Process Intensification Methodologies Applied to Liquid-Liquid Systems in Structured Equipment – Concept, Objectives and Selected Results of the FP7 EU-Project PILLS

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OUTLINE

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  • Basic project information
  • Starting point
  • Objectives
  • Project structure

• Selected project results
  • Process intensification in a cyclisation reaction
  • Reactor concepts for liquid/liquid processes
  • Scale-up considerations
  • Continuous work-up
  • Capillary microreactor with integrated ATR-IR sensor
  • Further insight in the project

• Summary
BASIC PROJECT INFORMATION

• Grant agreement no. NMP2-SL-2008-214599
• Project costs: 5.5 Mio. €
• Project funding: 3.6 Mio. €
• Run time: 01.01.09 – 31.12.11
• Project partners:
Two phase liquid-liquid reactions represent important chemical processes.

Their operation and control can be problematic. Often batch or semi-batch processing with sub-optimal operation of the process is performed.

Thereby, the process is often run to the limitations of existing equipment.

Continuous processing using structured equipment (e.g. microreactors) has the potential to overcome such limitations.

While there are numerous examples at research level, the are only few, if any, compelling examples of processes run at manufacturing scale.
### OVERVIEW MICROREACTOR APPLICATIONS IN PILOT- AND PRODUCTION SCALE - 1


<table>
<thead>
<tr>
<th>Application</th>
<th>Who?</th>
<th>Process type</th>
<th>Reactor configuration</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrogen peroxide synthesis</td>
<td>UOP LLC, Des Plaines, USA</td>
<td>g/l/s</td>
<td>mini-trickle bed reactor</td>
<td>lab and pilot tests (no details about scale), basic engineering design for 150000 t H2O2/a</td>
</tr>
<tr>
<td>Hydrogen peroxide synthesis</td>
<td>FMC Corporation, Princeton, USA</td>
<td>g/l/s</td>
<td>microchannel filled with catalyst particles or with wallcoating</td>
<td>lab and pilot tests (no details about scale); further work in progress</td>
</tr>
<tr>
<td>Organolithium exchange reaction</td>
<td>Lonza Ltd., Visp, Switzerland</td>
<td>1</td>
<td>Corning multi-injection reactor</td>
<td>production (250 kg product in a few weeks)</td>
</tr>
<tr>
<td>Organolithium coupling reaction</td>
<td>Lonza Ltd., Visp, Switzerland</td>
<td>1</td>
<td>Corning multi-injection reactor; corning single-injection reactor</td>
<td>production (several kg in a week)</td>
</tr>
<tr>
<td>Nitration reaction</td>
<td>Lonza Ltd., Visp, Switzerland</td>
<td>1</td>
<td>Corning multi-injection reactor</td>
<td>production (few kg in 24 h)</td>
</tr>
<tr>
<td>Chlorination</td>
<td>Lonza Ltd., Visp, Switzerland</td>
<td>g/l</td>
<td>Falling film reactor</td>
<td></td>
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<tr>
<td>Dehydrogenation</td>
<td>Lonza Ltd., Visp, Switzerland</td>
<td>g/l/s</td>
<td>tube filled with cat. particles</td>
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<tr>
<td>Organolithium coupling reaction</td>
<td>Lonza Ltd., Visp, Switzerland</td>
<td>1</td>
<td>small CSTR</td>
<td></td>
</tr>
<tr>
<td>Simmons-Smith reaction</td>
<td>Lonza Ltd., Visp, Switzerland</td>
<td>1</td>
<td>continuous launch production unit R-01 (up to 150 kg/h, multi-purpose): with static mixer and minitube heat exchanger</td>
<td>tons of product; production ran over several weeks</td>
</tr>
<tr>
<td>Organolithium coupling reaction</td>
<td>Lonza Ltd., Visp, Switzerland</td>
<td>1</td>
<td>continuous launch production unit R-01 (up to 150 kg/h, multi-purpose): with static mixer in adiabatic regime</td>
<td>similar amount of product as for the Simmons-Smith example</td>
</tr>
<tr>
<td>Polyacrylate formation</td>
<td>Arkva (now Siemens), Frankfurt, Germany</td>
<td>1</td>
<td>micromixer + static mixer combination</td>
<td></td>
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<tr>
<td>Butyl lithium-based alkylation reaction (two step: halogen exchange - coupling)</td>
<td>Lonza Ltd., Visp, Switzerland</td>
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</tr>
<tr>
<td>Suzuki coupling for the production of OLED</td>
<td>Covion (now Merck), Darmstadt, Germany</td>
<td>1</td>
<td>first step: microreactor; second step: static mixer; (c-SSP; multipurpose; c-GMP; ATEX)</td>
<td>lab process development; pilot phase in continuous small-scale production unit (c-SSP); typ. flow rate in c-SSP 100 g/min - 70 kg product/week</td>
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<tr>
<td>Process</td>
<td>Location</td>
<td>Scale</td>
<td>Reactor Type</td>
<td>Notes</td>
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<tr>
<td>Ozonolysis</td>
<td>Degussa (now Evonik Degussa), Hanau, Germany</td>
<td>g/l</td>
<td>falling film microreactor</td>
<td>Lab process development (100 ml - 1 l/h liquid throughput); pilot scale: 10 l/h</td>
</tr>
<tr>
<td>H2S addition to EO</td>
<td>BASF, Ludwigshafen, Germany</td>
<td>l (mainly)</td>
<td>microstructured two temperature zone heat exchanger</td>
<td></td>
</tr>
<tr>
<td>Ozonolysis of a steroid</td>
<td>Schering (Bayer Health Care), Germany</td>
<td>g/l, l</td>
<td>falling film microreactor, interdigital mixer-microchannel reactor</td>
<td>100-200 g/d</td>
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<tr>
<td>followed by reduction with NaBH4</td>
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<tr>
<td>Germinal difluorination of a 17-keto steroid</td>
<td>Schering (Bayer Health Care), Germany</td>
<td>l</td>
<td>micromixer-tube reactor (caterpillar micromixer; 1-5 mm inner diameter, up to 20 m)</td>
<td>5 - 10 kg/d using three parallel modules in parallel</td>
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<tr>
<td>Microphotoreactor</td>
<td>BTS Ehrfeld Mikrotechnik</td>
<td>l</td>
<td></td>
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<td>Ionic liquid production</td>
<td>InLiTec</td>
<td>l</td>
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<tr>
<td>Methacrylate manufacture</td>
<td>Idemitsu Kosan, Chiba, Japan</td>
<td>l</td>
<td>mixer-tube</td>
<td>10 t/a; eight microreactor blocks with each three tube reactors with inner dimensions of 500 µm and a length of 2 m</td>
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<tr>
<td>Craynard exchange reaction</td>
<td>(Kyoto University), Japan</td>
<td>l</td>
<td>micromixer and a microheat exchanger (55 micromixers (id 490 µm, l = 20 cm)</td>
<td>Pilot 0.5 kg/6 h i.e. 730 kg/a</td>
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<tr>
<td>Halogen-lithium</td>
<td>(Kyoto University), Japan</td>
<td>l</td>
<td></td>
<td>Pilot 0.5 kg/6 h i.e. 730 kg/a</td>
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<tr>
<td>Swern-Moffit oxidation</td>
<td>Ube Industries Ltd, Yamanouchi, Japan (Kyoto University)</td>
<td>l</td>
<td>sequence of three micromixers followed by tube sections</td>
<td>Lab about 8 ml/min; pilot plant with 10t/a capacity</td>
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<td>Yellow naph pigment synthesis</td>
<td>Fuji, Tokyo, Japan (Kyoto University)</td>
<td>l</td>
<td></td>
<td>Production 70 t/a</td>
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<td>Polycondensation (two)</td>
<td>MCFT, Japan</td>
<td>l</td>
<td></td>
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<tr>
<td>Friedel-Crafts alkylation</td>
<td>MCFT, Japan</td>
<td>l</td>
<td>T-mixer/interdigital micromixer/K-M mixer</td>
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<td>Oxidation of 2-methylnaphthalene</td>
<td></td>
<td>l</td>
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<td>Direct fluorination of ethyl 3-oxobutanoate</td>
<td>g/l</td>
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<tr>
<td>Propene oxide formation</td>
<td>g/s</td>
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<td><strong>(divers., see chapter)</strong></td>
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<tr>
<td>Production of polymer intermediates, Ritter</td>
<td>DSM Fine Chemicals GmbH, Linz, Austria</td>
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<td><strong>Synthesis of diazo</strong></td>
<td>Clariant, Germany</td>
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<tr>
<td>Nitroglycerine production</td>
<td>Xi'an Huian Industrial Group, Xian, China</td>
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<td>Fine chemical production</td>
<td>(Microinnova KG, Graz, Austria)</td>
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<td>Grignard-based enolate formation</td>
<td>Merck, Darmstadt, Germany</td>
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<td>Encapsulation</td>
<td>P&amp;G</td>
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<td>Liquid fabric enhancer production</td>
<td>P&amp;G</td>
<td>vesicular dispersion</td>
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<td>Ionic liquid synthesis</td>
<td>Solvent Innovation (now Merck)</td>
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<tr>
<td>Sulfonation</td>
<td>P&amp;G</td>
<td>g/s; l</td>
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</table>

- From 45 examples only 5 address the topic of l/l-reactions
- Scale max. 15 l/h
- Scale-up often not detailed
Development and validation of a process design methodology for two-phase liquid-liquid reactions,
in linkage with the development of a new generation of high performance process equipment (micro through meso structured) for continuous processing.

Topics to be addressed:
- mixing, mass and heat transfer in such equipment and
- physical chemistry effects on reaction yield and quality that the achievable mixing, mass and heat transfer may cause

The output of the project will be demonstrated on 2 different industrial systems to show the wide applicability.
Two commercially significant processes (A & B). Both are substantially exothermic. Aimed is to achieve process intensification and to demonstrate this at scales relevant to commercial production.

- A: representative for processing in a multipurpose plant (speciality / fine chemicals)
- B: improved first stage reactor to limit by-product formation to the extent that opens the prospect to replace costly, energy-intensive separation processes; high-tonnage process (commodity chemicals).

In the context of the project a modular, flexible and expandable multipurpose plant for specialty chemical production (A) and an experimental research facility (ERF) (B) will be designed and realized as one key activity.
OBJECTIVES OF THE PROJECT 3

- It is aimed at an improved fundamental understanding
  - of these multiphase processes and
  - of the design and operation of appropriate micro/mesostructured reactors
- and the codification of this learning.
- Development of whole process design approaches tailored to continuous liquid-liquid processes to allow application to a wide range of manufacturing environments – aiming at a wider application of process intensification approaches in the European chemical industry.
- Education activities: e-learning program and practical demonstration on an educational micro system
PROJECT STRUCTURE

WP1: Project coordination

WP3: Design of tailored structured devices
- Micro- & milli-structured reactors
- Netmix®-derived meso-structured reactors

WP4A: Device development and characterisation
- Speciality fine chemicals
- Commodity chemicals

WP4B: Final device and plant testing
- Multipurpose plant reactor, separator, crystalliser, etc.
- Experimental research facility

WP2: Modelling and process description
Mathematical modelling and numerical simulations to develop understanding of interaction between subprocesses and equipment structures

WP5: Generic knowledge/toolkit development
Develop generic understanding for development of processes and equipment

WP6: Training activities
E-learning, demonstrations, website, dissemination events, degree module
PROCESS EXAMPLE A: CYCLIZATION REACTION

- Highly exothermic reaction (-120 kJ/mol)
- Quenching similar challenging

Similar process in literature:

- Semi-batch process in the hour range
- In microreactor: 4 s

→ Process intensification


M.N. Kashid et al. (EPFL, GIV, IMM), Abstract for CHISA2010.
GENERIC CONSIDERATIONS:
PRINCIPLES OF L/L-CONTACTING IN
MICROSTURUCTURED REACTORS

- **Continuous phase**
- **Disperse phase**

**emulsification**
- a) membrane
- micromixer
- hydrophobic surface
- hydrophilic surface

**contact flow**
- about 60 s

**segmented flow**
- about 10 s


Extraction of phenol from dodecane to water
COMPARISON OF DISPERSION PERFORMANCE OF DIFFERENT MICROMIXERS

Slit Interdigital Micro Mixer Version 2 – SIMM V2

Caterpillar Micro Mixer - CPMM

Starlaminator15 – StarLam15

System: Heptane/Water (SDS)
Flow rate ratio: 1:5

Y. Okubo et al., 2008
One reactor concept: redispersion microreactor

CPMM-V1.2-R300/12-wt for initial dispersion

Proof of basic principle

Derived reactor concept: metal foam filled reactor
SCALE-UP APPROACHES FOR THE MICROMIXERS

Smart increase in characteristic size

Internal numbering-up (equalling-up)

Caterpillar micro mixer

StarLam micro mixer
CONTINUOUS WORK-UP SYSTEM
FROM THE BMBF-PROJECT POKOMI

caterpillar micro-mixer

1. settler

pump

caterpillar micro-mixer

2. settler

pump

3. settler

pH-sensor

water pumps
• Slug flow generation in a T- or Y-junction
• Each slug represents a reaction volume on its own with
  • defined interfacial area (and therewith mass and heat transport) and
  • defined residence time
• Internal circulation flows improve mass and heat transfer → potential for process intensification
• Concepts for numbering-up by a factor of 5-10 are described in literature
• Capillary microreactor not discussed for large scale production
• Tool for process investigations and optimisation
The challenges:

• The adaptation of the system to the specific operation conditions in the project context.
• The operation of the complete set-up under higher pressure.
• Integration of an in-line sensor after the flow splitter/phase separation.
EXPERIMENTAL SET-UP

- Flow through cell with implemented ATR-IR probe
- Flow splitter
- Capillary microreactor, tube-in-tube for HEX
- Slug flow generation in T-junction
capillary microreactor: ID = 0.8 mm, l = 5.6 m

excess of organic reactant to aqueous reactant: molar ratio: 1.89, i.e. max. conversion of organic reactant: 53%

Counter check of ATR-IR results with GC analysis: some refinement works still necessary
APPLICATION TO MODEL SYSTEM: INTRODUCTION

- Acid catalysed hydrolysis of benzal chloride to benzaldehyde

- Former investigations can be used as reference

Interdigital slit glass micromixer
APPLICATION TO MODEL SYSTEM: FORMER RESULTS

- Of interest: comparison of reactor performance: dispersive flow and slug flow

APPLICATION TO MODEL SYSTEM: ESTABLISHMENT OF IR-ANALYTICS

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FURTHER INSIGHT IN THE PROJECT:
UPCOMING CHISA CONFERENCE

• Specialised symposia no. 26 (EU project “F3 Factory”) of the 19th Int. Congress of Chemical and Process Engineering CHISA 2010, August 28 to September 1, 2010, Prague, Czech Republic. Contribution of PILLS partners:

  • Introduction presentation: “Process Intensification methodologies applied to Liquid-Liquid Systems in structured equipment – concept, objectives and status of the EU project PILLS”
    Patrick Löb, Steve Fletcher, Derek Lindsay, Jeremy Double, Jacques Membrez, Liouba Kiwi-Minsker, Asier Rodriguez, José Carlos B. Lopes, Jerzy Baldyga, Paulo Araújo, Cristina Gaudêncio Baptista
  • “Two phase micro-structured reactors for intensification of instantaneous exothermic cyclization of pseudoionone”
    M. N. Kashid, I. Yuranov, P. Raspail, P. Prechtl, J. Membrez, R. Haidar, P. Löb, A. Renken, L. Kiwi-Minsker
  • “Insights in heterogeneous liquid-liquid reactions against the background of bulk chemical production”
    C. G. Baptista, T. Mendes, C. Dias, N. Oliveira, M. S. Reis, A. Rodriguez, P. Araújo, G. Menges, P. Löb, J.C. Lopes
  • “Application of the NETmix® Technology to Liquid-Liquid Heterogeneous Reactions”
    Carlos M. Fonte, Erdem Demir, Paulo A. Quadros, Madalena M. Dias, José Carlos B. Lopes
  • “Modelling of complex liquid-liquid heterogeneous reactions”
    Jerzy Bałdyga, Wioletta Podgórska, Magdalena Jasińska, Wojciech Kowaliński

Introduction to the EU-project PILLS given

Structured reactors have the potential for process intensification in the case of liquid/liquid processes

Diverse basic reactor concepts exist:
  - Guidelines required for equipment selection but also for equipment design and process mode
  - Further development of reactor concepts especially with regard to scale-up

Capillary microreactors can be combined with inline ATR-IR sensor

Dissemination events of PILLS:
  - Special session during CHISA/ECCE conference in Prague (28.08.-01.09.10)
  - Mid-term dissemination event in December in Coimbra, Portugal

Thank you for your attention! – Contact: loeb@imm-mainz.de