The FP7 EU-Project PILLS (Process Intensification Methodologies Applied to Liquid-Liquid Systems in Structured Equipment) – An Introduction into the Technical Aspects

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Starting point

- 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.

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Overview microreactor applications in pilot and production scale 1

Application	Who?	Process type	Reactor configuration	Level
Hydrogen peroxide synthesis	UOP LLC, Des Plaines, USA	g/l/s	mini-trickle bed reactor	lab and pilot tests (no details about scale), basic engineering design for 150000 t H2O2/a
Hydrogen peroxide synthesis	FMC Corporation, Princeton, USA	g/l/s	microchannel filled with catalyst particles or with wallcoating	lab and pilot tests (no details about scale); further work in progress
Organolithium exchange reaction	Lonza Ltd., Visp, Switzerland	l	Corning mulit-injection reactor	production (250 kg product in a few weeks)
Organolithium coupling reaction	Lonza Ltd., Visp, Switzerland	l	Corning mulit-injection reactor; corning single-injection reactor	production (several kg in a week)
Nitration reaction	Lonza Ltd., Visp, Switzerland	l/l	Corning mulit-injection reactor	production (few kg in 24 h)
Chlorination	Lonza Ltd., Visp, Switzerland	g/l	Falling film reactor	
Dehydrogenation	Lonza Ltd., Visp, Switzerland	g/l/s	tube filled with cat. particles	
Organolithium coupling reaction	Lonza Ltd., Visp, Switzerland	l	small CSTR	
Simmons-Smith reaction	Lonza Ltd., Visp, Switzerland	l	continuous launch production unit R-01 (up to 150 kg/h, multi-purpose): with static mixer and mintube heat exchanger	tons of product, production ran over several weeks
Organolithium coupling reaction	Lonza Ltd., Visp, Switzerland	l	continuous launch production unit R-01 (up to 150 kg/h, multi-purpose): with static mixer in adiabatic regime	similar amount of product as for the Simmons-Smith example
Polyacrylate formation	Axiva (now Siemens), Frankfurt, Germany	l	micromixer - static mixer combination	lab testing would correspond to 50 t/a (8000 h of operation); prebasic design for 2000 t/a
Butyl lithium-based alkylation reaction (two step: halogen exchange - coupling)	Lonza Ltd., Visp, Switzerland	l	first step: microreactor; second step: static mixer; (c-SSP; multipurpose; c-GMP; ATEX)	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
Suzuki coupling for the production of OLED	Covion (now Merck), Darmstadt, Germany	l/l		
Ozonolysis	Degussa (now Evonik Degussa), Hanau, Germany	g/l	falling film microreactor	lab process development (100 ml - 1 l/h liquid throughput); pilot scale: 10 l/h
H2S addition to EO	BASF, Ludwigshafen, Germany	l (mainly)	microstructured two temperature zone heat exchanger	
Ozonolysis of a steroid followed by reduction with NaBH4	Schering (Bayer Health Care), Germany	g/l, l	falling film microreactor; interdigital mixer-microchannel reactor	lab 100-200 g/d

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Overview microreactor applications in pilot and production scale 2

Geminal difluorination of a 17-keto steroid	Schering (Bayer Health Care), Germany	l	micromixer-tube reactor (caterpillar micromixer; 1-5 mm inner diameter; up to 20 m)	5 - 10 kg/d using three parallel modules in parallel
Microphotoreactor	BTS Ehrfeld Mikrotechnik	l		
Ionic liquid production	IoLiTec	includes also l/l		
Methylmethacrylate manufacture	Idemitsu Kosan, Chiba, Japan	l	mixer-tube	10 t/a; eight microreactor blocks with each three tube reactors with inner dimensions of 500 µm and a length of 2 m
Grignard exchange reaction	(Kyoto University), Japan	l	micromixer and a microheat exchanger (55 microtubes (id 490 µm, l = 20 cm)	pilot 0.5 kg/6 h i.e. 730 kg/a
Halogen-lithium	(Kyoto University), Japan	l		pilot 0.5 kg/6 h i.e. 730 kg/a
Swern-Moffat oxidation	Ube Industries Ltd, Yamaguchi, Japan (Kyoto University)	l	sequence of three micromixers followed by tube sections	lab about 8 ml/min; pilot plant with 10t/a capacity
Yellow nano pigment synthesis	Fuji, Tokyo, Japan (Kyoto University)	l		production 70 t/a
Polycondensation (two	MCPT, Japan	l		
Friedel-Crafts alkylation	MCPT, Japan	l	T-mixer/interdigital micromixer/K-M mixer	
Oxidation of 2-methylnaphthalene		l/l		
Direct fluorination of ethyl 3- oxobutanoate		g/l		
Propene oxide formation		g/s		
(divers, see chapter				
Production of polymer intermediates, Ritter	DSM Fine Chemicals GmbH, Linz, Austria	l		
Synthesis of diazo	Clariant, Germany	l		
Nitroglycerine production	Xi´an Huian Industrial Group, Xian, China	l/l		production 15 kg/h
Fine chemical production	(Microinnova KEG, Graz, Austria)	l		
Grignard-based enolate formation	Merck, Darmstadt, Germany	l		
Encapsulation	P&G	l/l		
Liquid fabric enhancer pfoduction	P&G	vesicular dispersion		
Ionic liquid synthesis	Solvent Innovation (now Merck)	l		
Sulfonation	P&G	g/s; l		

- From 45 examples only 5 address the topic of l/l-reactions
- Scale max. 15 l/h
- Scale-up often not detailed

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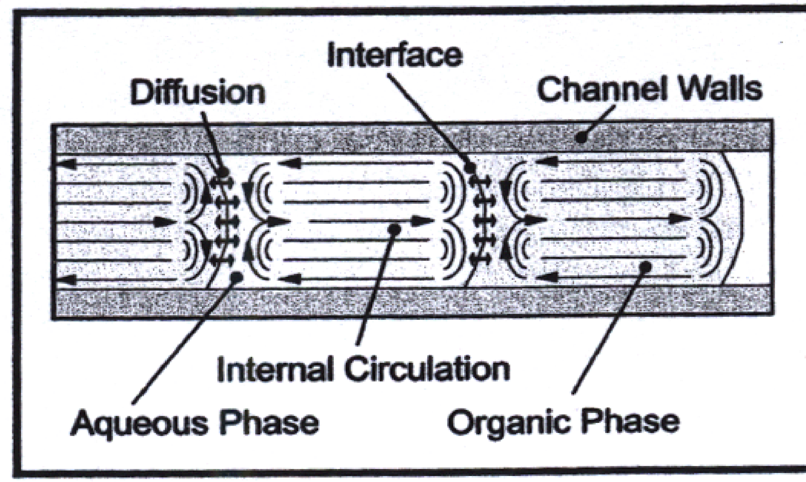
- Development and validation of a process design methodology for two-phase liquid-liquid reactions in linkage with the development of a new generation and high performance process equipment (micro through meso structured) for continuous processing.
- Topics to be addressed:
  - mixing, mass and heat transfer in such equipment and
  - physical chemistry effects on reaction yield and quality that the achievable mixing, mass and heat transfer may cause
- A generic approach will be developed involving practical, theoretical and modeling aspects.
- The output of the project will be demonstrated on 2 different industrial systems to show the wide applicability at development stage, scale-up and high-tonnage chemical production.

Slug flow reactor

Burns, J. R., Ramshaw, C.; Lab on a Chip **1**, (2001) 10-15
Burns, J. R., Ramshaw, C.; Trans. Inst. Chem. Eng. **77**, 5/A (1998) 206-21
See also: Agar, D. W., Wörz, et al.; Catalysis Today (2003)



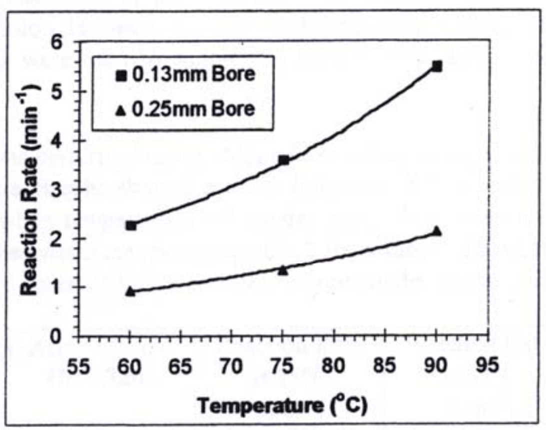
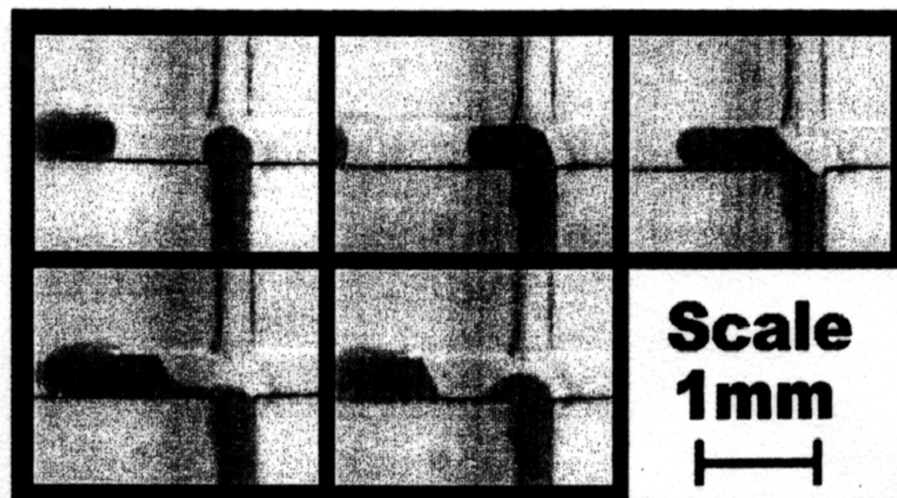


Figure 6 – Observed reaction rates for benzene nitration in a stainless steel capillary rea
(Experiments conducted with 83% H_2SO_4)



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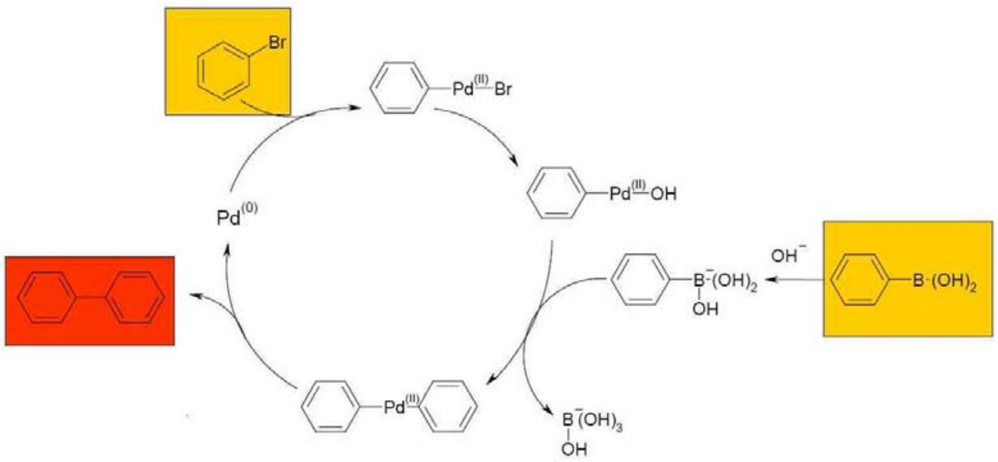
Exemplary reactor concepts for l/l-reactions from the BMBF-project POKOMI - 1

Application: synthesis of OLED materials via Suzuki polycondensation (200 g/d)

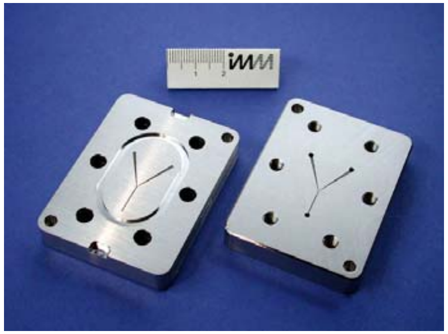


Reaction and process engineering issues:

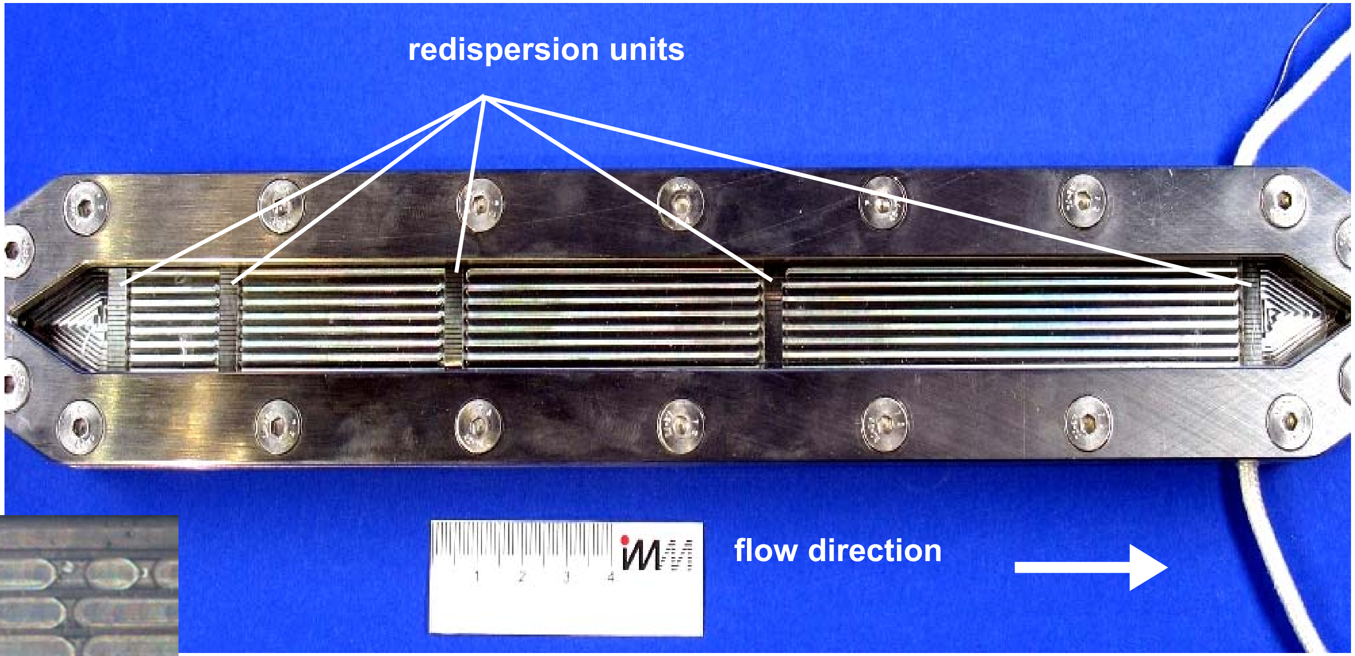
- Biphasic liquid/liquid contacting with problem of fast coalescence
- Reaction needs constant sufficiently large interfacial area to avoid mass transfer limitation
- Increase in viscosity in the course of the polymerization needs to be taken into account

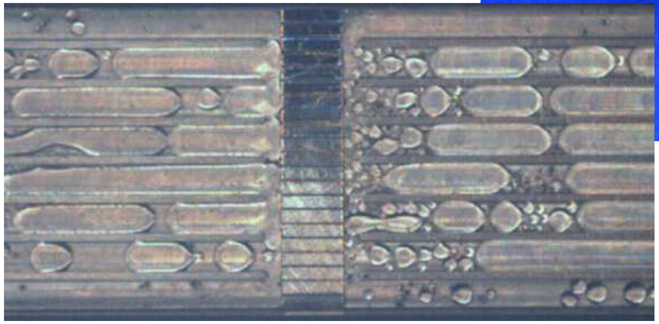
PILLS Exemplary reactor concepts for l/l-reactions from the BMBF-project POKOMI - 2

One reactor concept: redispersion microreactor



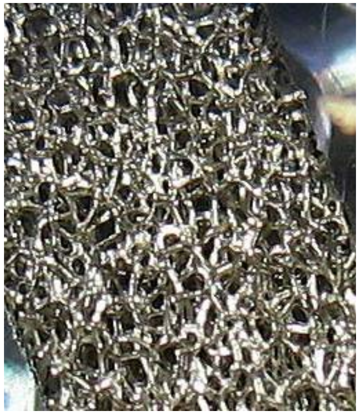
CPMM-V1.2-R300/12-wt
for initial dispersion





Proof of basic principle

Derived reactor concept: metal foam filled reactor



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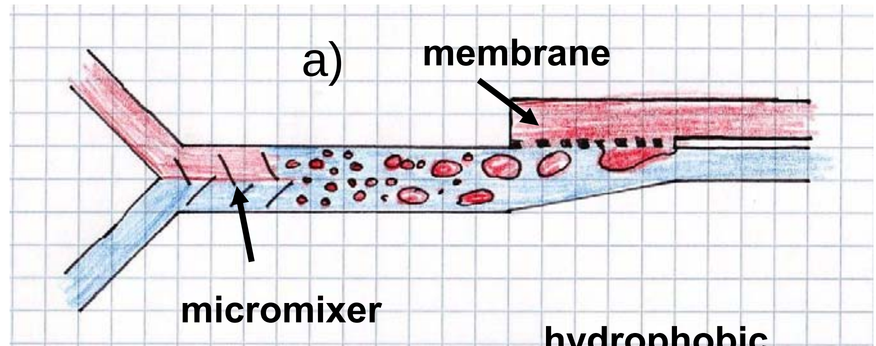
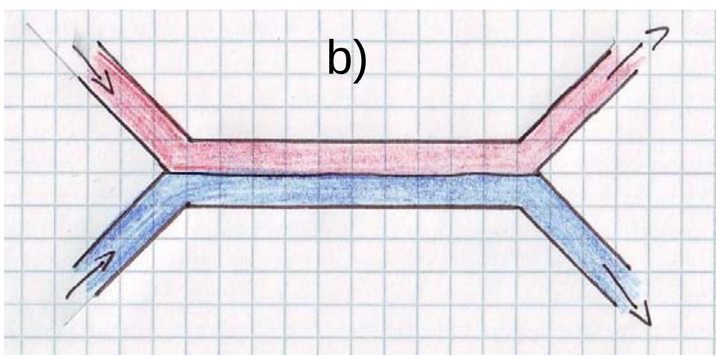
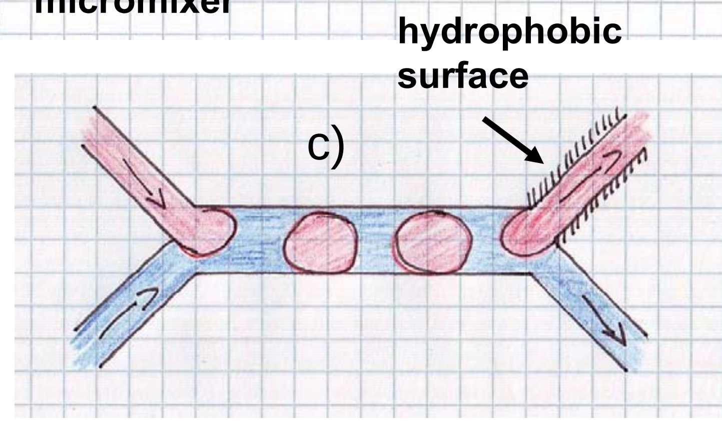
Generic considerations

- Continuous phase
- Disperse phase







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Exemplary reactor concept StarLam mixer and open issues

Smart increase in characteristic size

Larger platelets

≤ 150 l/h

≤ 900 l/h

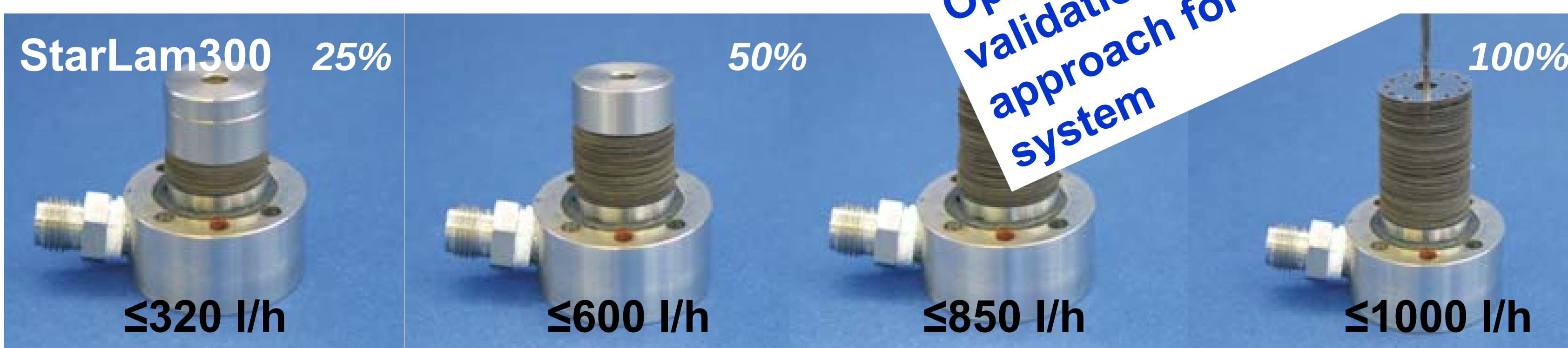
≤ 4000 l/h

'/h

Internal numbering-up (equalling-up)

More pl

Open: selection and validation of scale-up approach for two phase system



Objectives of the project 2

- 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
  - 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.
- 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.

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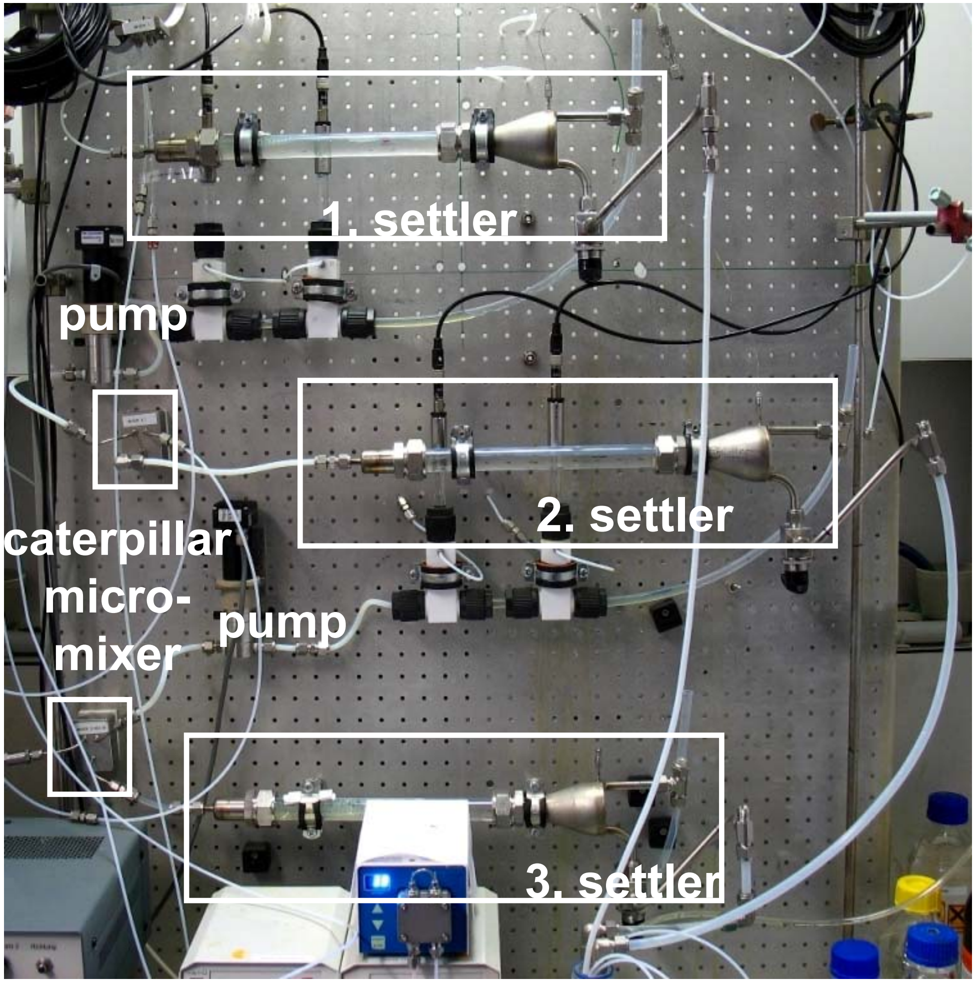
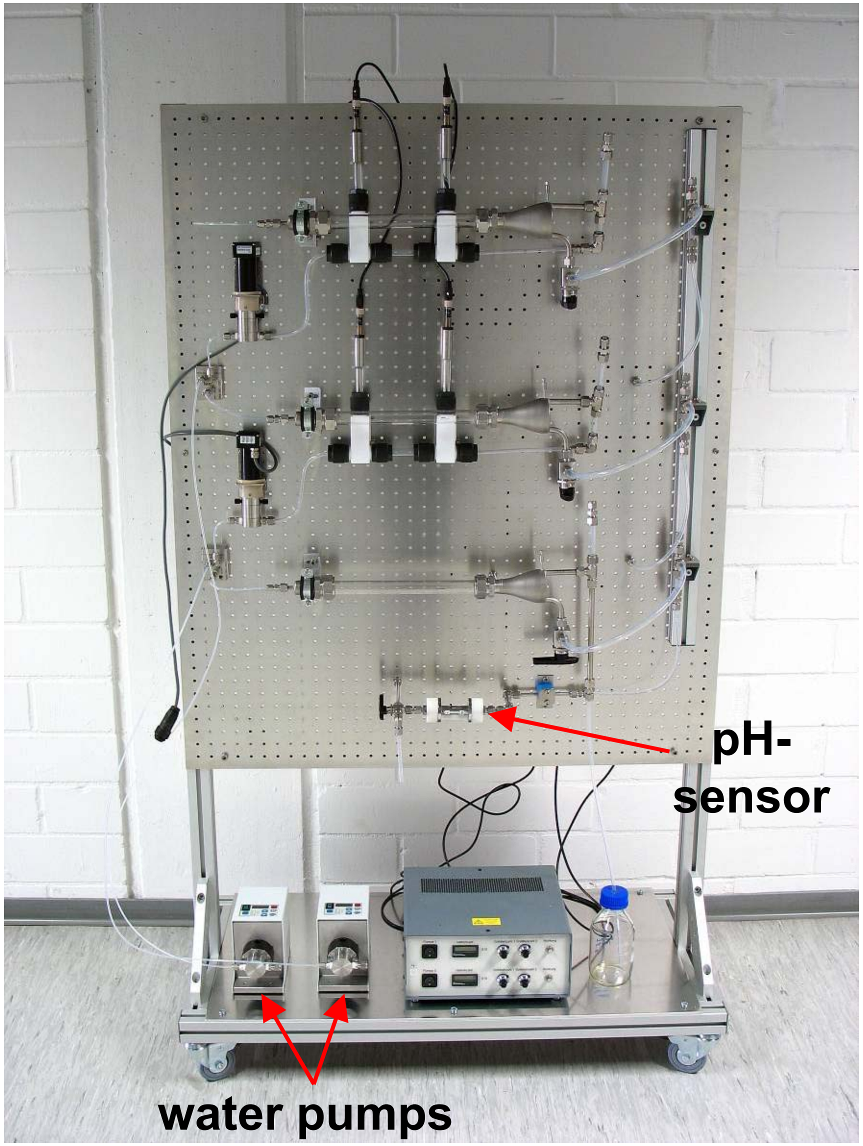
POKOMI project: continuous work up system with three settlers





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

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Aimed progress in the area modelling & whole system design approach

- Determination and description of flow patterns in structured devices allowing an a priori prediction of the different flow patterns for specific geometries
- Analysis of mass transfer for different devices and flow patterns (supported by CFD simulations and modelling of micro mixing)
- Multiphase reactor models for the selected chemistries
- Combination of the latter two
- Extension of the IMPULSE methodologies to processes involving two immiscible liquid phases.
  IMPULSE developed methodologies for whole process design, equipment selection and design and assessment of process for safety, environmental sustainability and business optimization. However, the case of liquid-liquid reactions has not been studied in this project.

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IMPULSE methodology – outline presented during CHISA 2008

- Risk exposure: a multi-dimensional metric for use in design
- Generic learning from the IMPULSE project in the area scale-out concepts in chemical micro process engineering
- Sustainable intensification/miniaturization through multi-scale structuring: the scientific rationale
- Characterisation of microstructured heat exchangers and micromixers
- Equipment selection within the IMPULSE multiscale process design framework
- Business decision support for intensified processes and multi-scale equipment with particular emphasis on SHE aspects
- Guidance on safety/health for process intensification including MS-design – analysis of thermo chemical hazards
- Risk analysis and safety methodology applied to intensified processes and multi-scale equipment
- Multiscale design: methods and tools for the sustainable chemical industry of the future

Aimed progress in the area continuous processing of liquid-liquid systems

- Realisation of basic functional units with systematic variation of geometry and dimensions and experimental investigation of diespersion performance and dispersion stability in the reactor.
- Development of pilot-scaled reactors
- Selection of dispersion structures also suited for higher throughputs or as base unit for numbering-up.
- A sufficient understanding of the impact of structure dimension on the dispersion performance
- Proven scale-up concept for the developed structures including proof of sufficient equal distribution
- Concept for dispersing structures also capable for high throughput
- Availability of tailored reactors
- **In total it is expected that the barrier for implementing structured devices also for two phase liquid-liquid reactions will be lowered.**

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Thank you for your attention!

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Coffee and Networking