cascades for HMF production from glucose has been proposed and evaluated. The process flowsheet is characterized by using glucose isomerase (EC 5.3.1.5) to convert glucose into fructose with a biphasic reaction for dehydration of fructose into HMF with recycle of the aqueous phase back to the enzymatic reaction. Costing analysis indicates the HMF production cost by the designed process is very sensitive to the dehydration reaction yield, the amount of solvent used in the whole process and the glucose price. In addition, increasing scale is also help to decrease the HMF production cost.

Using an ionic liquid (IL) route for HMF production has been evaluated with the dehydration reaction in [BMIm]Cl with different options starting from fructose and glucose with different initial concentrations. The HMF production cost is highly affected by the recycle of IL and catalyst. Processes with a high feed concentration show better economic potential than processes with a low feed concentration. IL processes starting from fructose are more costly than IL processes starting from glucose. A high concentration feed of glucose showed the best economic potential.
To sum up, the dehydration reaction yield is found to be the key important factor to achieve a feasible production cost of HMF. The use of the organic solvent can not be avoided and plays a very important role in determining the process economics. Recycling (unconverted sugar, reaction medium and solvent) become essential issues for HMF processes to reach a feasible production cost. Future directions and suggestions for the synthesis of HMF from sugar in a large-scale have been proposed. The developed methodology is helpful in evaluation and giving research directions. The methodology can be applied to other chemical process design and evaluation problems and in particular those for the next generation of production processes.

5.1.6: *Philip Lutze, 2012, "An Innovative Synthesis Methodology for Process Intensification", Ph.D. thesis (PEC12-22) PROCESS-CAPEC*

Process intensification (PI) has the potential to improve existing processes or create new process options, which are needed in order to produce products using more sustainable methods. A variety of intensified equipment has been developed which potentially creates a large number of options to improve a process. However, to date only a limited number have achieved implementation in industry, such as reactive distillation, dividing wall columns and reverse flow reactors. A reason for this is that the identification of the best PI option is neither simple nor systematic. That is to decide where and how the process should be intensified for the biggest improvement. Until now, most PI has been selected based on case-based trial-and-error procedures, not comparing different PI options on a quantitative basis.
Therefore, the objective of this PhD project is to develop a systematic synthesis/design methodology to achieve PI. It allows the quick identification of the best PI option on a quantitative basis and will push the implementation and acceptance of PI in industry. Such a methodology should be able to handle a large number of options. The method of solution should be efficient, robust and reliable using a welldefined screening procedure. It should be able to use already existing PI equipment as well as to generate novel PI equipment.
This PhD-project succeeded in developing such a synthesis/design methodology. In order to manage the complexities involved, the methodology employs a decomposition-based solution approach. Starting from an analysis of existing processes, the methodology generates a set of PI process options. Subsequently, the initial search space is reduced through an ordered sequence of steps. As the search space decreases, more process details are added, increasing the complexity of the mathematical problem but decreasing its size. The best PI options are ordered in terms of a performance index and a related set are verified through detailed process simulation. Two building blocks can be used for the synthesis/design which is PI unit-operations as well as phenomena. The use of PI unit-operations as building block aims to allow a quicker implementation/retrofit of processes while phenomena as building blocks enable the ability to develop novel process solutions beyond those currently in existence. Implementation of this methodology requires the use of a number of methods/algorithms, models, databases, *etc*., in the different steps which

have been developed. PI unit-operations are stored and retrieved from a knowledge-base tool. Phenomena are stored and retrieved from a phenomena library.
The PI synthesis/design methodology has been tested for both building blocks on a number of case studies from different areas such as conventional and bio-based bulk chemicals as well as pharmaceuticals.

5.1.7: *Albert Emili Cervera Padrell, 2012, "Moving from batch towards continuous organic-chemical pharmaceutical production", Ph.D. thesis (PEC12-23) PROCESS-CAPEC*

Pharmaceutical ingredients have traditionally been produced in batches using multipurpose stirred vessels. Reactions and separations have typically been tailored to fit these units, facing multiple limitations when transferring synthetic routes from the laboratory to industrial scale. Scaling up thus resulted in many cases in low reaction yields and separation efficiencies. These limitations were however compensated by a relatively fast process implementation. For the pharmaceutical industry this meant that new drug products could be exclusively marketed for a longer time period, resulting in higher benefits than those that could be obtained with a highly optimized process requiring extra development time. Being the first to commercialize a product also meant a fundamental marketing advantage, since healthcare professionals commonly related pharmaceutical products to the original trademark. Furthermore, once a pharmaceutical product was approved, changes to the original production process could only be achieved at the expense of revalidating the whole process in a worldwide market, which typically prevented pharmaceutical companies from optimizing already existing manufacturing processes.
Today, however, the pharmaceutical industry is facing a globalized market where national health institutions increasingly favor the prescription of low-cost generics, and it is more and more expensive to develop new pharmaceutical ingredients with the potential to become, for a few years, *blockbusters*. Fierce competition has therefore resulted in a need to reduce manufacturing costs and optimize the efficiency of production processes. In addition, ethical reasons and ever stricter legislations demand the development of sustainable processes with the lowest possible environmental footprint.
Continuous pharmaceutical manufacturing has been proposed as a way to facilitate process development and scale up, resulting in higher yields, improved quality, lower risks and reduced environmental impacts. Regulatory agencies, such as the FDA, have encouraged the transition towards novel technologies through increased process understanding. Developing a process within a more flexible *design space* based on sound engineering judgment potentially allows process optimization once the product has already been approved. Micro- and mini-chemical systems have been envisaged as the optimal scale for pharmaceutical production, due to improved heat and mass transfer allowing safer operation in a larger design space. Scaling up to high throughputs could then be performed by replicating small-scale units as required.
However, significant uncertainties arise. For example, when should continuous processes be selected?
Where are the highest benefits found? How can a continuous process be designed and implemented? Are continuous processes compatible with slow reactions? Do they allow problem free processing of solid particles? What is the cost needed to implement a continuous process?
This PhD thesis tries to answer some of those questions through the development of a systematic framework that takes advantage of continuous processing technologies and process systems engineering for the efficient design of continuous pharmaceutical

processes. The framework consists of a step-by-step procedure that guides the user from drug discovery and the initial process development steps towards process implementation. Guidelines are suggested for the selection of the most suitable operating mode. Conceptual continuous processes can then be compared against traditional batch-wise processes in order to evaluate potential cost savings and/or lower environmental footprints.
The design framework has been applied to a process originally developed by H. Lundbeck A/S to produce zuclopenthixol, an active pharmaceutical ingredient. The synthetic process includes four reaction steps (alkylation by a Grignard reaction, hydrolysis of the alkoxide product, dehydration and hydroamination) with very different kinetics and thermodynamics, and several separation and solvent exchange steps. The implementation of continuous processes provided improved product quality without the need of some of the product isolation and purification steps, resulting in a significant simplification of the process. The process mass intensity (kg of raw materials used per kg of product obtained) could then be reduced to at least half the original value.
In this thesis, three of the unit operations included in the zuclopenthixol process were studied in detail. Specifically, the continuous alkylation reaction was achieved using a filter reactor coupled with a side-entry tubular reactor, using real-time in-line near-infrared (NIR) spectroscopy for monitoring the reaction and ensuring the right product quality. A subsequent hydrolysis of the alkoxide product was performed in continuous mode in a tubular reactor with segmented flow. The product of the hydrolysis reaction was fed to a hydrophobic membrane separator where the organic and aqueous phases were split. The organic phase was then dehydrated in continuous mode in a pressurized tubular reactor where the reaction rate of an otherwise slow reaction could be optimized by increasing the temperature above the normal boiling point of the solvent. These three unit operations could potentially be employed in similar reaction and separation steps, thus constituting 'continuous-flow building blocks' for the design of novel continuous pharmaceutical processes.

5.1.8: *Martina Heitzig, 2012, "Computer-aided modeling for efficient and innovative product-process engineering", Ph.D. thesis (PEC12-24) CAPEC*

Model-based computer aided product-process engineering has attained increased importance in a number of industries, including pharmaceuticals, petrochemicals, fine chemicals, polymers, biotechnology, food, energy and water. This trend is set to continue due to the substantial benefits computer-aided methods provide. The key prerequisite of computer-aided product-process engineering is however the availability of models of different types, forms and application modes. The development of the models required for the systems under investigation tends to be a challenging, time-consuming and therefore cost-intensive task involving numerous steps, expert skills and different modelling tools. The objective of this project is to systematize the process of model development and application thereby increasing the efficiency of the modeller as well as model quality.
The main contributions of this thesis are a generic methodology for the process of model development and application, combining in-depth algorithmic work-flows for the different modelling tasks involved and the development of a computer-aided modelling framework. This framework is structured, is based on the generic modelling methodology, partially automates the involved work-flows by integrating the required tools and, supports and guides the user through the different work-flow steps. Supported modelling tasks are the establishment of the modelling objective, the collection of the required system information, model construction including numerical analysis, derivation of solution strategy and

connection to appropriate solvers, model identification/ discrimination as well as model application for simulation and optimization. The computer-aided modelling framework has been implemented into an user-friendly software.
A variety of case studies from different areas in chemical and biochemical engineering have been solved to illustrate the application of the generic modelling methodology, the computer-aided modelling framework and the developed software tool.

5.1.9: *Paloma de Gracia Andrade Santacoloma, 2012, "Multi-enzyme Process Modeling", Ph.D. thesis (PROCESS)*

systematically guide mathematical model building for better understanding of multi-enzyme processes. In this way, opportunities for process improvements can be identified by analyzing simulations of either existing or potential process configurations operated under different conditions. In these cases, process engineering, enzyme immobilization and protein engineering are presented as fields that can offer feasible solutions for better process configurations or biocatalyst modification to enhance actual process implementation, especially at an industrial level.
Multi-enzyme processes are characterized by a high degree of complexity due to the mixture of enzymes that catalyze several reactions. Therefore, it is necessary to understand how enzymes act in a coordinated and interactive way, and also how enzymes are affected (in a positive or negative way) by the presence of the other enzymes and compounds in the media.
In this thesis the concept of multi-enzyme in-pot term is adopted for processes that are carried out by the combination of enzymes in a single reactor and implemented at pilot or industrial scale. In order to understand the difference between multi-enzyme processes, a number of concepts are discussed in the second chapter of this thesis and has also been published as a review. Furthermore, a classification of multi-enzyme processes is suggested to clarify the ambiguous definitions found in the scientific literature.
Reliable mathematical models of such multi-catalytic schemes can exploit the potential benefit of these processes. In this way, the best outcome of the process can be obtained understanding the types of modification that are required for process optimization. An effective evaluation of these processes is achieved by applying a methodological framework which provides a systematic way of modeling, a structure, guidance, documentation and support to the modeler.
The methodological framework developed here brings many benefits to multienzyme process modeling. This framework identifies generic features of the process and provides the information required to structure the process model by using a step-by-step procedure with the required tools and methods. In this way, this framework increases efficiency of the model development process with respect to time and resources needed (fast and effective model development). Furthermore, this methodology incorporates state-of-the-art methods and provides background and insight into their applications for model development purposes.
The methodological framework, which comprises five steps, is the main result of this thesis. The novel feature of this methodology is the emphasis on the multi-enzyme process concepts that is introduced in all steps. In this way, the most relevant and necessary modeling issues can be precisely identified in order to achieve reliable mathematical structures of the processes. In the same way, specific mathematical techniques, for model quality evaluation such as uncertainty and sensitivity analyses, are included in this methodology. Multienzyme process modeling is tremendously benefited with the

introduction of these analyses which mark a big difference in the formulation of reliable models for the multi-enzyme processes. In this way the model parameters that drives the mai n dynamic behavior can be identified and thus a better understanding of this type of processes.
In order to develop, test and verify the methodology, three case studies were selected, specifically the bi-enzyme process for the production of lactobionic acid, the bi-enzyme process for the production of N-acetyl-D-neuraminic acid, and the tri-enzyme process for the production of 1-phenylethylamine. Furthermore, different capabilities of the methodology are developed due to the valuable contributions of each case study. In this way, the methodology was also proven to be useful for a fast model formulation of multi-enzyme processes. Additionally, programming codes were developed using MATLAB (The Mathworks, Natick, MA) which were also used as computational tools to support the implementation, solution and analysis of all the mathematical problems faced in the case studies.

5.1.10: *Mads Orla Albæk, 2012, "Evaluation of the efficiency of alternative enzyme production technologies", Ph.D. Thesis (PROCESS)*

Enzymes are used in an increasing number of industries. The application of enzymes is extending into the production of lignocellulosic ethanol in processes that economically can compete with fossil fuels. Since lignocellulosic ethanol is based on renewable resources it will have a positive impact on for example the emission of green house gasses. Cellulases and hemi-cellulases are used for enzymatic hydrolysis of pretreated lignocellulosic biomass, and fermentable sugars are released upon the enzymatic process. Even though many years of research has decreased the amount of enzyme needed in the process, the cost of enzymes is still considered a bottleneck in the economic feasibility of lignocellulose utilization. The purpose of this project was to investigate and compare different technologies for production of these enzymes. The filamentous fungus *Trichoderma reesei* is currently used for industrial production of cellulases and hemi-cellulases. The aim of the thesis was to use modeling tools to identify alternative technologies that have higher energy or raw material efficiency than the current technology.
The enzyme production by *T. reesei* was conducted as an aerobic fed-batch fermentation. The process was carried out in pilot scale stirred tank reactors and based on a range of different process conditions, a process model was constructed which satisfactory described the course of fermentation. The process was governed by the rate limiting mass transfer of oxygen from the gas to the liquid phase. During fermentation, filamentous growth of the fungus lead to increased viscosity which hindered mass transfer. These mechanisms were described by a viscosity model based on the biomass concentration of the fermentation broth and a mass transfer correlation that incorporated a viscosity term. An analysis of the uncertainty and sensitivity of the model indicated the biological parameters to be responsible for most of the model uncertainty.
A number of alternative fermentation technologies for enzyme production were identified in the open literature. Their mass transfer capabilities and their energy efficiencies were evaluated by use of the process model. For each technology the scale-up enzyme production was simulated at industrial scale based on equal mass transfer. The technical feasibility of each technology was assessed based on prior knowledge of successful implementation at industrial scale and mechanical complexity of the fermentation vessel. The airlift reactor was identified as a potential high energy efficiency technology for enzyme production with excellent chances for success.

Two different pilot plant configurations of the airlift reactor technology were tested in nine fermentations. The headspace pressure was varied between 0.1 and 1.1 barg and the superficial gas velocity in the airlift riser section was varied between 0.02 and 0.06 m/s. The biological model developed in the stirred tank reactor was shown to apply to the airlift reactor with only small modifications: The mass transfer of oxygen in the airlift reactor was studied and a mass transfer correlation containing the superficial gas velocity and the apparent viscosity of the fermentation broth was shown to describe the experimental data well. The mass transfer rate was approximately 20% lower than the literature data for airlift reactors. Mixing in the pilot scale airlift reactor was also studied. As the mixing time was of the same order of magnitude as the characteristic time for oxygen transfer, mixing could also be limiting the process at that scale. The process model for the airlift reactor was also shown to describe the experimental data well for a range of process conditions.
A cost function for oxygen transfer including the equipment cost and running cost for nutrients and electricity was developed for both the stirred tank reactor and the airlift reactor. The cost function was used to identify an optimum range of reactor configuration and process conditions for industrial scale enzyme production fermentors. It was shown that compared to the stirred tank reactor 22% of the electricity cost might be reduced for the airlift reactor, and the capital cost might also be somewhat lower. However, since the electricity cost is a relatively minor part of the total cost, there might currently not be an obvious fiscal motive to change technology. The cost of nutrients is considerably larger than the electricity cost and was shown to be independent of the technology and process conditions. If the cost structure changes in the future and the airlift reactor is chosen as the alternative production technology, suggestions on the practical scale-up procedure are given. These include the use of Computational Fluid Dynamics (CFD) and scale-down models of the production environment.

5.1.11: *Yuan Xu, 2012, "Process Technology for Immobilized Lipasecatalyzed Reactions" Ph.D. thesis (PROCESS)*

Biocatalysis has attracted significant attention recently, mainly due to its high selectivity and potential benefits for sustainability. Applications can be found in biorefineries, turning biomass into energy and chemicals, and also for products in the food and pharmaceutical industries. However, most applications remain in the production of high-value fine chemicals, primarily because of the expense of introducing new technology. In particular lipasecatalyzed synthesis has already achieved efficient operations for high-value products and more interesting now is to establish opportunities for low-value products. In order to guide the industrial implementation of immobilized-lipase catalyzed reactions, especially for highvolume low-value products, a methodological framework for dealing with the technical and scientific challenges and establishing an efficient process via targeted scale-down experimental work is described in this thesis. The methodology uses economic targets to test options characterized via a set of tools.
In order to validate the methodology, two processes based on immobilized lipase-catalysis have been studied: transesterification and esterification of vegetable oils for the production of biodiesel. The two processes are focused on the conversion of the two main components of vegetable oil materials, glyceride esters and free fatty acids respectively, into fatty acid alkyl esters. Although biodiesel is conventionally prepared via chemical-catalyzed transesterification of vegetable oils with methanol to produce fatty acid methyl esters (FAME), this work has been focused on the production of fatty acid ethyl esters (FAEE) with bioethanol due to the expected improved sustainability of this type of biodiesel.

A key reaction characteristic of the immobilized lipase-catalyzed transesterification is that it is multi-phasic system. The by-product glycerol can potentially impose inhibitory effects on immobilized lipases and likewise the un-dissolved ethanol can inhibit the lipase. The options for addressing these issues can be used as the basis for selecting the biocatalyst and the reactor (e.g. a hydrophobic carrier for the immobilized lipase and the capabilities to provide sufficient mixing as well as stepwise/continuous feeding of ethanol to the reactor).
An STR is efficient for batch operation while a PBR is efficient for a continuous production.
An STR can more easily provide sufficient external mass transfer for a reaction, but will lead to more mechanical damage of the biocatalyst particles, than a PBR. A reactor combination of CSTR with PBR can couple the advantages of both, delivering an efficient continuous process.
The second case study (esterification) shares some similar process characteristics to the first case (e.g. the multi-phasic nature). However, instead of glycerol, water shows a great impact on the extent of reaction. The removal of water should therefore be feasible during the operation of the reactor, either intermittently or preferably *in situ*. Highly anhydrous reaction conditions and the smaller substrates for this reaction place particular requirements on the lipase.
In order to validate the established processes at a larger scale, both lipase-catalyzed transesterification and esterification developed in the lab-scale STRs have been carried out in pilot-scale STRs. Results in both scale STRs correlate well with respect to the biocatalyst performance and mechanical stability.
Once the technical and scientific challenges of the process have been addressed, it is of course important to evaluate its economic and environmental feasibility. To that end, process evaluation has been performed for six processes composed of transesterification and product purification for making 'in-spec' biodiesel and the conventional chemical process is taken as a bench mark for comparison. The optimal process is a process composed of lipase-catalyzed transesterification with 'in-spec' biodiesel product as output with less feedstock input and waste production and much saved energy from the absence of product purification.

5.2 Publications Record

The last 12-months have seen a big increase for CAPEC in the number of peer-reviewed journal publications. 72 published paper from 2011 to present (plus 38 "in press" or "submitted") have been published in major chemical engineering journals (see Appendix 7.3). There have been 14 plenary or keynote lectures international conferences and 104 presentations have been made in important international conferences. This has given CAPEC greater visibility and attracted more attention to the research results published by CAPEC coworkers. CAPEC continues to have an open policy with respect to the publication of model parameters (especially, the CAPEC developed property models). The new version of ICAS 15.0 has all the latest property models and updated property model parameters.

6. Future Developments & Opportunities

For the industrial consortium, CAPEC and PROCESS are working on developing and analyzing new products and their corresponding processes together with achieving further process-product improvements through application of green chemistry principles and sustainability measures. Several joint-projects have been initiated to achieve this. First, however, a brief overview on PSE/CAPE and its relation to the CAPEC-PROCESS industrial consortium is given, followed by the current and future research plans within the identified focus areas.

6.1 Relation to PSE/CAPE

Process systems engineering promotes the solution of a problem in a systematic manner. In this way, although it has traditionally been applied by the chemical engineering community to solve problems for the oil and petrochemical industries, its potential application range is much wider. This is because the word "process" also implies, among others, the process of solving a problem; design of a biochemical / biological process for conversion of biomaterial to specific chemicals; and, the process of finding/designing chemicals with desired properties.

Most of the earlier developments can be linked to chemical processes involved with the manufacture of high volume bulk chemicals and the related industries (such as the oil and gas, petrochemical and chemical industries). To a lesser extent, these methods and tools have also been applied to the manufacture of low volume specialty chemicals. Since its formation, CAPEC has contributed by providing systematic, reliable and efficient models, methods and tools that have now become standard for the chemical process industries as well as in chemical engineering education. CAPEC software, employing CAPEC models and methods, such as ProPred (property prediction software), ProCAMD (molecular design-solvent selection software), SustainPro (sustainable process design software), ProCAFD (process flowsheet design/synthesis), ICAS (Integrated Computer Aided System), are routinely used by the CAPEC consortium members and more than 50 universities outside of Denmark.

The question therefore arises, what next? Where are the new challenges for CAPEC and what could be the new directions for research and education? Through collaboration with the CAPEC industrial member companies and academic partners, CAPEC conducted a "gap-analysis" with respect to identifying the current trends and the future needs with respect to chemical products, the processes that manufacture them and the models, methods and tools needed to design, analyze and operate them. The conclusions are briefly summarized below.

"*To satisfy the needs of the modern society, it is necessary to continuously develop better and significantly improved chemicals based products. The bulk chemicals as well as the specialty chemicals have important roles. For example, the bulk chemicals act as raw materials, solvents, process fluids, etc., are needed in the manufacture of specialty chemicals that may become an active ingredient for a pharmaceutical and/or drug product. Therefore improved designs of continuous processes (needed for the manufacture of bulk chemicals) are as important as designs of batch operations (needed for the manufacture of specialty chemicals). Also, alternative production routes from renewable feed materials*

and retrofit of processes for changes in feed materials while focusing on energy, water and environmental issues will need special attention."

6.2 Future Plans

Based on the above, CAPEC-PROCESS research collaboration will address the following questions:

- How does one identify the chemicals and their synthesis routes that will help to meet future economic demands, taking into account, also the questions of sustainability and protection of the environment (*eg.*, energy conservation and water resources)?
- How does one find their replacements for feedstocks and reagent as well as product and the processes to manufacture the products? The sources for many of the raw materials used, especially those derived from oil, gas, and some plants/animals continue to be depleted and may soon be economically infeasible to use (*eg.*, bio-refinery and green chemistry).
- How to develop and provide the necessary models, methods and tools through which the future problems can be addressed (*eg.*, multiscale modelling & integration/intensification)?

CAPEC and PROCESS plans to invest heavily in the following areas:

- Product-process modelling: Development of a generic computer aided modelling framework through which product-process models of different forms and scale can be generated/created with significantly less time and resources than current practice.
- Product-process design: Use of a multidisciplinary approach because the process-product knowledge (including data) will come from different sources and the performance criteria, factors, etc., will involve other research groups (expertise). The opportunity for CAPEC and PROCESS is that it can play the role of the "integrator" or "glue".
- Sustainable and greener process development: Develop systematic solution approaches that combine methods and tools from different sources into problem specific flexible, reliable and efficient systems.

More specifically, for CAPEC and PROCESS to meet the challenges for the future, the following topics will have higher priority:

- computer aided frameworks for generation and use of multi-scale models (further extension of the predictive-generic property-product–process models)
- methods for design of experiments to collect and analyze data (efficient use of resources in data collection) and, verification by experiments (through collaboration between CAPEC and PROCESS)
- methods & tools for process-product monitoring/control systems (and their design)
- sustainable process-product development (such as, hybrid processes, green chemistry, process intensification)
- systematic methods for product discovery (further extension of computer aided molecular and mixture design)
- evaluation of alternative processes for sustainability, retrofit and process modification

- evaluation tools to identify biocatalytic process bottlenecks and strategies to improve the biocatalyst (in collaboration with others) and process.

6.3 Managing the complexity through a systems approach

Product-process design and development in the life sciences, pharmaceutical, food and related industries, as opposed to the oil and petrochemical industries, is principally dependent on experiment-based trial and error approaches. Furthermore, unlike the oil and petrochemical industries in the life sciences, pharmaceutical, food and related industries, problems associated with product-process design and development involve, among others, the following distinct features:

- Multi-scale: important data related to the chemicals come from different sources, at different scales of time and size; for example, the properties that define the product characteristics are based on the microstructure of the molecule or material, while the process behaviour that needs to be monitored and controlled during operation is defined by the macroscopic (end-use) properties of the chemical system.
- Multidiscipline: the conversion of the biomaterial through biocatalysis requires knowledge of organic synthesis, enzymes, reaction catalysis, bioreactor design and operation – information about these topics come from different disciplines.
- Computer-aided techniques: lack of models to predict the behaviour of the chemicals at different scales, of enzymes during organic synthesis, of reaction kinetics, etc., means that appropriate model-based computer aided techniques have not been developed and use of experiment-based techniques is the only option.

Advances have been made on each of the above issues on specific areas of chemical and biochemical engineering. For example, multiscale polymerization reactors have been developed to investigate the operation of reactors; techno-economic assessment related to sustainability biofuels have been made using data from engineers, economists and scientists; computer-aided systems have been developed to perform routine mass and energy balances of chemical and biochemical processes. The demand for improved chemical-based products, made from more sustainable raw material resources and employing more efficient processes to make them, however, requires the above issues and others to be tackled in an integrated manner. This means that methods and tools suitable for current and future product-process development need to manage complex situations that require handling of data and knowledge from different sources and at different time and size scales. That is, the dimensions of the problems we need to solve have become larger. Therefore, a systems approach that can efficiently “manage the complexity” becomes very desirable.

The multi-dimensional and multi-scalar nature of problems is highlighted through Fig. 5.1, where, it can be noted that at the micro- and meso- scales, the related problems are dealing with the microstructure of the molecules or materials and their properties; at the macro-scale (traditional area of application of chemical engineering), the related problems are mainly dealing with the process and its operation to produce a desired chemical; at the mega-scale, the related problems are, among others, dealing with enterprise wide optimization and supply chain issues. Many of the problems of current interest, such as, finding the optimal biorefinery, sustainable chemical process-product design, use of green solvents, process (energy and water) integration, etc., involve the macro- and mega-scales.

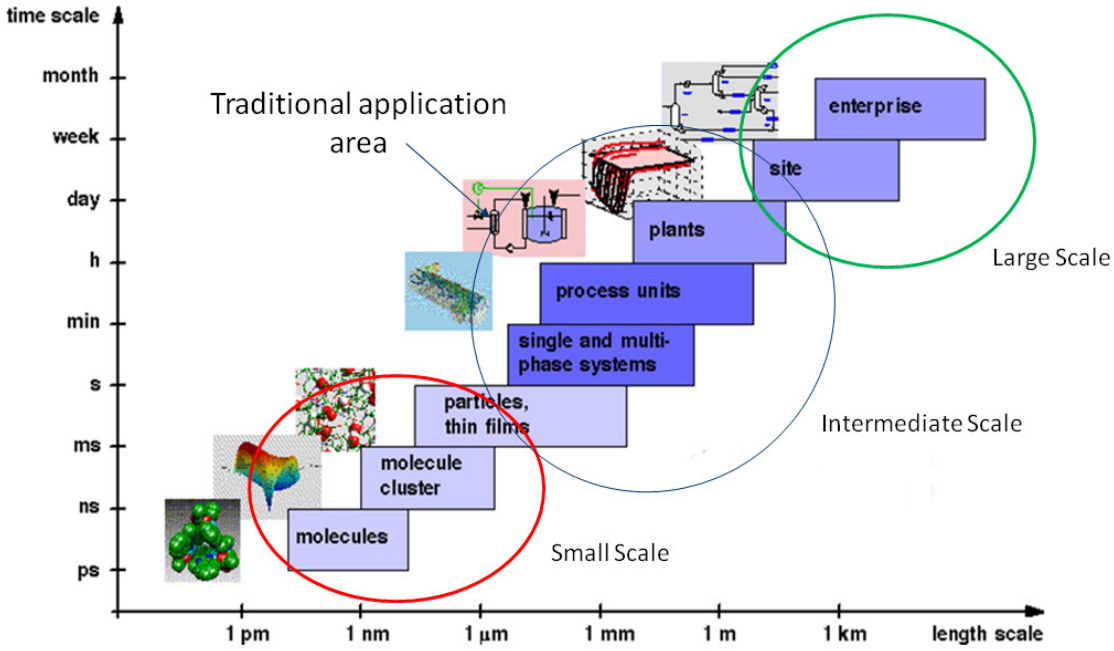


Figure 5.1: Multiscale nature of product-process design problems

To manage the complexity, a systems approach would develop a framework (the architecture of the software) for handling the diverse set of methods and tools needed to solve a wide range of problems, for a potential computer-aided system. Such systems need to have a knowledge base of data (for example, of the active ingredients, solvents, polymers, etc.); a library of models (for example, models to predict properties – in case data is not available - of active ingredients, solvents, polymers, etc.; models to predict the controlled release from the microcapsule; models to predict the behaviour of the mixing process); a design method (for example, guiding the engineer/scientist through the sequence of steps needed to identify the best solution); and, other associated methods-tools (such as a tool to analyze data; a tool to create the missing model; a tool to screen feasible alternatives). The principal idea here is to decompose a complex problem into a set of sub-problems that are easier to solve and identify those that can be solved through model-based solution approaches. Solving these sub-problems according to a pre-determined sequence helps to reduce the search space through each subsequent sub-problem solution, until a sub-problem cannot be solved with models anymore. At this point, the experiment-based trial and error approach takes over to determine the final solution. The advantage of this combined hybrid (systems approach) is that during the early stages, where enough data and models are available (or could be easily generated), the search space is rapidly reduced. In the later stages, where quantitative values become important and data/models become more unreliable, the experimental resources are employed, sometimes only to evaluate a few feasible alternatives to identify the truly innovative and best solution. Several examples of such computer aided systems can be found at CAPEC and current research is expanding on this approach through the development of a collection of methods and tools.

6.4 Some specific plans (CAPEC-PROCESS coworkers) for the future

Major collaboration between CAPEC and PROCESS will be established in the areas of thermodynamics of biocatalytic processes; in the development of generic process plants and in the development of the integrated biorefinery concept. At the same time, the current collaboration between CAPEC and PROCESS in the areas of crystallization modeling, control and monitoring; tailor-made blend design; process intensification; control and monitoring of biodiesel processes, and wastewater management will be continued. Collaboration with member companies in the areas of property prediction; process synthesis, design and intensification; solvents; integrated economic-business solutions; and the development of model based applications will continue. Specific projects in the areas of computer aided molecular and blend design; integrated biorefinery; water networks; process intensification and properties prediction are also set-up with collaboration partners from academia.

7. Appendix

7.1 PROCESS lab and Pilot plant

The PROCESS experimental facilities are based in a laboratory in building 227 and also the pilot hall in building 228. The possibility of batch, fed-tach and continuous process operations of biocatalystic reactions at miniature, lab and pilot scale is being developed. Both packed bed and stirred reactors are available. Analytical equipment is in place.

Figure 7.1: The main laboratory of the Process group

Figure7. 2: One of the HPLC setups

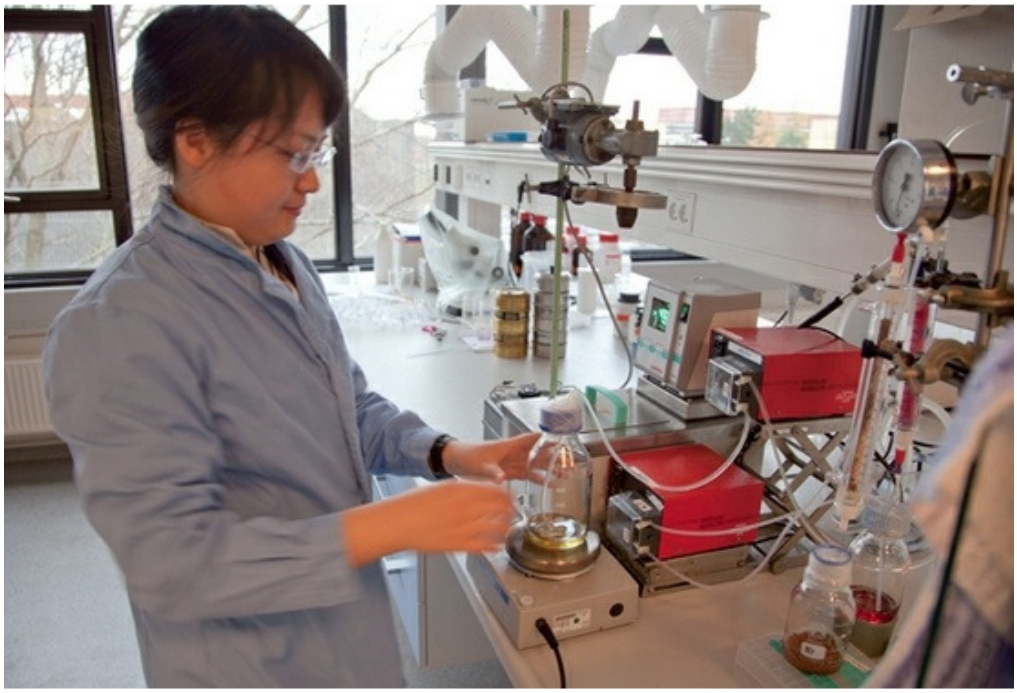


Figure 7.3: The former PhD student Yuan Xu is producing Biodiesel in a Batch Reactor

Figure 7.4: A group of students discussing the enjoyable latest results

7.2 CAPEC Control Lab

The main purpose of the CAPEC Control Lab is to give our students hands-on experience with process control problems. The laboratory is presently undergoing a complete renovation.

Two facilities are in use:

- a 4-tank exercise, and
- a distillation column

With the 4-tank exercise (used as a 2-tank system), students make two experiments. The first day they determine the dynamics of the system. Then they go to the computer lab to configure a PI-controller by simulation. On the second day they try out their controller settings on the real system. This setup is used in all our introductory teaching; about 75 students each year.

A HTST pasteurizer has also been established

The distillation column is used in an intensive 3-weeks course. This course teaches the participants to:

- Plan and execute start-up of the chemical plant.
- Apply a Distributed Control System for chemical plant operation.
- Simulate and document the operation of a chemical plant.
- Reason on process behaviour during start-up and operation.

4 tank exercise

HTST pasteurizer

Indirect Vapour Recompression Distillation Pilot Plant

7.3 Publication list (2011-2012)

Publications listed under PECxx-yy indicate CAPEC publications where one or more authors are CAPEC members, whether or not PROCESS is involved. Publications listed under PROCESS indicate PROCESS publications where there is no joint activity with CAPEC.

	A - Ph.D. Theses and Monographs
PEC10-24 Book chp.	Manuel Pinelo, Gunnar Jonsson, Anne S. Meyer, 2011, "Advances in the effective application of membrane technology in the food industry", in "Separation, extraction and concentration processes in the food, beverage and nutraceutical industries", S.S.H. Rizvi (Ed), Woodhead Publishing, Chapter 6, pp. 180-201
PROCESS	Muhd. Nazrul Hisham Zainal Alam, 2011, "Continuous Membrane Microbioreactor for Development of Integrated Pectin Modification and Separation Processes", Ph.D. thesis
PEC11-02	Mohd. Kamaruddin bin Abd. Hamid, 2011, "Model-Based Integrated Process Design and Controller Design of Chemical Processes", Ph.D. thesis
PEC11-03	Rasmus Wedberg, 2011, "Molecular Modeling of Enzyme Dynamics Towards Understanding Solvent Effects", Ph.D. thesis
PEC11-13	Martin D. Ellegaard, 2011, "Molecular thermodynamics using fluctuation solution theory", Ph.D. thesis
PROCESS	Bodil Voss, 2011, "Value-added Chemicals from Biomass by Heterogeneous Catalysis", Ph.D. thesis
PEC11-14 Book chp.	Ricardo Morales-Rodriguez, Rafiqul Gani, Stéphane Déchelotte, Alain Vacher and Olivier Baudouin, 2011, "Interoperability between Modelling Tools (MoT) with Thermodynamic Property Prediction Packages (Simulis® Thermodynamics) and Process Simulators (ProSimPlus) Via CAPE-OPEN Standards" in "Thermodynamics", ISBN: 978-953-307-544-0, Volume 1, Chapter 20, pp. 425-440
PEC11-16 Book chp.	Krist V. Gernaey, Ingmar Nopens, Gürkan Sin, and Ulf Jeppsson, 2011, "Chapter 11. Wastewater Systems", in "Handbook of Ecological Models used in Ecosystem and Environmental Management", Edited by Sven Erik Jørgensen, CRC Press , pp. 277–322, Print ISBN: 978-1-4398-1812-1, eBook ISBN: 978-1-4398-1813-8
PEC11-21 Book	Ian T. Cameron, Rafiqul Gani, 2011, "Product and Process Modelling : A Case Study Approach", Elsevier, The Boulevard, Langford Lane, Kidlington, Oxford OX5 1GB, UK, Radarweg 29, PO Box 211, 1000 AE Amsterdam, The Netherlands, ISBN: 978-0-444-53161-2
PEC11-23	Carlos Axel Díaz-Tovar, 2011, "Computer-Aided Modeling of Lipid Processing Technology", Ph.D. thesis
PEC11-24	Alicia Román-Martínez, 2011, "A model-based framework for design of intensified enzyme-based processes", Ph.D. thesis

PEC11-45	Linfeng Yuan, 2011, “Membrane Assisted Enzyme Fractionation”, Ph.D. thesis
PEC11-46	Wenjing Fu, **2012**, “Process Design and Evaluation for Chemicals Based on Renewable Resources”, Ph.D. thesis
PEC12-22	Philip Lutze, **2012, “**An Innovative Synthesis Methodology for Process Intensification”, Ph.D. thesis
PEC12-23	Albert Emili Cervera Padrell, **2012**, "Moving from batch towards continuous organic-chemical pharmaceutical production”, Ph.D. thesis
PEC12-24	Martina Heitzig, **2012**, “Computer-aided modeling for efficient and innovative product-process engineering”, Ph.D. thesis
PROCESS	Paloma de Gracia Andrade Santacoloma, **2012**, “Multi-enzyme Process Modeling”, Ph.D. thesis
PROCESS	Mads Orla Albæk, **2012**, “Evaluation of the efficiency of alternative enzyme production technologies”, Ph.D. Thesis
PROCESS	Yuan Xu, **2012**, “Process Technology for Immobilized Lipasecatalyzed Reactions” Ph.D. thesis

	B - Reviewed publications in International Journals
PEC09-42	Jakob Kjøbsted Huusom, Håkan Hjalmarsson , Niels Kjølstad Poulsen, Sten Bay Jørgensen, 2011, ”A Design Algorithm using External Perturbation to Improve Iterative Feedback Tuning Convergence”, Automatica, 47(12), pp. 2665-2670
PEC10-03	Bao Lin, Sten Bay Jørgensen, 2011, “Soft sensor design by multivariate fusion of image features and process measurements”, Journal of Process Control, 21, pp. 547-553
PEC10-08	Gürkan Sin, Krist V. Gernaey, Marc B. Neumann, Mark C.M. van Loosdrecht and Willi Gujer, 2011, ”Global sensitivity analysis in wastewater treatment plant model applications: Prioritizing sources of uncertainty”, Water Research, 45(2), pp. 639-651
PEC10-16	C.A. Diaz Tovar, R. Gani, B. Sarup, 2011, “Lipid technology: Property prediction and process design/analysis in the edible oil industries”, Fluid Phase Equilibria, 302, pp. 284-293
PEC10-18	A.A. Mustaffa, G.M. Kontogeorgis, R. Gani, 2011, “Analysis and application of GC plus models for property prediction of organic chemical systems”, Fluid Phase Equilibria, 302, pp. 274-283
PEC10-19	Elisa Conte, Rafiqul Gani and Tahir I. Malik, 2011, “The virtual product-process design laboratory to manage the complexity in the verification of formulated products”, Fluid Phase Equilibria, 302, pp. 294-304
PEC10-22	Morales Rodriguez, Ricardo; Gernaey, Krist; Meyer, Anne S.; Sin, Gürkan, 2011, ”A Mathematical Model for Simultaneous Saccharification and Co-fermentation (SSCF) of C6 and C5 Sugars”, Chinese Journal of Chemical Engineering 19(2), pp. 185-191

PEC10-27	Martin D. Ellegaard, Jens Abildskov, John P. O'Connell, 2011, "Solubilities of gases in ionic liquids using a corresponding-states approach to Kirkwood-Buff solution theory", Fluid Phase Equilibria, Special Issue PPEPPD 2010, 302, pp. 93-102
PEC10-29	Corominas L., Sin G., Puig S., Balaguer M.D., Vanrolleghem P.A., Colprim J., 2011, "Modified calibration protocol evaluated in a model-based testing of SBR flexibility", Bioprocess and Biosystems Engineering, 34(2), pp. 205-214
PEC10-30	Rasmus Wedberg, John P. O'Connell, Günther H. Peters, Jens Abildskov, 2011, "Total and Direct Correlation Function Integrals from Molecular Simulation of Binary Systems", Fluid Phase Equilibria, 302(1-2), pp. 32-42
PEC10-31	Prado-Rubio, O.A.; Jørgensen, S.B. and Jonsson, G., 2011, "Model based investigation of the potential lactate recovery using Electro-Enhanced Dialysis-Static analysis", Separation and Purification Technology Journal, 78, pp. 113-124
PEC10-32	Prado-Rubio, O.A.; Jørgensen, S.B. and Jonsson, G., 2011, "Reverse Electro-Enhanced Dialysis for lactate recovery from a fermentation broth", Journal of Membrane Science, 374(1-2), pp. 20–32
PEC10-33	Ricardo Morales-Rodriguez, Anne S. Meyer, Krist V. Gernaey, Gürkan Sin, 2011, "Dynamic Model-Based Evaluation of Process Configurations for Integrated Operation of Hydrolysis and Co-Fermentation for Bioethanol Production from Lignocellulose", Bioresource Technology Journal, 102(2), pp. 1174-1184
PEC10-34	Conte E., Gani R. and Ng K. M., 2011, "Design of formulated products: a systematic methodology", AIChE Journal, 57(9), pp. 2431-2449
PEC10-38	Noor Asma Fazli Abdul Samad, Ravendra Singh, Gürkan Sin, Krist V. Gernaey, Rafiqul Gani, 2011, "A generic multi-dimensional model-based system for batch cooling crystallization processes", Computers & Chemical Engineering, 35(5), pp. 828-843
PEC10-41	Heitzig, Martina; Sin, Gurkan; Sales Cruz, Mauricio; Glarborg, Peter; Gani, Rafiqul, 2011, "A computer-aided modeling framework for efficient model development, analysis and identification: Combustion and reactor modeling", Industrial & Engineering Chemistry Research Puigjaner Special Issue, 50(9), pp. 5253–5265
PEC10-42	Philip Lutze, Alicia Román-Martinez, John M. Woodley, Rafiqul Gani, **2012**, "A systematic synthesis and design methodology to achieve process intensification in (bio) chemical processes", Computers & Chemical Engineering, 36, pp. 189-207
PEC10-43	E. Conte, R. Gani, Y. S. Cheng, K. M. Ng, **2012**, "Design of Formulated Products: Experimental Component", AIChE Journal, 58(1), pp. 173-189
PEC10-46	M. V. Ruano, J. Ribes, J. Ferrer and G. Sin, 2011, "Application of the Morris method for screening the influential parameters of fuzzy controllers applied to wastewater treatment plants", Water Science & Technology, Vol. 63(10), pp. 2199–2206
PEC10-47	Iskandar Halim, Ana Carvalho, Rajagopalan Srinivasan, Henrique Matos, Rafiqul Gani, 2011, "A Combined Heuristic and Indicator-based Methodology for Design of Sustainable Chemical Process Plants", Computers and Chemical Engineering Journal (Special Issue: Energy & Sustainability), 35(8), pp. 1343-1358

PEC10-48	E. Zondervan, Mehboob Nawaz, André B de Haan, John M Woodley, Rafiqul Gani, 2011, "Optimal design of a multi-product biorefinery system", Computers and Chemical Engineering Journal (Special Issue: Energy Systems Engineering), 35(9), pp. 1752-1766
PEC10-49	Amnart Jantharasuk, Rafiqul Gani, Andrzej Górak, Suttichai Assabumrungrat, 2011, "Methodology for Design and Analysis of Reactive Distillation Involving Multielement Systems", Chemical Engineering Research and Design, 89(8), pp. 1295-1307
PEC10-66	Abildskov J., O'Connell J.P., 2011, "Molecular Thermodynamic Modeling and Design of Microencapsulation Systems for Drug Delivery", J. Chem. Eng. Data, 56, pp. 1229-1237
PEC11-01	Yuan, Hao ; Sin, Gürkan, 2011, "Uncertainty and Sensitivity Analysis of Filtration Models for Non-Fickian transport and Hyperexponential deposition", Chemical Engineering Journal, 168(2), pp. 635-648
PEC11-05	Santacoloma P.A., Sin G., Gernaey K.V., Woodley J.M., 2011, "Multienzyme-catalyzed processes: Next-generation biocatalysis", Organic Process Research & Development, 15, pp. 203-212
PEC11-08	Yung-Chieh Su, Y. A. Liu, Carlos Axel Diaz Tovar and Rafiqul Gani, 2011, "Selection of Prediction Methods for Thermophysical Properties for Process Modeling and Product Design of Biodiesel Manufacturing", Industrial Engineering and Chemistry Research, 50(11), pp. 6809-6836
PEC11-12	Tolga Us, Niels Jensen, Morten Lind, Sten B. Jørgensen, 2011, "Fundamental Principles of Alarm Design", International Journal of Nuclear Safety and Simulation, 2, pp. 44-51
PEC11-15	Wedberg R., O'Connell J.P., Peters G.H., Abildskov J., 2011, "Pair Correlation Function Integrals: Computation and Use", J. Chem. Phys., 135, 084113
PEC11-17	S. Sansonetti, T.J. Hobley, V. Calabrò, J. Villadsen and G. Sin, 2011, "A biochemically structured model for ethanol fermentation by Kluyveromyces marxianus: A batch fermentation and kinetic study", Bioresource Technology, 102(16), pp. 7513-7520
PEC11-20	Zainal Alam, M.N.H., Pinelo M., Samanta K., Jonsson G., Meyer A. and Gernaey K.V., 2011, "A continuous membrane microbioreactor system for development of integrated pectin modification and separation processes", Chemical Engineering Journal, 167, pp. 418-426
PEC11-47	Marta L. S. Batista, Catarina M. S. S. Neves, Pedro J. Carvalho, Rafiqul Gani, João A.P. Coutinho, 2011, "Chameleonic Behavior of Ionic Liquids and Its Impact on the Estimation of Solubility Parameters", The Journal of Physical Chemistry B, 115 pp. 12879-12888
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PEC10-12	P. Tansutapanich, P. Malakul, R. Gani, 2011, “Sustainable process design for lignocellulosic-based bioethanol using life cycle assessment technique”, (Paper presented at ISSPPE-2010, Hangzhou, China 9-12 May 2010), Internal Report
PEC10-53	Jakob Kjøbsted Huusom, Dawid Bialas, John Bagterp Jørgensen and Gürkan Sin, 2011, ”Towards benchmarking of multivariable controllers in chemical/biochemical industries: Plantwide control for ethylene glycol production”, 21st European Symposium on Computer Aided Process Engineering, ESCAPE21, (only on CD)
PEC11-04	Gürkan Sin, Rafiqul Gani, 2011, “Model-based engineering for product-process design – dealing with uncertainties”, Chemical Engineering, AIDIC, ISBN 978-88-95608-10-5, pp. 227-286
PEC11-25	Rafiqul Gani and John Woodley, 2011, “CAPEC-PROCESS Research Report 2011”, CAPEC-PROCESS Internal Report, DTU-KT, Lyngby, Denmark
PEC11-39	Rafiqul Gani, 2011,”Chemical Engineering Education in a Bologna Three Cycle Degree System”, unreviewed conference proceedings of XXXII National Meeting and 1st International Congress , AMIDIQ-2011 Proceedings, AMIDIQ, Mexico, pp. 24-25
PEC11-40	Rafiqul Gani, 2011, “Systematic methods for synthesis and design of sustainable chemical and biochemical processes”, unreviewed conference proceedings of XXXII National Meeting and 1st International Congress, AMIDIQ-2011 Proceedings, AMIDIQ, Mexico, pp. 55-56
PEC11-41	Alberto Vergara-Fernández, José Rebolledo-Castro, Ricardo Morales-Rodriguez, 2011, “Multiscale Modelling Approach for a Fungal Biofilter Unit for the Hydrophobic Abatement of Volatile Organic Compounds”, unreviewed conference proceedings of XXXII National Meeting and 1st International Congress AMIDIQ-201
PEC11-42	Ricardo Morales-Rodriguez, Chien-Tai Tsai, Anne S. Meyer, Krist V. Gernaey, Gürkan Sin, 2011, “Validation of Inhibition Effect in the Cellulose Hydrolysis: a Dynamic Modelling Approach”, unreviewed conference proceedings of XXXII National Meeting and 1st International Congress AMIDIQ-2011

PEC11-43	Ricardo Morales-Rodriguez, Anne S. Meyer, Krist V. Gernaey, Gürkan Sin, 2011, "Technology Evaluation of Process Configurations for Second Generation Bioethanol Production using Dynamic Model-based Simulations", unreviewed conference proceedings of XXXII National Meeting and 1st International Congress AMIDIQ-2011
PEC11-44	Ricardo Morales-Rodriguez, Anne S. Meyer, Krist V. Gernaey, Gürkan Sin, 2011, "Modelling Framework for the Identification of Critical Variables and Parameters under Uncertainty in the Bioethanol Production from Lignocellulose", unreviewed conference proceedings of XXXII National Meeting and 1st International Congress AMIDIQ-2011
PEC11-50	Rafiqul Gani, 2012, "A systems engineering approach to manage the complexity in sustainable chemical product-process design", electronic unreviewed proceedings to 13th Industrialist's Conference, info on USB stick
PEC11-51	Sin Gürkan, 2012, "An integrated knowledge-based framework for synthesis and design of enterprise-wide processing networks", electronic unreviewed proceedings to 13th Industrialist's Conference, info on USB stick
	Valverde-Pérez, B. Mauricio-Iglesias, M. Sin, G., **2012**, "Modelling and control design for SHARON/Anammox reactor sequence", Proceedings of Nordic Process and Control Workshop 17 (NPCW17), Technical University of Denmark, Kgs Lyngby, Denmark, pp. 176-184
	Ane H. Mollerup, M. Mauricio-Iglesias, N. B. Johansen, D. Thornberg, P. S. Mikkelsen and G. Sin, **2012**, "Model-based analysis of control performance in sewer systems", Proceedings of Nordic Process and Control Workshop 17 (NPCW17), Technical University of Denmark, Kgs Lyngby, Denmark, pp. 123-127
	Prado-Rubio, O.A., Jørgensen, S.B. and Jonsson, **2012**, "On controllability of an integrated bioreactor and periodically operated membrane separation process", Proceedings of Nordic Process and Control Workshop 17 (NPCW17), Technical University of Denmark, Kgs Lyngby, Denmark, p. 207
	Remus M. Prunescu, Mogens Blanke, Jakob M. Jensen, Gürkan Sin, **2012**, "Temperature Modelling of the Biomass Pretreatment Process", Proceedings of the 17th Nordic Process Control Workshop (NPCW17), Technical University of Denmark, Kgs Lyngby, Denmark pp. 8-17
	Sten Bay Jørgensen and Morten Lind, **2012**, "Modeling Operating Modes during Plant Life Cycle", Proceedings of the 17th Nordic Process Control Workshop (NPCW17), Technical University of Denmark, Kgs Lyngby, Denmark p. 60
	Mads O. Albaek, Krist V. Gernaey, Morten S. Hansen, Stuart M. Stocks, **2012**, "Modelling Fungal Fermentations For Enzyme Production", Proceedings of the 17th Nordic Process Control Workshop (NPCW17), Technical University of Denmark, Kgs Lyngby, Denmark, p. 185
	Jason A. Price, Jakob Kjøbsted Huusom, Mathias Nordblad, John Woodley, **2012**, "Operation and Control of Enzymatic Biodiesel Production", Proceedings of the 17th Nordic Process Control Workshop (NPCW17), Technical University of Denmark, Kgs Lyngby, Denmark, pp. 186
	Guofeng Zhou, Jakob K. Huusom, John Bagterp Jørgensen, 2012, "State Estimation for the Automotive SCR Process", Proceedings of the 17th Nordic Process Control Workshop (NPCW17), Technical University of Denmark, Kgs Lyngby, Denmark, p. 204

PEC12-25	Rafiqul Gani and John Woodley, **2012**, "CAPEC-PROCESS Research Report 2012", CAPEC-PROCESS Internal Report, DTU-KT, Lyngby, Denmark
PROCESS	Gernaey K.V. (2011) Bioreactor design and optimization – a future perspective. Biotechnology International, Feb.-March 2011, 21-23.
PROCESS	Cervera-Padrell A.E., Skovby T., Kiil S. and Gernaey K.V. (2011) Kontinuerlig lægemiddelproduktion af små molekyler via organisk syntese. Dansk Kemi, 92(11): 18-20
PROCESS Unrev.	Gernaey K.V. (2011) Bioreactor design and optimization – a future perspective. Biotechnology International, Feb.-March 2011, 21-23.
PROCESS Unrev.	Cervera-Padrell A.E., Skovby T., Kiil S. and Gernaey K.V. (2011) Kontinuerlig lægemiddelproduktion af små molekyler via organisk syntese. Dansk Kemi, 92(11): 18-20

	F - Conference Presentations 2011
2011-1 (poster)	Nor Alafiza Yunus, Krist V. Gernaey, John M. Woodley, Rafiqul Gani, 2011, "Design of Tailor-made Fuel Blends of Gasoline and Bio-fuels", International Congress on Sustainability Science and Engineering (ICOSSE'11), Tucson, Arizona, 9-12 January
2011-2	Chandrakant B. Panchal, John C. Prindle, Jing Huang, Robert W. Lyczkowski, Richard D. Doctor, Emmanuel A. Dada, Philip Lutze, Rafiqul Gani and John M. Woodley, 2011, "Heat-Integrated Reactive Distillation", AIChE Spring Meeting, Chicago, Illinois, USA, 13-17 March
2011-3	Philip Lutze, Rafiqul Gani, John M. Woodley, 2011, "Phenomena-Based Process Synthesis and Design to Achieve Process Intensification", AIChE Spring Meeting, Chicago, Illinois, USA, 13-17 March
2011-4	I. Mitrofanov, G. Sin, R. Gani, 2011, "Computer-Aided Solvent Selection Framework", CAPE forum-2011, Bradford, UK, 21-22 March
2011-5	Jakob Kjøbsted Huusom, 2011, "The Role of Mechanistic and Statistic Models in Predictive Control Applications", CAPE forum-2011, Bradford, UK, 21-22 March
2011-6	Rafiqul Gani, 2011, "Model based process-product design and analysis", International Conference on Modeling, Simulation and Applied Optimization, ICMSAO 2011, Kuala Lumpur, Malaysia, 19-21 April **(Plenary Lecture)**
2011-7	Nor Alafiza Yunus, Rafiqul Gani, John Woodley, 2011, "Tailor-made Design of Chemical Blends using Decomposition-based Computer-aided Approach", International Conference on Modeling, Simulation and Applied Optimization, ICMSAO 2011, Kuala Lumpur, Malaysia, 19-21 April

2011-8	Carlos Axel Diaz-Tovar, Azizul Azri Mustaffa, Amol Hukkerikar, Alberto Quaglia, Gürkan Sin, Georgios Kontogeorgis, Bent Sarup, Rafiqul Gani, 2011, "Building a Multilevel Modeling Network for Lipid Processing Systems", International Conference on Modeling, Simulation and Applied Optimization, ICMSAO 2011, Kuala Lumpur, Malaysia, 19-21 April
2011-9	Noor Asma Fazli Samad, Gürkan Sin, Krist V. Gernaey, Rafiqul Gani, 2011, "Systematic Procedure for Generating Operational Policies to Achieve Target Crystal Size Distribution (CSD) in Batch Cooling Crystallization", International Conference on Modeling, Simulation and Applied Optimization, ICMSAO 2011, Kuala Lumpur, Malaysia, 19-21April **(Best Paper)**
2011-10	Noor Asma Fazli Abdul Samad, Ravendra Singh, Gürkan Sin, Krist V. Gernaey and Rafiqul Gani, 2011, "Systematic Modelling and Crystal Size Distribution Control for Batch Crystallization Processes", 2nd European Conference on Process Analytics and Control Technology (EuroPACT 2011), Glasgow, Scotland, 26-29 April
2011-11	Rafiqul Gani, 2011,"Chemical Engineering Education in a Bologna Three Cycle Degree System", XXXII National Meeting and 1st International Congress AMIDIQ-2011, Riviera Maya, Mexico, 3-6 May **(Invited Lecture)**
2011-12	Rafiqul Gani, 2011, "Systematic methods for synthesis and design of sustainable chemical and biochemical processes", XXXII National Meeting and 1st International Congress AMIDIQ-2011, Riviera Maya, Mexico, 3-6 May **(Plenary Lecture)**
2011-13 (poster)	Alberto Vergara-Fernández, José Rebolledo-Castro, Ricardo Morales-Rodriguez, 2011, "Multiscale Modelling Approach for a Fungal Biofilter Unit for the Hydrophobic Abatement of Volatile Organic Compounds", XXXII National Meeting and 1st International Congress AMIDIQ-2011, Riviera Maya, Mexico, 3-6 May
2011-14 (poster)	Ricardo Morales-Rodriguez, Chien-Tai Tsai, Anne S. Meyer, Krist V. Gernaey, Gürkan Sin, 2011, "Validation of Inhibition Effect in the Cellulose Hydrolysis: a Dynamic Modelling Approach", XXXII National Meeting and 1st International Congress AMIDIQ-2011, Riviera Maya, Mexico, 3-6 May
2011-15 (poster)	Ricardo Morales-Rodriguez, Anne S. Meyer, Krist V. Gernaey, Gürkan Sin, 2011, "Technology Evaluation of Process Configurations for Second Generation Bioethanol Production using Dynamic Model-based Simulations", XXXII National Meeting and 1st International Congress AMIDIQ-2011, Riviera Maya, Mexico, 3-6 May
2011-16 (poster)	Ricardo Morales-Rodriguez, Anne S. Meyer, Krist V. Gernaey, Gürkan Sin, 2011, "Modelling Framework for the Identification of Critical Variables and Parameters under Uncertainty in the Bioethanol Production from Lignocellulose", XXXII National Meeting and 1st International Congress AMIDIQ-2011, Riviera Maya, Mexico, 3-6 May
2011-17	Jakob Kjøbsted Huusom, 2011, "Model Based Monitoring and Control of Chemical and Biochemical Processes", Model Based Control Conference, DTU, Lyngby, Denmark, 5 May
2011-18	Philip Lutze, Rafiqul Gani, John M. Woodley, 2011, "A systematic synthesis and design methodology to achieve process intensification in (bio)chemical processes", Process Intensification Network (PIN) – NL Spring Session, Utrecht, The Netherlands, 11 May

2011-19	Jakob Kjøbsted Huusom, Niels Kjølstad Poulsen, Sten Bay Jørgensen and John Bagterp Jørgensen, 2011, "Systematic identification and robust control design for uncertain time delay processes", 21th European Symposium on Computer Aided Process Engineering, ESCAPE21, Chalkidiki, Greece, 29 May -1 June
2011-20	Elisa Conte, Rafiqul Gani, 2011, "Chemical-Based Formulation Design: Virtual Experimentation", Proceedings 21st European Symposium on Computer Aided Process Engineering, ESCAPE 21, Chalkidiki, Greece, 29 May -1 June
2011-21	Chiara Piccolo, Patrick M. Piccione, Rafiqul Gani, 2011, "Modeling and design of reacting systems with phase transfer catalysis", 21th European Symposium on Computer Aided Process Engineering, ESCAPE21, Chalkidiki, Greece, 29 May -1 June
(poster) 2011-22	Oscar Andres Prado-Rubio, Sten Bay Jorgensen and Gunnar Jonsson, 2011, "Systematic Procedure for Integrated Process Operation: Reverse Electro-Enhanced Dialysis (REED) during Lactic Acid Fermentation", 21th European Symposium on Computer Aided Process Engineering, ESCAPE21, Chalkidiki, Greece, 29 May -1 June
(poster) 2011-23	Albert E. Cervera, Rafiqul Gani, Søren Kiil, Tommy Skovby, Krist V. Gernaey, 2011, "A systematic methodology for the design of continuous active pharmaceutical ingredient production processes", 21th European Symposium on Computer Aided Process Engineering, ESCAPE21, Chalkidiki, Greece, 29 May -1 June
(poster) 2011-24	Ravendra Singh, Raquel Rozada-Sanchez, Tim Wrate, Frans Muller, Krist V. Gernaey, Rafiqul Gani, John M. Woodley, 2011, "A retrofit strategy to achieve "Fast, Flexible, Future (F3)" pharmaceutical production processes", 21th European Symposium on Computer Aided Process Engineering, ESCAPE21, Chalkidiki, Greece, 29 May -1 June
(poster) 2011-25	Klaus Reinholdt Nyhuus Hansen, Martin Grunow, Rafiqul Gani, 2011, "Robust Market Launch Planning for a Multi-Echelon Pharmaceutical Supply Chain", 21th European Symposium on Computer Aided Process Engineering, ESCAPE21, Chalkidiki, Greece, 29 May -1 June
2011-26	Carlos A. Diaz-Tovar, Azizul A. Mustaffa, Amol Hukkerikar, Alberto Quaglia, Gürkan Sin, Georgios Kontogeorgis, Bent Sarup, Rafiqul Gani, 2011, "Lipid Processing Technology: Building a Multilevel Modeling Network", 21th European Symposium on Computer Aided Process Engineering, ESCAPE21, Chalkidiki, Greece, 29 May -1 June
2011-27	Brock C. Roughton, Kyle V. Camarda, and Rafiqul Gani, 2011, "Simultaneous Design of Ionic Liquids and Azeotropic Separation for Systems Containing Water", 21th European Symposium on Computer Aided Process Engineering, ESCAPE21, Chalkidiki, Greece, 29 May -1 June
2011-28	Noor Asma Fazli Abdul Samad, Ravendra Singh, Gürkan Sin, Krist V. Gernaey, Rafiqul Gani, 2011, "Integration of Generic Multi-dimensional Model and Operational Policies for Batch Cooling Crystallization", 21th European Symposium on Computer Aided Process Engineering, ESCAPE21, Chalkidiki, Greece, 29 May -1 June
2011-29	Susilpa Bommareddy, Mario R. Eden, Rafiqul Gani, 2011, "Computer Aided Flowsheet Design using Group Contribution Methods", 21th European Symposium on Computer Aided Process Engineering, ESCAPE21, Chalkidiki, Greece, 29 May -1 June

2011-30	Martina Heitzig, Christopher Gregson, Gürkan Sin, Rafiqul Gani, 2011, "Application of computer-aided multi-scale modelling framework – Aerosol case study", 21th European Symposium on Computer Aided Process Engineering, ESCAPE21, Chalkidiki, Greece, 29 May -1 June
2011-31	Mehboob Nawaz, Edwin Zondervan, John Woodley and Rafiqul Gani, 2011, "Design of an Optimal Biorefinery", 21th European Symposium on Computer Aided Process Engineering, ESCAPE21, Chalkidiki, Greece, 29 May -1 June
(poster) 2011-32	Philip Lutze, Rafiqul Gani, John M. Woodley, 2011, "Phenomena-based Process Synthesis and Design to achieve Process Intensification", 21th European Symposium on Computer Aided Process Engineering, ESCAPE21, Chalkidiki, Greece, 29 May -1 June
2011-33	Ricardo Morales-Rodriguez, Anne S. Meyer, Krist V. Gernaey, Gürkan Sin, 2011, "A framework for model-based optimization of bioprocesses under uncertainty: Identifying critical parameters and operating variables", 21th European Symposium on Computer Aided Process Engineering, ESCAPE21, Chalkidiki, Greece, 29 May -1 June
PROCESS	Krist V. Gernaey, Albert E. Cervera and John M. Woodley, 2011, "PSE in pharmaceutical process development", 21th European Symposium on Computer Aided Process Engineering, ESCAPE21, Chalkidiki, Greece, 29 May -1 June
(poster) 2011-34	Dawid Jan Białas, Jakob Kjøbsted Huusom, John Bagterp Jørgensen, Gürkan Sin, 2011, "Model predictive control for plant-wide control of a reactor-separation-recycle system", 21th European Symposium on Computer Aided Process Engineering, ESCAPE21, Chalkidiki, Greece, 29 May -1 June
2011-35	Andrade Santacoloma, Paloma de Gracia; Roman Martinez, Alicia; Sin, Gürkan; Gernaey, Krist; Woodley, John, 2011, "Methodological Approach for Modeling of Multienzyme in-pot Processes", 21th European Symposium on Computer Aided Process Engineering, ESCAPE21, Chalkidiki, Greece, 29 May -1 June
2011-37	Elham Ramin, Gürkan Sin, Peter Steen Mikkelsen, Benedek Gy. Plósz, 2011, "Significance of uncertainties derived from settling tank model structure and parameters on predicting WWTP performance - A global sensitivity analysis study", Watermatex, San Sebastian, Spain, 19-23 June
2011-38	Anna Katrine Vangsgaard, Miguel Mauricio Iglesias, Krist V. Gernaey, Barth F. Smets, and Gürkan Sin, 2011, "Framework for Construction of Multi-scale Models for Biological Wastewater Treatment Processes", Watermatex 2011, 8th IWA Symposium on Systems Analysis and Integrated Assessment, San Sebastian, Spain, 20-22 June
2011-39	Amol Hukkerikar, Bent Sarup, Gürkan Sin and Rafiqul Gani, 2011, "Estimation of Properties of Pure Components Using Improved Group Contribution Based and Atom Connectivity Index Based Models and Uncertainty Analysis", 25th European Symposium on Advanced Thermodynamics (ESAT), Saint Petersburg, Russia, 24-27 June
2011-40	Jakob Kjøbsted Huusom, Niels Kjølstad Poulsen, Sten Bay Jørgensen and John Bagterp Jørgensen, 2011, "Adaptive Disturbance Estimation for Offset-Free SISO Model Predictive Control", American Control Conference ACC, San Francisco, USA, 29 June -1 July
2011-41	Gunnar Jonsson, Oscar Prado Rubio, 2011, "Modeling and operation of dynamic membrane processes", ICOM2011, Amsterdam, Holland, 23-29 July, Keynote

PROCESS	Yuan, Linfeng; Korsholm, Lars; Jakobsen, Sune; Woodley, John; Jonsson, Gunnar Eigil, 2011, "Electro-membrane filtration: An Alternative Way to Fractionate Industrial Enzymes", ICOM2011, Amsterdam, Holland, 23-29 July
2011-42	Morten Lind, Hidekazu Yoshikawa, Sten Bay Jørgensen, Ming Yang, Kiyoshi Tamayama, Kyoichi Okusa, 2011, "Multilevel Flow Modeling of Monju Nuclear Power Plant", ICI2011 (ISOFIC, CSEPC, ISSNP 2011), Daejeon, Korea, 21-25 August
2011-43	Jakob K. Huusom, Niels K. Poulsen, Sten B. Jørgensen & John B. Jørgensen, 2011, "Noise Modelling and MPC Tuning for Systems with Infrequent Step Disturbances", 18th IFAC World Congress, Milan, Italy, 28 August - 2 September
2011-44	Chiara Piccolo, George Hodges, Patrick M. Piccione, Rafiqul Gani, 2011, "Modelling and design of phase transfer catalytic processes", 8th European Congress of Chemical Engineering (ECCE-8/ECAB-1), Berlin, Germany, 25-29 September, **Keynote**
(poster) 2011-45	Chiara Piccolo, Patrick M. Piccione, Andrew Shaw, George Hodges, Rafiqul Gani, 2011, "Systematic computation of phase partition and solubilities in phase transfer catalytic processes", 8th European Congress of Chemical Engineering (ECCE-8/ECAB-1), Berlin, Germany, 25-29 September
2011-46	Elisa Conte, Rafiqul Gani, Peter Crafts, 2011, "A framework for API solubility modelling", 8th European Congress of Chemical Engineering (ECCE-8/ECAB-1), Berlin, Germany, 25-29 September
2011-47	Alberto Quaglia, Bent Sarup, Gürkan Sin and Rafiqul Gani, 2011, "A systematic framework for CAFD and resources allocation optimisation using MINLP in vegetable oil processing", 8th European Congress of Chemical Engineering (ECCE-8/ECAB-1), Berlin, Germany, 25-29 September
2011-48	Martina Heitzig, Christopher Gregson, Gürkan Sin, Rafiqul Gani, 2011, "Systematic multi-scale model development strategy for fragrance spraying process and transport", 8th European Congress of Chemical Engineering (ECCE-8/ECAB-1), Berlin, Germany, 25-29 September, **Keynote**
2011-49	Philip Lutze, Rafiqul Gani, John M. Woodley, 2011, "Application of a Synthesis and Design Methodology to achieve Process Intensification", 8th European Congress of Chemical Engineering (ECCE-8/ECAB-1), Berlin, Germany, 25-29 September
2011-50	Ravendra Singh, Raquel Rozada-Sanchez, Frans Muller, Tim Wrate, Krist V. Gernaey, Rafiqul Gani, John M. Woodley, 2011, "Substrates adoption methodology (SAM) to achieve "Fast, Flexible, Future (F^3)" pharmaceutical production processes", 8th European Congress of Chemical Engineering (ECCE-8/ECAB-1), Berlin, Germany, 25-29 September
2011-51	K. Haas-Santo, B. Vankayala, R. Dittmeyer, R. Singh, K.V. Gernaey, R. Gani, J.M. Woodley, 2011, "Development of a fast and flexible generic process for the reduction of nitro compounds", 8th European Congress of Chemical Engineering (ECCE-8/ECAB-1), Berlin, Germany, 25-29 September
2011-52	Amol Hukkerikar, Bent Sarup, Gürkan Sin, and Rafiqul Gani, 2011, "A Systematic Methodology for Uncertainty Analysis of Group Contribution Based and Atom Connectivity Index Based Models for Estimation of Properties of Pure Components", 8th European Congress of Chemical Engineering (ECCE-8/ECAB-1), Berlin, Germany, 25-29 September

2011-53	Mauricio-Iglesias M, Johanssen, K. Jørgensen, S.B. Sin, G., 2011, "Modelling and control of heat-integrated distillation columns: An industrial case study", 8th European Congress of Chemical Engineering (ECCE-8/ECAB-1), Berlin, Germany, 25-29 September
2011-54	Prado-Rubio, O.A., Jørgensen, S.B. and Jonsson, G., 2011, "Model based design and operation of a membrane bioreactor for lactic acid production", 8th European Congress of Chemical Engineering (ECCE-8/ECAB2011), Berlin, Germany, 26-29 September
2011-55	Ricardo Morales-Rodriguez, Anne S. Meyer, Krist V. Gernaey, Gürkan Sin, 2011, "An integral analysis for second generation bioethanol production via a dynamic model-based simulation approach: stochastic nonlinear optimisation", 8th European Congress of Chemical Engineering (ECCE-8/ECAB2011), Berlin, Germany, 26-29 September
2011-56	R. Lencastre Fernandes, M. Carlquist, L. Lundin, A.L. Heins, A. Dutta, I. Nopens, S.J. Sorensen, A.D. Jensen, A. Eliasson Lantz, K.V. Gernaey, 2011, "Heterogeneous microbial populations: using flow cytometric data for building dynamic distributed models", 8th European Congress of Chemical Engineering (ECCE-8/ECAB2011), Berlin, Germany, 26-29 September
2011-57	Y. Xu, M. Nordblad, J. Brask, J.M. Woodley, 2011, "Development of Process Technology for Two-stage Enzymatic FAEE-biodiesel Production", 8th European Congress of Chemical Engineering (ECCE-8/ECAB2011), Berlin, Germany, 26-29 September
2011-58	A. Bolic, A.E. Lantz, K. Rottwitt, K.V. Gernaey, 2011, "Uniform and reproducible stirring in a microbioreactor", 8th European Congress of Chemical Engineering (ECCE-8/ECAB2011), Berlin, Germany, 26-29 September
(poster) 2011-59	J. Lima-Ramos, P. Tufvesson, J.W. Woodley, 2011, "Process considerations and economic evaluation of biocatalytic production of chiral amines using transaminases", 8th European Congress of Chemical Engineering (ECCE-8/ECAB2011), Berlin, Germany, 26-29 September
2011-60	M. Albaek, K.V. Gernaey, M.S. Hansen, S. Stocks, 2011, "Investigations of the efficiency of enzyme production technologies using modelling tools", 8th European Congress of Chemical Engineering (ECCE-8/ECAB2011), Berlin, Germany, 26-29 September
PROCESS	Tufvesson, Pär; Lima Ramos, Joana; Jensen, Jacob Skibsted; Woodley, John, 2011, "Operating windows for transaminase processes using thermodynamic and biocatalyst constraints", 10th International Symposium on Biocatalysis and Biotransformations (BIOTRANS 2011), Giardini Naxos, Italy, 2-6 October
PROCESS	Xue, Rui; Mikkelsen, Jørn Dalgaard; Meyer, Anne S.; Woodley, John, 2011, "Reactor selection for multi-enzymatic processes", 10th International Symposium on Biocatalysis and Biotransformations (BIOTRANS 2011), Giardini Naxos, Sicily, Italy, 2-6 October
2011-61	Igor Mitrofanov, Elisa Conte, Jens Abildskov, Gürkan Sin and Rafiqul Gani, 2011, "Computer Aided Solvent Selection and Design Framework", AIChE Annual Meeting, Minneapolis, MN, USA, 16-21 October
2011-62	Elisa Conte, Rafiqul Gani, Peter A. Crafts, Sascha Sansonetti, 2011, "Efficient, Reliable and Predictive Solvent Design for Pharmaceutical Processes", AIChE Annual Meeting, Minneapolis, MN, USA, 16-21 October

2011-63	Kresten Troelstrup Meisler, Noor Asma Fazli Abdul Samad, Krist V. Gernaey, Nicolas von Solms, Rafiqul Gani, 2011, ”Generic Model and Data Based Framework for Analysis and Development of Crystallization Processes”, AIChE Annual Meeting, Minneapolis, MN, USA, 16-21 October
(poster) 2011-64	Azizul Azri Mustaffa, Rafiqul Gani, Jeong Won Kang, 2011, “Development and Analysis of Original UNIFAC-CI and Modified (Dortmund) UNIFAC-CI Models for Predictions of VLE and SLE Systems”, AIChE Annual Meeting, Minneapolis, MN, USA, 16-21 October
2011-65	Brock C. Roughton, Rafiqul Gani, Kyle V. Camarda, 2011, “Optimal Design of Ionic Liquid Entrainers for Extractive Distillation of Azeotrope Systems”, AIChE Annual Meeting, Minneapolis, MN, USA, 16-21 October
2011-66	Carlos Axel Diaz-Tovar, Azizul Azri Mustaffa, Georgios Kontogeorgis, Rafiqul Gani, Bent Sarup, 2011, “Lipid Processing Technology: Shifting From Waste Streams to High-Value Commercial by-Products”, AIChE Annual Meeting, Minneapolis, MN, USA, 16-21 October
2011-67	Elisa Conte, Sascha Sansonetti, Peter A. Crafts, Rafiqul Gani, 2011, “Rational Design of Pharmaceutical and Other Liquid Formulations”, AIChE Annual Meeting, Minneapolis, MN, USA, 16-21 October
2011-68	Amol Hukkerikar, Bent Sarup, Jens Abildskov, Gürkan Sin, Rafiqul Gani, 2011, ”Development of Property Models with Uncertainty Estimate for Process Design under Uncertainty”, AIChE Annual Meeting, Minneapolis, MN, USA, 16-21 October
2011-69	Cierra Hall, Martina Heitzig, Gürkan Sin, Rafiqul Gani, Andreas Linninger, 2011, ”Systematic Engineering Approach to Development and Identification of Physiologically-Based Pharmacokinetic Models”, AIChE Annual Meeting, Minneapolis, MN, USA, 16-21 October
2011-70	Sascha Sansonetti, Elisa Conte, Azizul A. Mustafa, Peter A. Crafts, Rafiqul Gani, 2011, “Verification and Prediction of Solubilities of Active (Pharmaceutical) Ingredients In Solvents and Solvent Mixtures”, AIChE Annual Meeting, Minneapolis, MN, USA, 16-21 October
2011-71	Philip Lutze, Deenesh K. Babi, John M. Woodley, Rafiqul Gani, 2011, “Achieving Process Intensification: A Phenomena-Based Synthesis/Design Methodology”, AIChE Annual Meeting, Minneapolis, MN, USA, 16-21 October
2011-72	Alberto Quaglia, Bent Sarup, Gürkan Sin, Rafiqul Gani, 2011, “Computer Aided Flowsheet Synthesis and Design Under Uncertainty In Vegetable Oil Production”, AIChE Annual Meeting, Minneapolis, MN, USA, 16-21 October
(poster) 2011-73	Ricardo Morales-Rodriguez, Miguel Mauricio-Iglesias, Anne S. Meyer, Krist V. Gernaey, Gürkan Sin, 2011, “A Framework for Optimization of Bioprocess Operation Under Uncertainty: A Lignocellulosic Ethanol Production Case Study”, AIChE Annual Meeting, Minneapolis, MN, USA, 16-21 October
2011-74	Miguel Mauricio-Iglesias, Kristoffer Johansen, Sten Bay Jørgensen, Gürkan Sin, 2011, ”A Systematic Methodology for the Assessment and Troubleshooting of Control Strategies and Operational Problems In Distillation Systems”, AIChE Annual Meeting, Minneapolis, MN, USA, 16-21 October

2011-75	Rita Lencastre Fernandes, Magnus Carlquist, Luisa Lundin, Anna-Lena Heins, Abhishek Dutta, Ingmar Nopens, Anker D. Jensen, Søren J. Johansen, Anna Eliasson Lantz, Krist V. Gernaey, 2011, "Heterogeneous Microbial Populations: Using Flow Cytometric Data for Building Dynamic Distributed Models", AIChE Annual Meeting, Minneapolis, MN, USA, 16-21 October
2011-76	Abhishek Dutta, Rita Lencastre Fernandes, Anna-Lena Heins, Anna Eliasson Lantz, Anker D. Jensen, Krist V. Gernaey, Ingmar Nopens, 2011, "Modeling the Residence Time Distribution In a Batch Fermentor: Comparison of CFD Prediction with Experiment", AIChE Annual Meeting, Minneapolis, MN, USA, 16-21 October
2011-77	Rafiqul Gani, 2011, "Property Modelling for Applications in Chemical Product and Process Design", VI Congresso Brasileiro de Termodinãmica Aplicada (CBTermo 2011), Salvador, Bahia, Brazil, 22-25 November, **Plenary Lecture**
2011-76	Rafiqul Gani, 2011, "Chemical Engineering Education - Current and Future Trends", 3rd International Conference of Chemical Engineering, 29-30 December , Dhaka, Bangladesh, **Plenary Lecture**
	F - Conference Presentations 2012
2012-1	Rafiqul Gani, 2012, "A systems engineering approach to manage the complexity in sustainable chemical product-process design", 13th Industrialist's Conference, Riyadh, Saudi Arabia, 17-19 January. **invited lecture.**
2012-2	Sin Gürkan, 2012, "An integrated knowledge-based framework for synthesis and design of enterprise-wide processing networks", 13th Industrialist's Conference, Riyadh, Saudi Arabia, 17-19 January. **invited lecture.**
2012-3	Rodríguez-Valverde, B. Mauricio-Iglesias, M. Sin, G., 2012, "A systematic methodology for controller tuning in wastewater treatment plants", Nordic Process and Control Workshop 17 (NPCW17), Lyngby, Denmark, 25-27 January
2012-4	Ane H. Mollerup, M. Mauricio-Iglesias, N. B. Johansen, D. Thornberg, P. S. Mikkelsen and G. Sin, 2012, "Model-based analysis of control performance in sewer systems", Nordic Process and Control Workshop 17 (NPCW17), Lyngby, Denmark, 25-27 January
2012-5 Poster	Prado-Rubio, O.A., Jørgensen, S.B. and Jonsson, 2012, "On controllability of an integrated bioreactor and periodically operated membrane separation process", Nordic Process and Control Workshop 17 (NPCW17), Lyngby, Denmark, 25-27 January
2012-6	Remus M. Prunescu, Mogens Blanke, Jakob M. Jensen, Gürkan Sin, 2012, "Temperature Modelling of the Biomass Pretreatment Process", Proceedings of the 17th Nordic Process Control Workshop (NPCW17), Technical University of Denmark, Kgs Lyngby, Denmark, 25-27 January
2012-7	Sten Bay Jørgensen and Morten Lind, 2012, "Modeling Operating Modes during Plant Life Cycle", Proceedings of the 17th Nordic Process Control Workshop (NPCW17), Technical University of Denmark, Kgs Lyngby, Denmark, 25-27 January
PROCESS	Mads O. Albaek, Krist V. Gernaey, Morten S. Hansen, Stuart M. Stocks, 2012, "Modelling Fungal Fermentations For Enzyme Production", Proceedings of the 17th Nordic Process Control Workshop (NPCW17), Technical University of Denmark, Kgs Lyngby, Denmark, 25-27 January

2012-8 Poster	Jason A. Price, Jakob Kjøbsted Huusom, Mathias Nordblad, John Woodley, 2012, "Operation and Control of Enzymatic Biodiesel Production", Proceedings of the 17th Nordic Process Control Workshop (NPCW17), Technical University of Denmark, Kgs Lyngby, Denmark, 25-27 January
2012-9 Poster	Guofeng Zhou, Jakob K. Huusom, John Bagterp Jørgensen, 2012, "State Estimation for the Automotive SCR Process", Proceedings of the 17th Nordic Process Control Workshop (NPCW17), Technical University of Denmark, Kgs Lyngby, Denmark, 25-27 January
PROCESS Poster	Bodla DK, Bolic A, Krühne U, Woodley JM and Gernaey KV, 2012, "Design of microfluidic reactors for biocatalytic reactions", IMRET 2012, Lyon. France, 20-22 February
PROCESS	Mitic A., Cervera Padrell A., Skovby T., Kiil S., Gani R., Dam-Johansen K. and Krist V. Gernaey, 2012, "Acceleration of pharmaceutical production by using micro-reactor technology in a continuous mode", The 12th International Conference on Microreaction Technology (IMRET12), Lyon, France, 20-22 February
PROCESS	Cervera-Padrell A.E., Mitic A., Morthensen S.T., Lewandowski D.J., Skovby T., Kiil S. and Gernaey K.V., 2012, "Continuous hydrolysis and L-L phase separation of an active pharmaceutical ingredient using a miniscale PTFE membrane separator", The 12th International Conference on Microreaction Technology (IMRET12), Lyon, France, 20-22 February
PROCESS	Bolić A., Bodla V.K., Eliasson Lantz A., Krühne U. and Gernaey K.V., 2012, "One-millilitre microbioreactor with impeller for improved mixing", The 12th International Conference on Microreaction Technology (IMRET12), Lyon, France, 20-22 February
2012-10	Rafiqul Gani, 2012, "A model-data based systems approach to process intensification", Inaugural scientific conference: Process Technology For The Future World – Building Bridges Across Boundaries, TU Delft Process Technology Institute, Delft, The Netherlands, 2 March, **Plenary Lecture**
2012-11	Nor Alafiza Yunus, Krist V Gernaey, John M Woodley & Rafiqul Gani, 2012, "Computer-aided approach for design of tailor-made blended products", 3rd International Gas processing Symposium, Doha, Qatar, 5-7 March
2012-12 Poster	Azizul Azri Mustaffa, Georgios Kontogeorgis, Rafiqul Gani, 2012, "Application of the UNIFAC-CI Model for Phase Equilibria Predictions of Organic Chemical System", Industrial Use of Molecular Thermodynamics (InMoTher 2012), Lyon, France, 19-20 March
2012-13	Amol Hukkerikar, Bent Sarup, Jens Abildskov, Gürkan Sin, and Rafiqul Gani, 2012, "Development of property models with uncertainty estimate for reliable product-process design", Proceedings of Industrial Use of Molecular Thermodynamics (InMoTher 2012), Lyon, France, 19-20 March
PROCESS	Tufvesson P, Janes K, Al-Haque N. Neto W, Lima-Ramos J, Santacoloma P and Woodley JM, 2012, "Process engineering tools to guide implementation and scale-up of transaminase cascades", MECP12, Graz, Austria, 10-13 April
PROCESS Poster	Janes K, Gernaey KV, Tufvesson P and Woodley JM, 2012, "A methodology for cascade selection for co-product removal in the ω-transaminase system", MECP12. Graz, Austria, 10-13 April

2012-14	Noor Asma Fazli Abdul Samad, Kresten T. Meisler, Gürkan Sin, Krist V. Gernaey & Rafiqul Gani, 2012, ”Quantifying uncertainties of nucleation and crystal growth models on PAT system performance for crystallization processes”, Advanced in Process Analytics and Control Technology (APACT-12), Newcastle UK, 25-27 April
PROCESS	Gernaey K.V., 2012, “Towards improved bioprocess operation: monitoring, modeling and control. Modeling approaches and recent developments”, Nordic Bioprocess Improvement Seminar 2 - Process optimization from parallel microbioreactors to large-scale bio-manufacturing, Kgs. Lyngby, Denmark, 26 April
2012-15 Poster	Noor Asma Fazli Abdul Samad, Kresten T. Meisler, Krist V. Gernaey, Nicolas von Solms & Rafiqul Gani, 2012, ”Framework for the analysis of crystallization operations”, Advanced in Process Analytics and Control Technology (APACT-12), Newcastle UK, 25-27 April
PROCESS	Nordblad M, Pedersen AK, Meyland LH, Xu Y and Woodley JM, 2012, ”Towards continuous enzyme-catalysed processes for the production of biodiesel”, 103rd AOCS Annual Meeting, Long Beach, CA, USA, 29 April-2 May, Invited
PROCESS	Törnvall U. Nordblad M, Tufvesson P and Woodley JM, 2012, “Enzyme stability: Process engineering requirements”, 9th Int Conf on Protein Stabilisation, Lisbon, Portugal, 2-4 May
PROCESS	Gernaey K.V., 2012, “PAT tools for fermentation processes”, Fifth pan-European QbD & PAT Sience Conference (EUPAT5), Gent, Belgium, 9-10 May 9-10 **(Invited Lecture)**
PROCESS	Mortier S.T.F.C., Van Hoey S., Cierkens K., De Beer T., Gernaey K.V. and Nopens I., 2012, “Application of model uncertainty analysis on the modelling of the drying behaviour of single pharmaceutical granules”, Fifth pan-European QbD & PAT Sience Conference (EUPAT5), Gent, Belgium, 9-10 May
PROCESS	Woodley JM, 2012, ”Process engineering for biocatalytic reactions and biotransformations”, SSCHE12, Tatranské Matliare, Slovakia, 21-25 May, **Invited plenary lecture**
PROCESS	Ramesh H, Tufvesson P and Woodley JM, 2012, ”Tools to evaluate processes for oxidase-based biocatalysis”, SSCHE12, Tatranské Matliare, Slovakia, 21-25 May

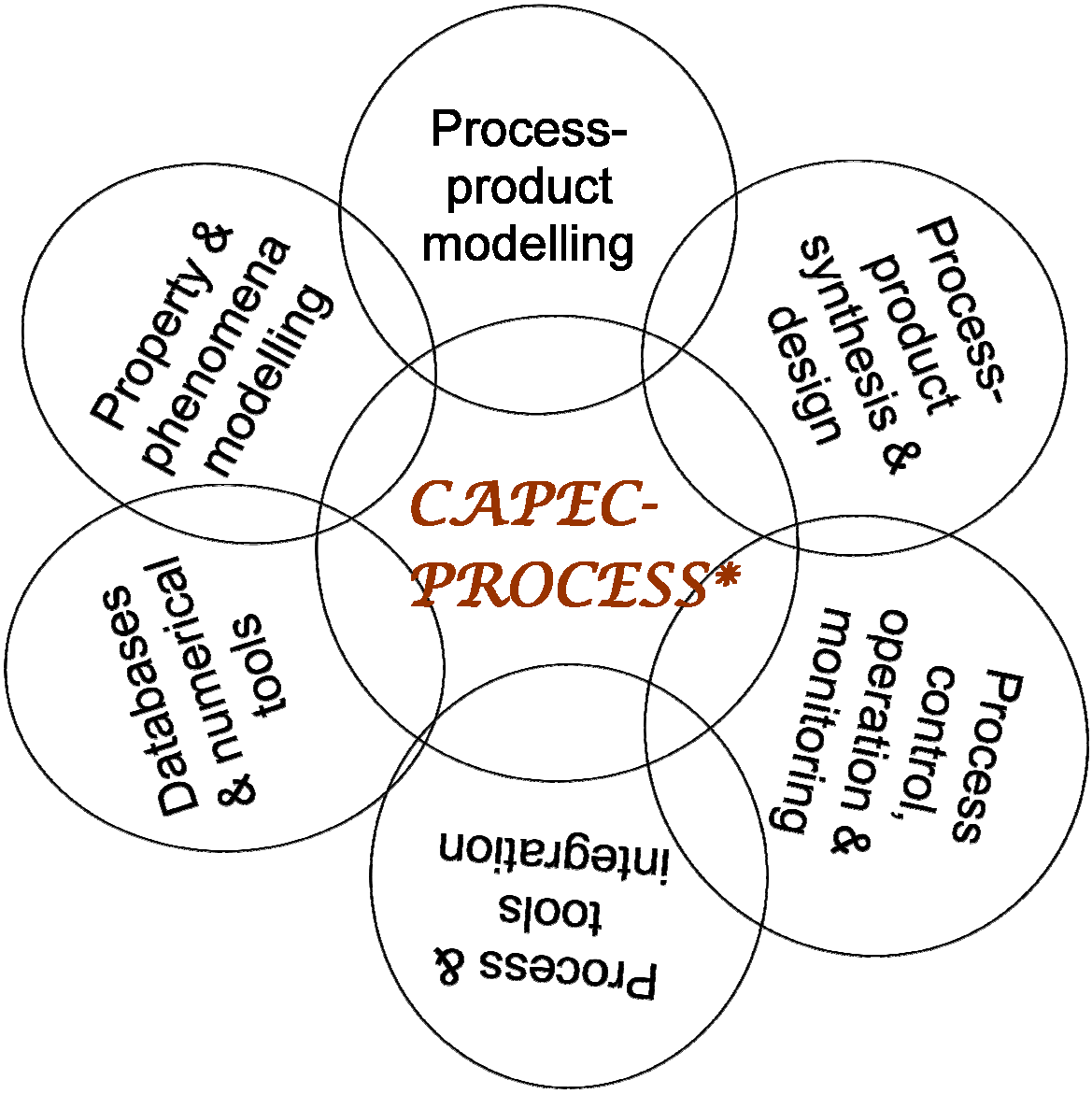
	G – Invited Seminars 2011
	Rafiqul Gani, 2011, “CAPEC Overview and Status - 2011”, DSM, The Netherlands, 27 January
	Rafiqul Gani, 2011, “CAPEC Overview and Status - 2011”, Lonza, Switzerland, 10 February
	Rafiqul Gani , 2011, “Managing the Complexity in Product and Process Engineering”, Departmental Seminar, NTUA, Athens, Greece, 17 March
	Rafiqul Gani, 2011, “Building and sustaining an Industrial Consortium – The experience of DTU-CAPEC”, UTM, Johar Bahru, Malaysia, 22 April 2011

Upcoming Conference presentations

Poster	Voss B, Schjødt NC, Grunwaldt J-D, Andersen SI and Woodley JM, 2012, "Kinetics of acetic acid synthesis from ethanol over a Cu/SiO2 catalyst", NSC 2012, Åland, Finland, 10-12 June
Poster	Alberto Quaglia, Bent Sarup, Gürkan Sin, Rafiqul Gani, 2012, "Synthesis and Design of Processing Networks: Stochastic Formulation and Solution", ESCAPE22, London, UK, 17-20 June
Poster	Nor Alafiza Yunus, Krist V. Gernaey, John M. Woodley and Rafiqul Gani, 2012, "An Integrated Methodology for Design of Tailor-Made Blended Products", ESCAPE22, London, UK, 17-20 June
Oral	Noor Asma Fazli Abdul Samad, Kresten Troelstrup Meisler, Gürkan Sin, Krist V. Gernaey, Rafiqul Gani, 2012, "A Generic Framework for Systematic Design of Process Monitoring and Control System for Crystallization Processes", ESCAPE22, London, UK, 17-20 June
Poster	Igor Mitrofanov, Sascha Sansonetti, Jens Abildskov, Gürkan Sin and Rafiqul Gani, 2012, "The Solvent Selection framework: solvents for organic synthesis, separation processes and ionic-liquids solvents", ESCAPE22, London, UK, 17-20 June
Poster	Chiara Piccolo, Andrew Shaw, George Hodges, Patrick M. Piccione, John P. O'Connell, Rafiqul Gani, 2012, "A framework for the design of reacting systems with phase transfer catalysis", ESCAPE22, London, UK, 17-20 June
Oral	Amol Shivajirao Hukkerikar, Bent Sarup, Jens Abildskov, Gürkan Sin, and Rafiqul Gani, 2012, "Estimation of Properties of Pure Components Using Improved Group-Contribution+ (GC+) Based Models and Uncertainty Analysis", 18th Symposium on thermo physical properties, Boulder, CO, USA, 24-29 June
Oral	Amol Hukkerikar, Mark Jones, Gürkan Sin, Rafiqul Gani, 2012, "Effect of Uncertainties in Physical Property Estimates on Process Design - Sensitivity Analysis", 18th Symposium on thermo physical properties, Boulder, CO, USA, 24-29 June
Oral	Neto W, Schwartze D, Tufvesson P, Vogel A and Woodley JM, 2012, "Process considerations for protein engineering of ω-Transaminase", ICCE 2012, Santander, Spain, 29-30 June
Oral	Babi DK, Lutze P, Woodley JM and Gani R, 2012, "Achieving process intensification form the application of a phenomena based synthesis: Design and intensification methodology", ICCE 2012, Santander, Spain, 29-30 June
Oral	Woodley JM, 2012, "Process engineering for transaminase-catalysed rections", Gordon Research Conference on Biocatalysis, Smithfield, RI, USA, 8-13 July, **Invited keynote lecture**
Oral	Mauricio-Iglesias, M., Jørgensen, S.B. Sin, G., 2012, "Asystematic methodology for controller tuning in wastewater treatment plants", The International Symposium on Advanced Control of Chemical Processes (AdChem), Singapore, 10-13 July
Poster	Guofeng Zhou, John Bagterp Jørgensen, Christophe Duwig, Jakob Kjøbsted Huusom, 2012, "State Estimation in the Automotive SCR DeNOx Process", The International Symposium on Advanced Control of Chemical Processes (AdChem), Singapore, 10-13 July

Oral	Rasmus Enemark-Rasmussen, David Cameron, Per Bagge Angelo and Gürkan Sin, 2012, "A simulation based engineering framework to facilitate HAZOP meetings for process safety analysis: Case studies from Oil and Gas industry", 11th International Symposium on Process Systems Engineering conference (PSE 2012), Singapore, 15-19 July
Poster	Amol Hukkerikar, Mark Jones, Bent Sarup, Jens Abildskov, Gürkan Sin, Rafiqul Gani, 2012, "Sensitivity of Process Design due to Uncertainties in Property Estimates", 11th International Symposium on Process Systems Engineering conference (PSE 2012), Singapore, 15-19 July
Oral	Lida Simasatitkul, Amornchai Arpornwichanop, and Rafiqul Gani, 2012, "Design methodology for bio-based processing: Biodiesel and fatty alcohol production", 11th International Symposium on Process Systems Engineering conference (PSE 2012), Singapore, 15-19 July
Poster	Michele Mattei, Georgios M Kontogeorgis, Rafiqul Gani, 2012, "A Systematic Methodology for Design of Emulsion Based Chemical Products", 11th International Symposium on Process Systems Engineering conference (PSE 2012), Singapore, 15-19 July
Oral	Philip Lutze, Deenesh K. Babi, John Woodley, Rafiqul Gani, 2012, "Phenomena-based Process Synthesis and Design to achieve Process Intensification", 11th International Symposium on Process Systems Engineering conference (PSE 2012), Singapore, 15-19 July
Poster	Ravendra Singh, Raquel Rozada-Sanchez, William Dean, Jacob Perkins, Frans Muller, Andy Godfrey, Krist V. Gernaey, Rafiqul Gani, John M. Woodley, 2012, "A generic process template for continuous pharmaceutical production", 11th International Symposium on Process Systems Engineering conference (PSE 2012), Singapore, 15-19 July
Oral	Noor Asma Fazli Abdul Samad, Kresten Troelstrup Meisler, Krist V. Gernaey, Nicolas Smit von Solms, Rafiqul Gani, 2012, "Systematic identification of crystallization kinetics within a generic modelling framework", 11th International Symposium on Process Systems Engineering conference (PSE 2012), Singapore, 15-19 July
	Rita Lencastre Fernandes, Ulrich Krühne, Ingmar Nopens, Anker D. Jensen, Krist V. Gernaey, **2012**, "Multi-scale modeling for prediction of distributed cellular properties in response to substrate spatial gradients in a continuously run microreactor", 11th International Symposium on Process Systems Engineering conference (PSE 2012), Singapore, 15-19 July
	Ulrich Krühne, Vijaya K. Bodla, Jacob Møllenbach, Steen Laursen, Naseem Theilgaard, Leif H. Christensen, Krist V. Gernaey, **2012**, "Computational Fluid Dynamics at work – Design and Optimization of Microfluidic Applications", 11th International Symposium on Process Systems Engineering conference (PSE 2012), Singapore, 15-19 July
	Pär Tufvesson, Ulrich Krühne, Krist V. Gernaey, John M. Woodley, **2012**, "PSE opportunities in biocatalytic process design and development", 11th International Symposium on Process Systems Engineering conference (PSE 2012), Singapore, 15-19 July
Oral	A. Quaglia, B. Sarup, G. Sin, R. Gani, 2012, "Synthesis and design of processing networks: decision making under uncertainty and sensitivity analysis", CHISA-2012, Prague, Czech Republic, 25-29 August

Oral	Mark Jones, Amol Hukkerikar, Gürkan. Sin, Rafiqul. Gani, 2012, "Sensitivity of process design to uncertainties in property models applied to extractive distillation", CHISA-2012, Prague, 25-29 August
Oral	Sin G. Advanced sensitivity and uncertainty analysis for computer-aided process engineering. CHISA-2012, Prague, 25-29 August. **Invited lecture.**
Oral	Vangsgaard, A.K., Mutlu, A.G., Gernaey, K.V., Smets, B.F. & Sin, G., 2012, "Calibration and validation of a model describing complete autotrophic nitrogen removal in granular sludge", IWA Nutrient Removal and Recovery 2012: Trends in NRR, September 2012, Harbin, China
Poster	Vangsgaard, A.K., Mauricio-Iglesias, M., Valverde Perez, B., Gernaey, K.V. & Sin, G., 2012, "pH variation and influence in a nitrogen converting biofilm dominated by autotrophs", IWA Nutrient Removal and Recovery 2012: Trends in NRR, September 2012, Harbin, China
Oral	Mutlu, A.G., Vangsgaard, A.K., Smets, B.F. & Sin, G., 2012, "Stoichiometric control strategy for operational decision-making in single-stage autotrophic nitrogen removing reactors", IWA World Water Congress & Exhibition, September 2012, Busan, South Korea



*** Systematic methods and tool**

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