

Technical notes: Lonza microreactor concept

Introduction

Microreactor technology is a continuous flow process based on plug flow reactors. It requires minimal volume of reagents while offering rapid dynamic responses and robustness. The system allows excellent temperature control and efficient mixing procedures. The characteristic mixing time and residence time of the reactor lead to the definition of three reaction classes suitable for microreactor technology:

- **Type A** instantaneous, mixing controlled
- **Type B** rapid (t~minutes), kinetically controlled
- **Type C** slow, with thermal hazard

Lonza developed modular microreactor system to cover a wide range of reactions. Not all reactions are feasible:

- very slow reactions,
- solids forming,

Microreactor technology furthermore delivers the following advantages: new chemical routes, less solvents, higher yields than conventional batch process and less change-over time.

Lonza designed Microreactor

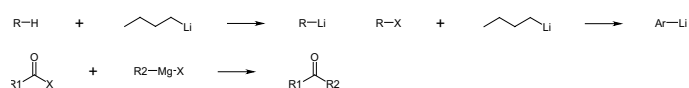
Design goals

- High flow rates (>100 g/min) with low pressure loss Δp
- Rapid mixing and high heat transfer rates
- Variable residence time
- Different mixing structures adapted to involved phases, kinetics and flow rates

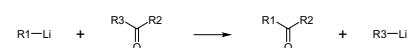
No scale-up issue: Lonza microreactors allow a process to be developed in lab and transferred to production environment.

Chemical examples

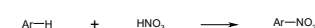
Metalations, Organolithium exchange, and Grignard reactions [Type A]



Organolithium coupling reaction [Type]

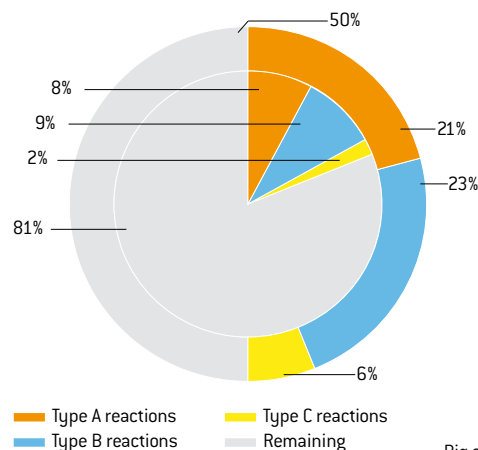
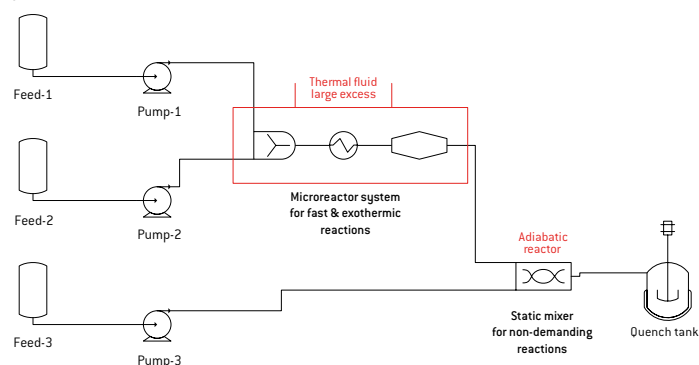


Nitration as hazardous reactions [Type C]



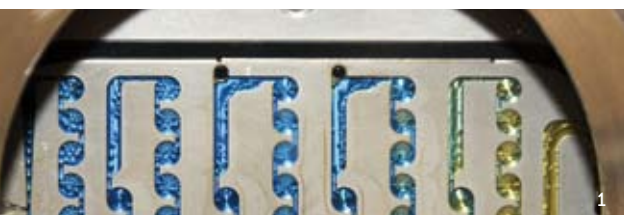
The toolbox concept

Integration of multipurpose microreactors needs toolbox concept. This reflects a fundamental change in production strategy for pharma and fine chemical industries.



Roberge et al., CE&T 28 (2005) 318

Big circle based on kinetics only
Inner circle based on kinetics and phases



1, 2 Lonza lab plate microreactor with acidbase test reaction
3 Lonza Mini and Lab reactor setups

Technical notes: Lonza microreactor concept

Batch (Unit operations)

Charging
Heating and cooling
Reaction batch or semi batch
Aging

Continuous (modules)

Dosage system (pumps)
Heat exchangers
Reactor and manifold
Residence time

Conclusions

In 2003 Lonza decided to enter the microreactor market and initiated a technology project for the production of fine chemicals and pharmaceuticals. The program materialized in the development of own microreactors (patents pending) on different scales.

Production environment



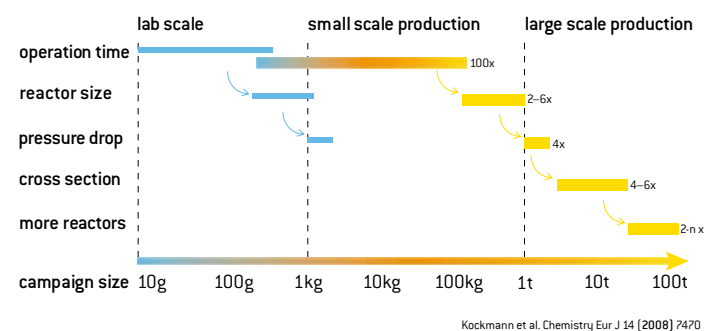
Up to three feed lines with flow rates 10 to 400g/min, $\Delta p < 8$ bar
– EX-environment and cGMP production feasible
– 24h shift operation allowing large campaign sizes > 2.5 mt

Lonza scale-up concept

- Feasibility, optimization, and kg-sample production in laboratory
- Production campaign with 24 h shift operation for several 100 kgs
- Dedicated microstructured devices for high ton-scale production

- Lonza is a leading company in chemical continuous manufacturing using microreactors and conventional technology
- The Lonza microreactor modules were designed to be a modular, multi-purpose “toolbox” for Type A and B reactions, adaptable to conventional technology (e.g. static mixers) for Type C reactions
- Customer approach with feasibility studies and parameter optimization, as well as large production campaigns
- In the scale-up strategy, a process can quickly be developed and transferred directly to production environment (0.1–2.5 ton product/campaign) with no scale-up issues

The novelty of the technology is that a large range of flow rates can be covered from few milliliters/min up to several hundred milliliters/min. As opposed to the current devices on the market, the Lonza system does not require external/internal parallelization for high flow applications. Thus, the Lonza microreactor is able to produce even multi-tons large-scale quantities with the same device.



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