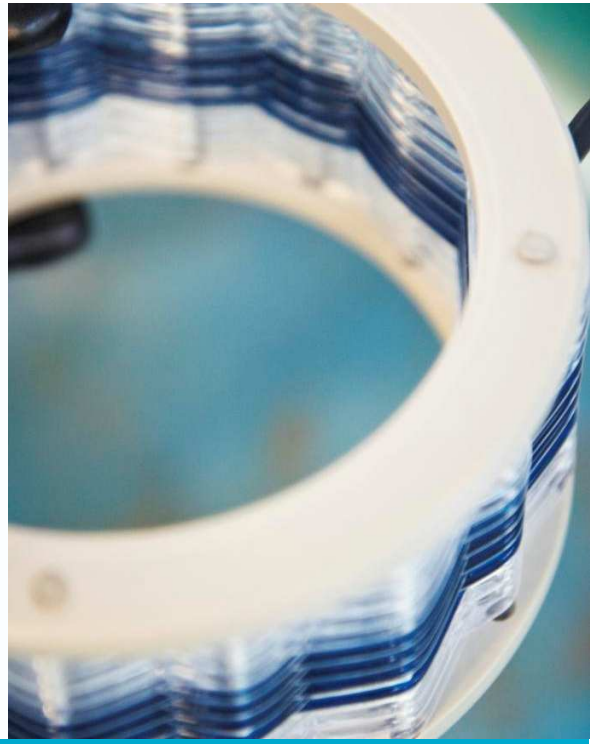


Process Intensification for Chemical Manufacturing using Continuous Flow Processing

Christian Hornung | Senior Research Scientist – Director, Centre for Industrial Flow Chemistry

31 May 2017

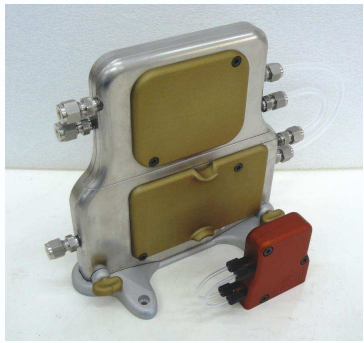
CSIRO MANUFACTURING
www.csiro.au

RSC Symposium: Continuous Flow Chemistry for Industrial Processes 2017
Chemspec Europe - Munich

Continuous Flow Processing at CSIRO – Lab Discovery

Vapourtec - Tubular Reactor Systems

Zaiput L-L Separators



Capabilities:

- Hom. Liquid Phase
- Liquid-Liquid
- Gas-Liquid
- Het. Catalysis
- (Slurry Reactions)

Chip & Tubular Reactor Modules

Uniqsis – Flow Reactors

Partners / Suppliers:

CHEMTRIX

vapourtec

CRD CAMBRIDGE REACTOR DESIGN

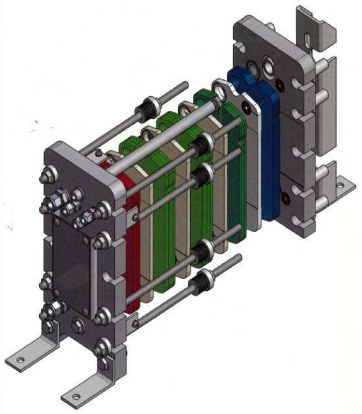
Zaiput Flow Technologies
Groundbreaking Innovations in Flow Chemistry

UNIQSIS
Accessible flow chemistry

Continuous Flow Processing at CSIRO – Scale-up

CRD Shell & Tube Reactors

up to 2 L reactor volume
➔ up to >2500 L/day



ChemTrix
Plate type Reactor

CSIRO Tubular Flow Reactor

FloWorks – CSIRO's Centre for Industrial Flow Chemistry

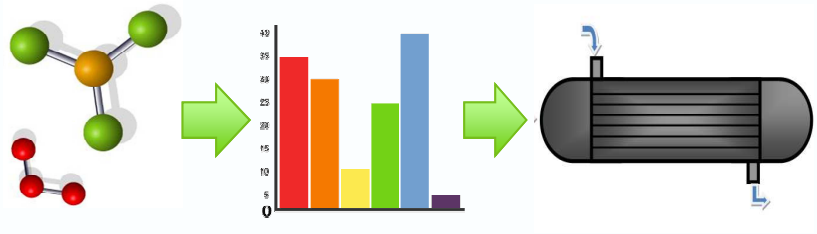
*The **Centre for Industrial Flow Chemistry,** based in Clayton, is a technology platform providing access to CSIRO's flow chemistry technology to chemical manufacturers.* ➔ ***from lab discovery to scale-up and production***

Services:

- process R&D operations for industrial clients
- managing the technology transfer to client site
- in-house training for industrial collaborators
- innovative research on new process technology for chemical manufacture

launched on 22nd November 2016

CHEMICAL DISCOVERY | **REACTION OPTIMISATION** | **PROCESS SCALE-UP**



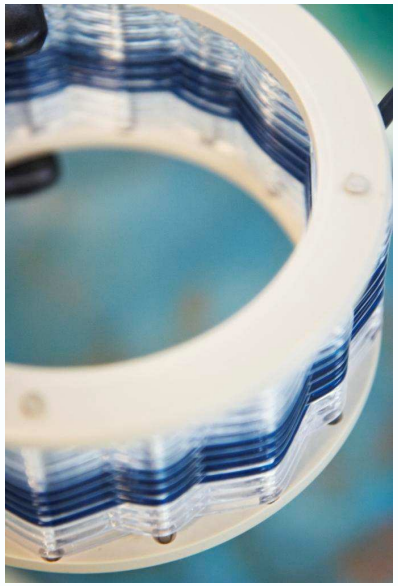
Project areas:

Pharmaceuticals
Fine Chemicals
Biofuels & Renewables
Food Additives
Health Care & Medical
Agrochemicals
Cosmetics
Catalysts
Nano-materials
Reactor Design
Polymers
Speciality Chemicals
Construction Materials

FloWorks – New Facility at Clayton, VIC

Partners:

- Academia (Monash, Deakin, …)
- Equipment Manufacturers (Cambridge Reactor Design, Chemitrix, …)
- Chemical Manufacturers (Boron Molecular, …)
- VCSCM, Chemistry Australia, …



➔ operation of **laboratory scale** and **industrial scale** flow chemistry equipment

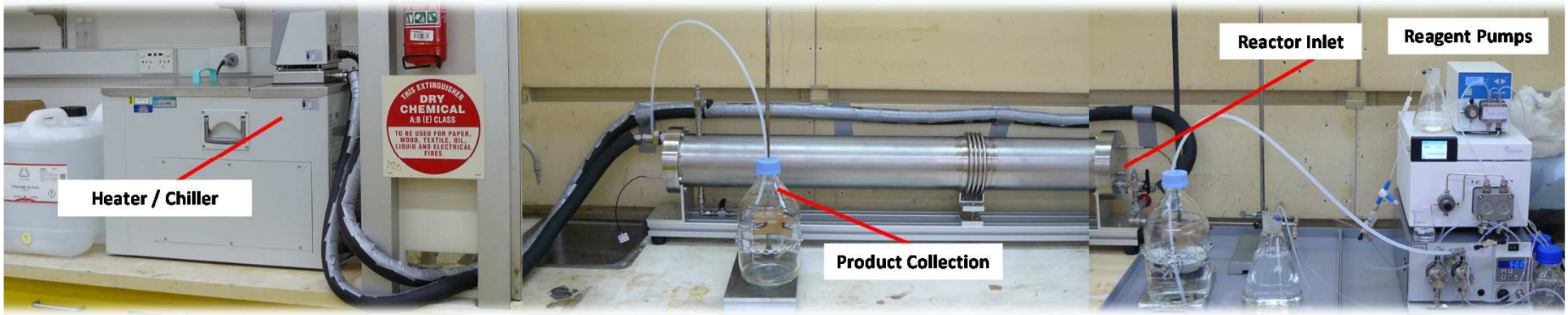
➔ accommodating **current** operations and development of **new** flow chemistry solutions

Recent commercial projects include...

- **Emulsion polymerisation**
  slow reaction, low temperature, high viscosity, intensified mixing required
- **Synthesis of polymers with very narrow polydispersity**
  fast reaction, SM difficult to handle, very precise process control needed
- **Synthesis of novel monomers**
  exothermic reaction, moisture sensitive compounds

Space Time Yield

$$STY = \frac{Product}{t_P \cdot V_R}$$

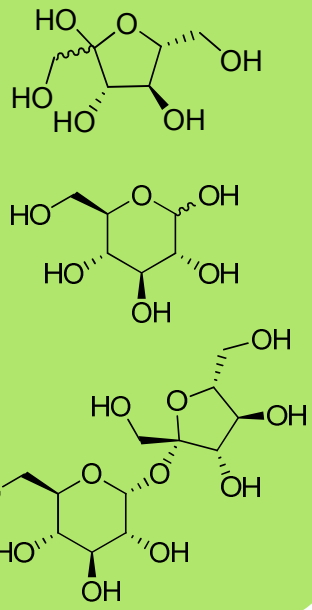


Process Improvements:	Reaction Time		Space Time Yield [g $L^{-1}h^{-1}$]	
	batch	*flow*	*batch*	*flow*
• Synthesis of RAFT precursor	8 h	10 min	0.69	768
• Synthesis of dye intermediate	n/a	30 min	7.6	235
• Synthesis of API precursor	7 d	10 min	0.44	1336

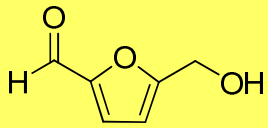
T. M. Kohl, C. H. Hornung, J. Tsanaktsidis. *Molecules* **2015**, 20, 17860–71.

Carbohydrates as Renewable Feedstock

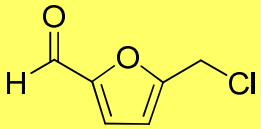
Biomass



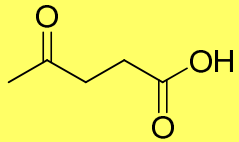
Bulk Chemicals & Biofuel



HMF
(5-(hydroxymethyl)furfural)



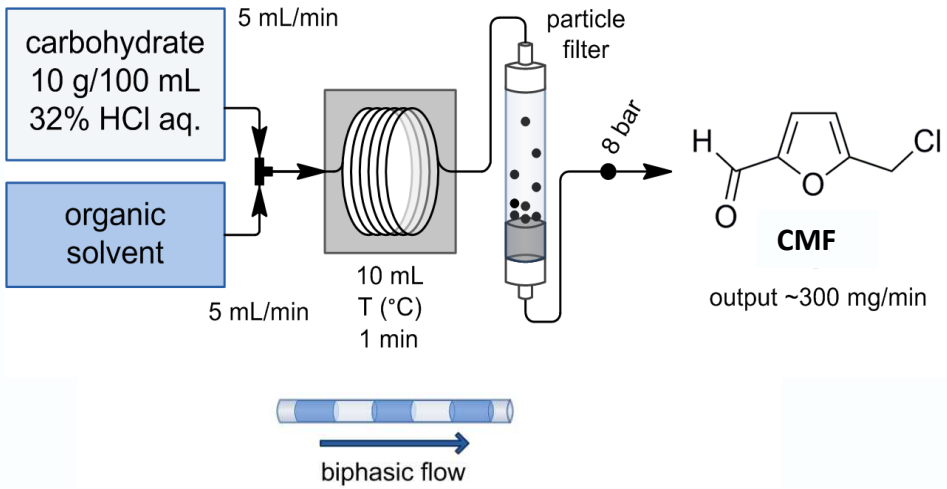
CMF
(5-(chloromethyl)furfural)



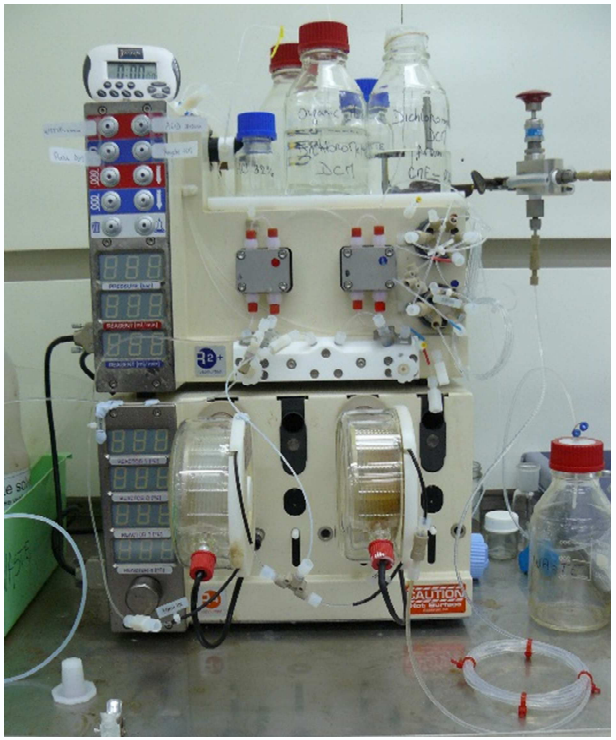
LA
(levulinic acid)

M. Brasholz, K. von Kaenel, C. H. Hornung, S. Saubern, J. Tsanaktsidis, *Green Chemistry*, **2011**, 13, 1114-1117.

Continuous Flow Dehydration of Sugar



Lab-Scale: 10 ml tubular reactor



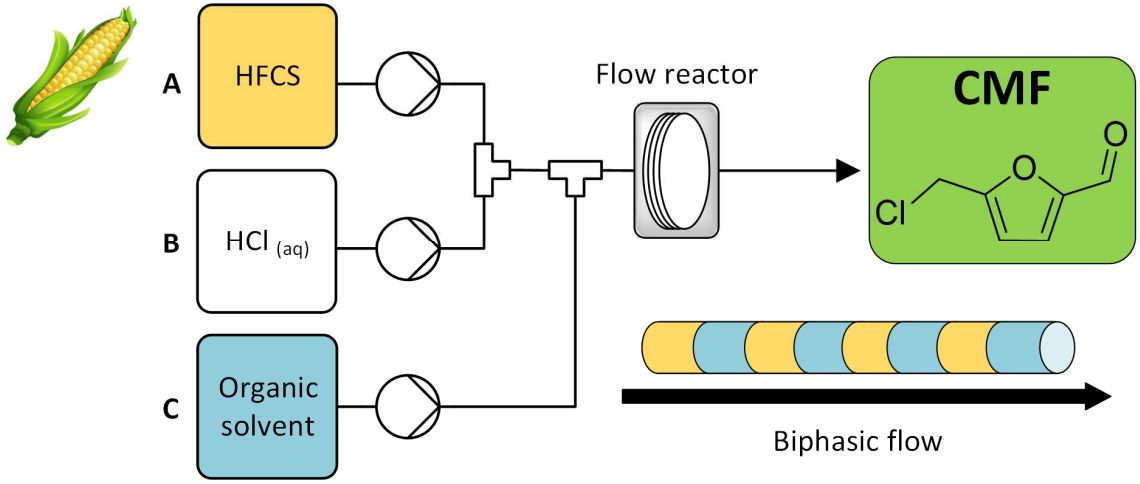
Vapourtec R2/R4 reactor system

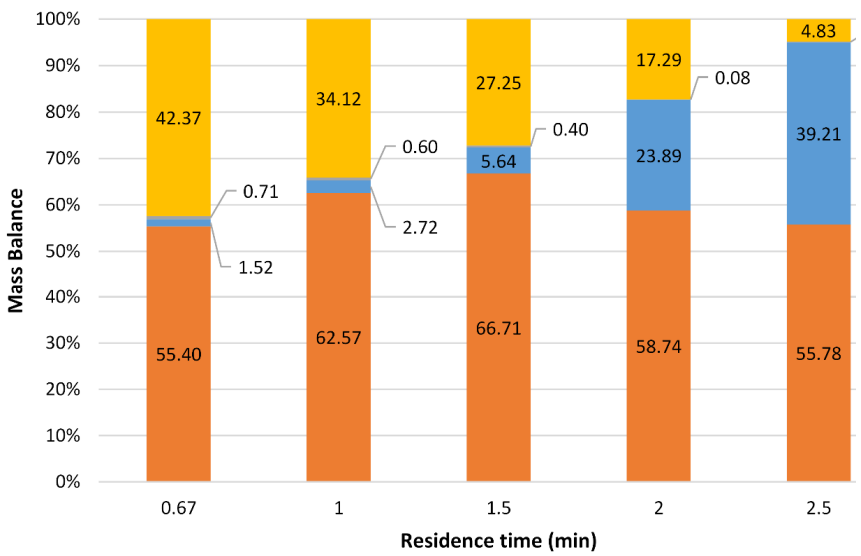
By-Product: **HUMIN**

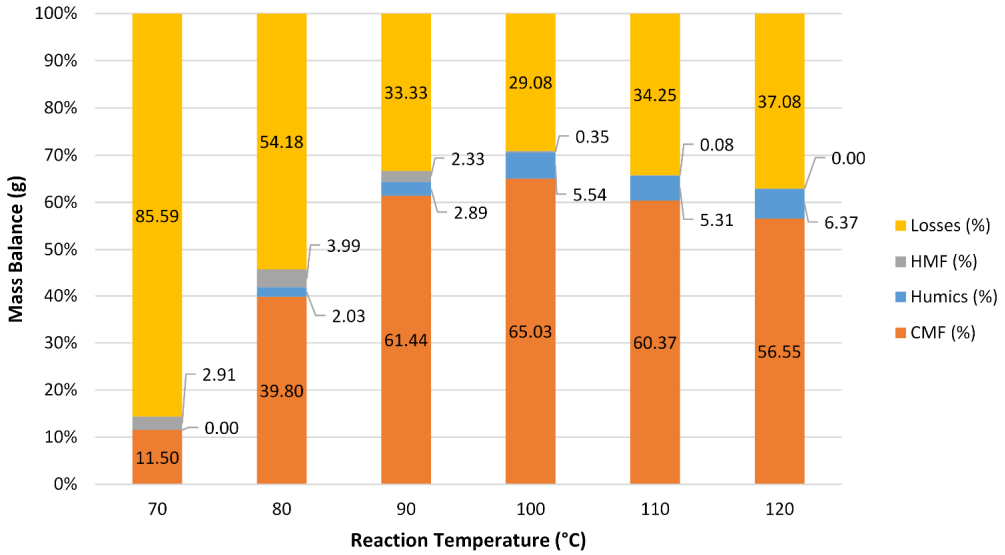
- aqueous + organic ➔ biphasic flow
- very short residence times: ~1 min
- moderate temperatures: ~100 °C
- inline filtration to remove by-product
- simple and efficient purification by liquid-liquid extraction

M. Brasholz, K. von Kaenel, C. H. Hornung, S. Saubern, J. Tsanaktsidis, *Green Chemistry*, **2011**, 13, 1114-1117.

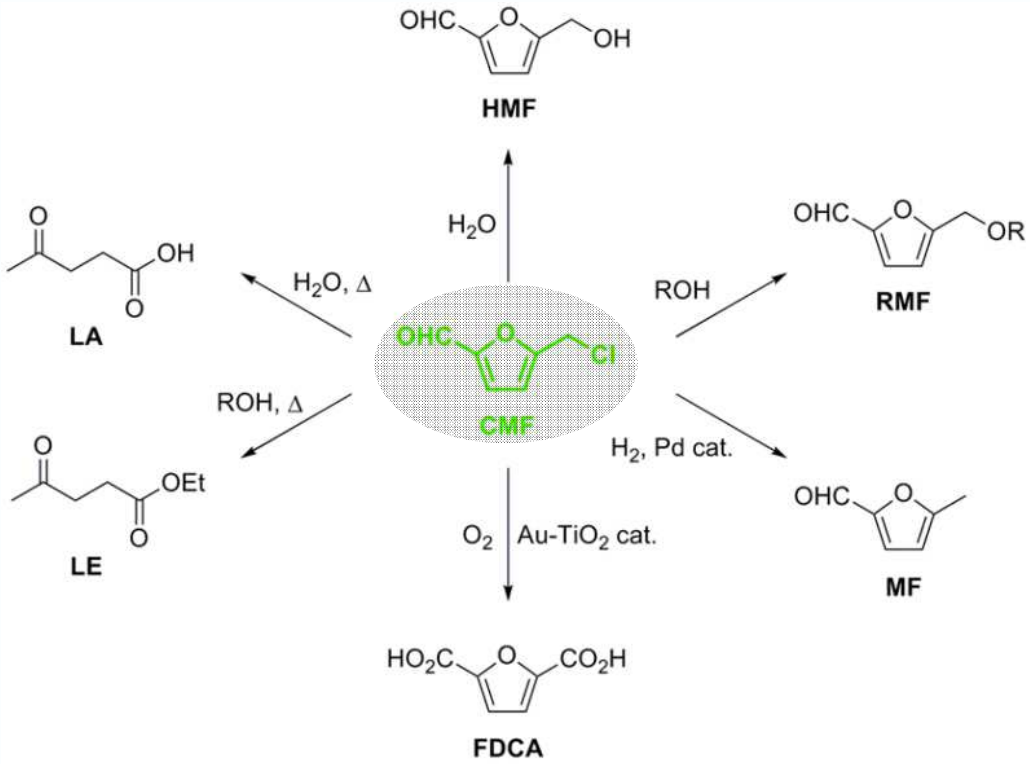
CMF from High Fructose Corn Syrup (HFCS) using Flow







CMF as a renewable platform chemical



Bio-refinery Concept for CMF

using lignocellulosic or sugar-based feedstocks from:

- Agricultural waste
- Food waste
- Refined renewable feed stocks (sucrose, HFCS)

... towards a chemical industry using renewable resources

Scale-up of the RAFT Process

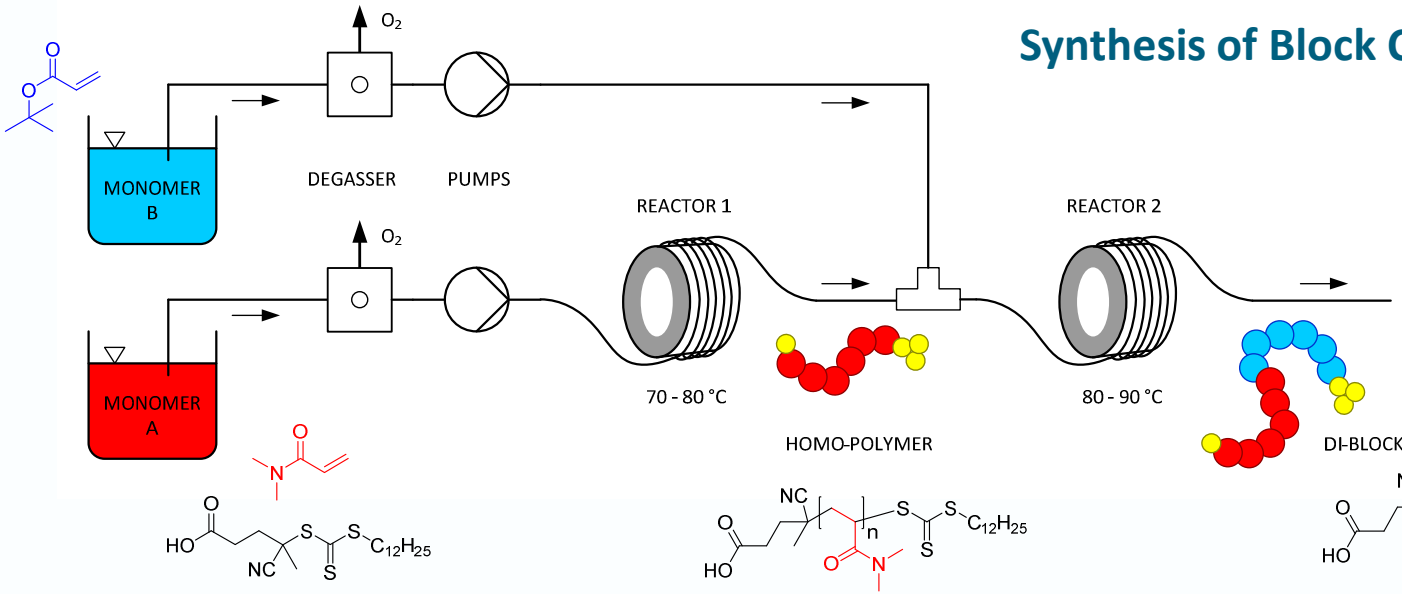
RAFT: Reversible Addition-Fragmentation Chain Transfer

Tubular Flow Reactor
with static mixers
(reactor volume 108 ml)

Benefits of RAFT polymerisation:

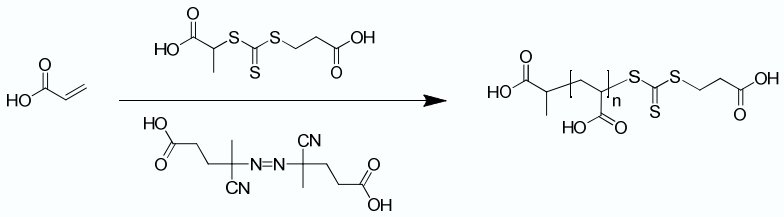
- 'Tailored' molecular weight (M_n ~ moles RAFT agent)
- Narrow mol. weight distribution
- Access to complex architectures: blocks, grafts, stars,...
- Conjugation to reactive molecules (drugs, biomolecules, etc.)

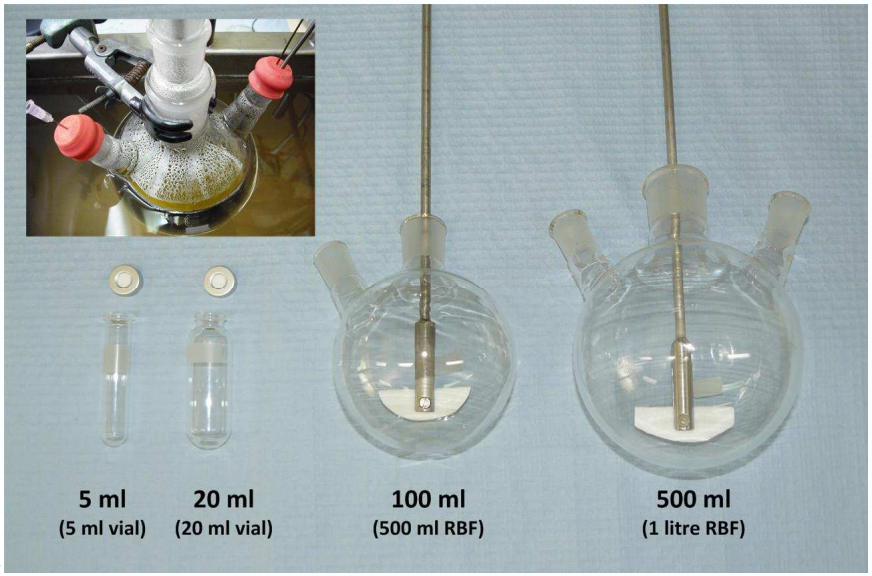
Synthesis of Block Copolymers in Flow



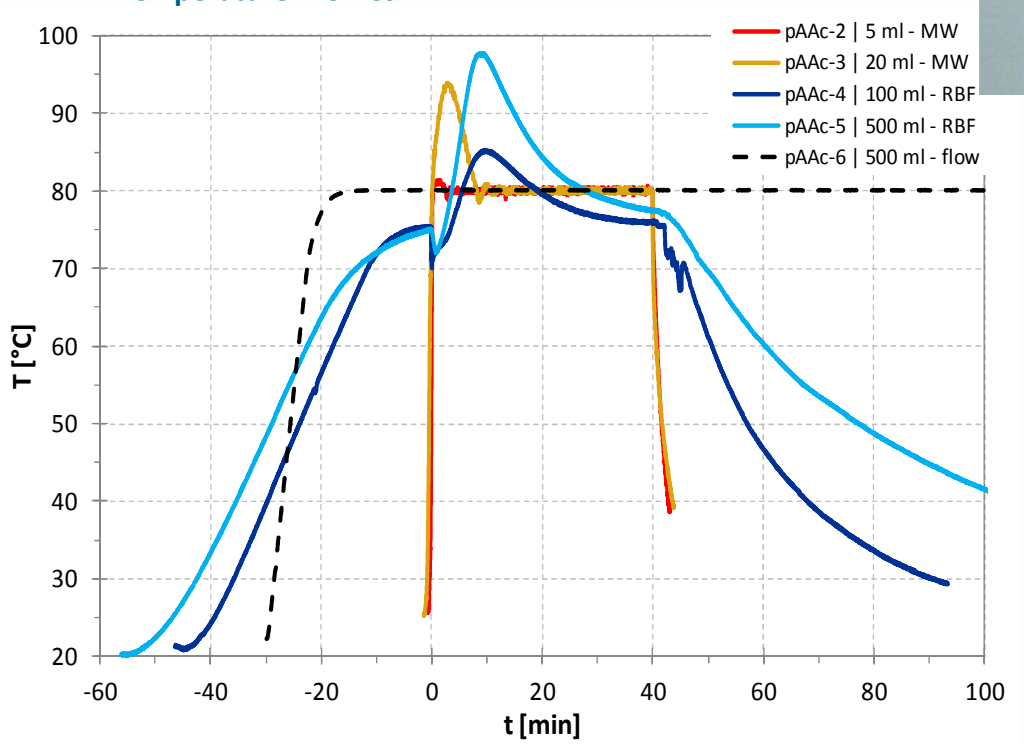
Reactor system:
Vapourtec - R2/R4
SS - 10 ml coils

Scale-up of the RAFT Process





Temperature Profiles:



Problems with scale-up in batch:

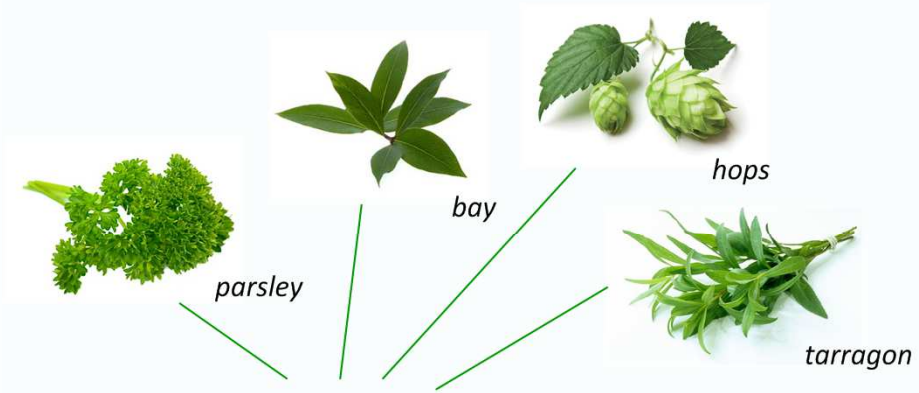
- temperature gradients
- concentration gradients
- dead zones
- inefficient mixing

small 'ideal' system
Laboratory

large 'non-ideal' system
Industry

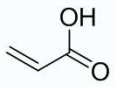
N. Micic, A. Young, J. Rosselgong, C.H. Hornung, *Processes,* **2014**, 2, 58-70.

Surfactants from Renewable Feedstock

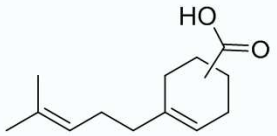


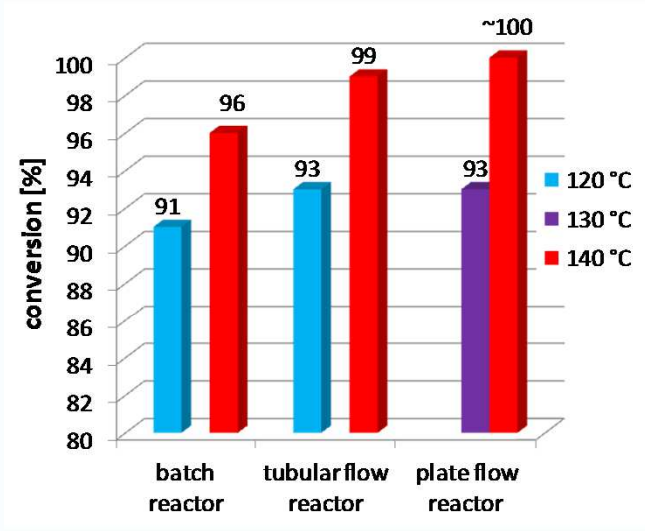
myrcene

+



Continuous Flow Process
100 – 160 °C

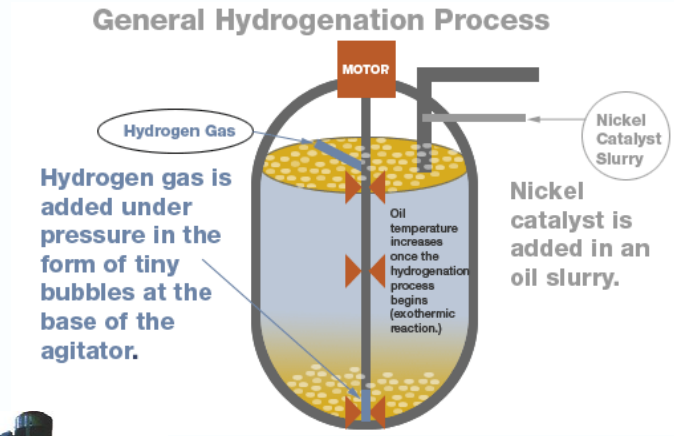


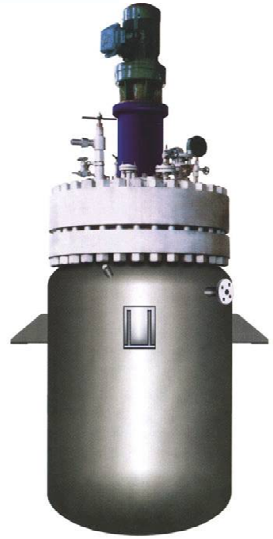


Surfactant for use in household products, e.g. as stain remover for expensive garments (wedding dresses and others)

Hydrogenation – Industrial Processes and a New Approach

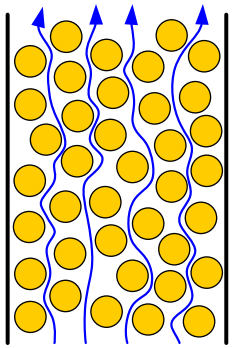
Heterogeneous catalysis - current state of the art:





slurry – stirred tank

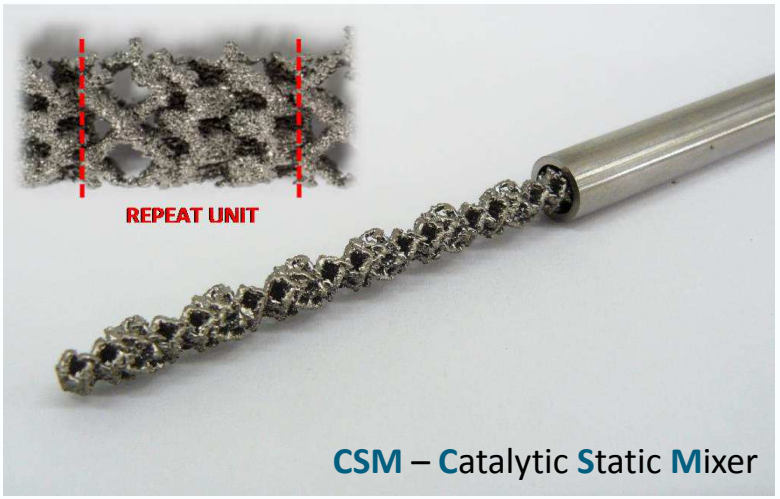
heterogeneous catalyst



fixed or fluidised bed

Our approach:

- continuous flow process
- tubular reactor system with inserts
  ➔ favorable flow / processing conditions
- heterogeneous catalyst supported on tubular inserts using metal deposition methods
- 3D metal printing for manufacture of inserts
- optimize fluid flow and heat and mass transfer by custom designed static mixer inserts and evaluate by CFD & EFD



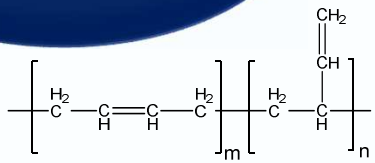
Impact – Industrial Applications of Hydrogenations

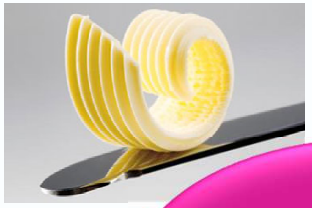
Pharmaceuticals

Petrochemicals

Fine Chemicals

Polymers





Food Processing

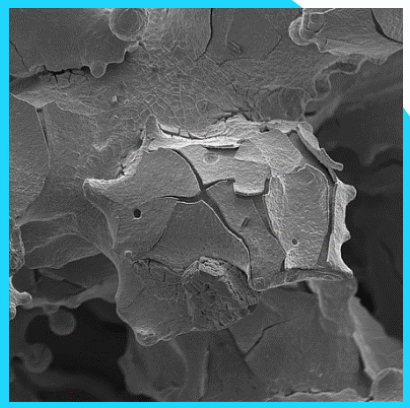
R&D

Hydrogenation Reactor – Project Plan & Resources

3D Metal Printing

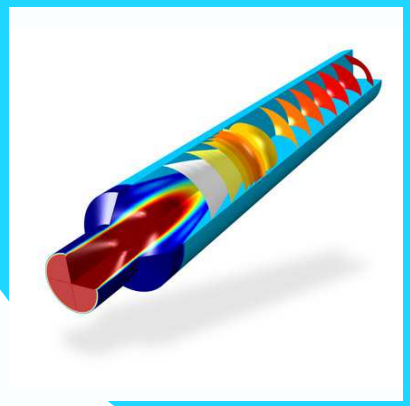
Additive Manufacturing

Metal Deposition

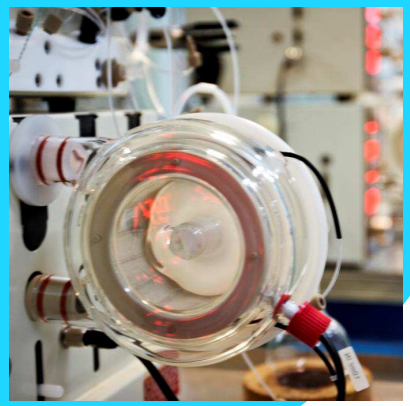


Electrodeposition &
Cold Spraying

CFD &
Experimental
Fluid Dynamics



Fluid Dynamics



Flow Chemistry

Organic Chemistry &
Reactor Engineering

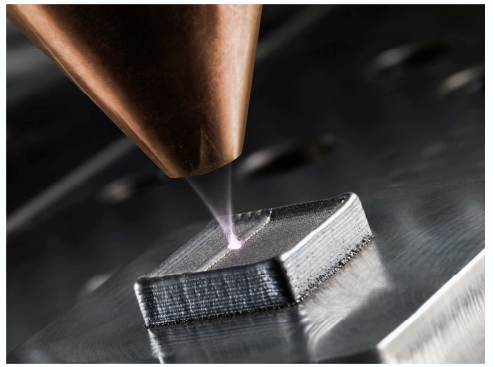
Catalytic Static Mixers (CSMs)

Different designs:
➔ maximize heat and mass transport for different reaction systems

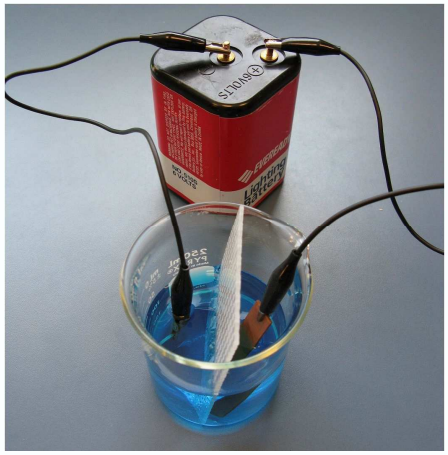
Substrate Materials:
Ti-alloy, CoCr-alloy, Al-alloy, 316 SS, …

Catalysts:
Ni, Pt, Pd, Cu, Au, Ag, …

3D Metal Printing

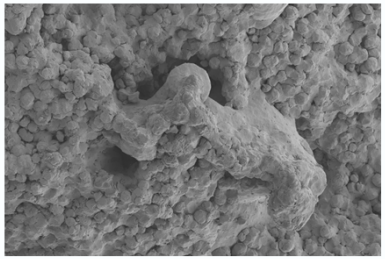


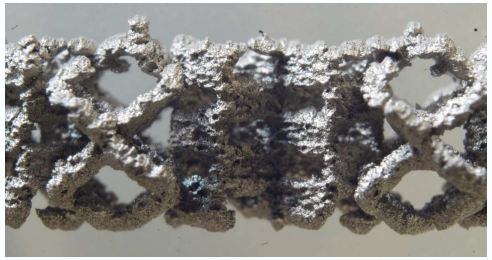
Electroplating

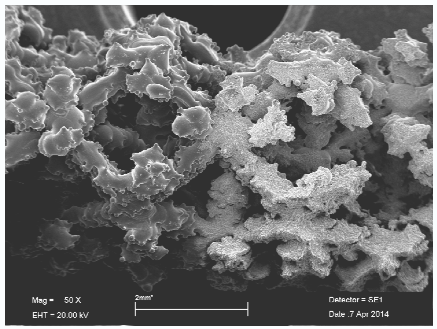


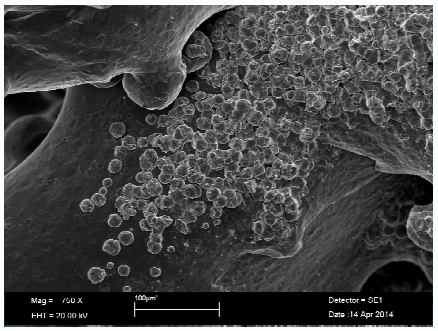
Cold Spray

Nickel – Cold Spray

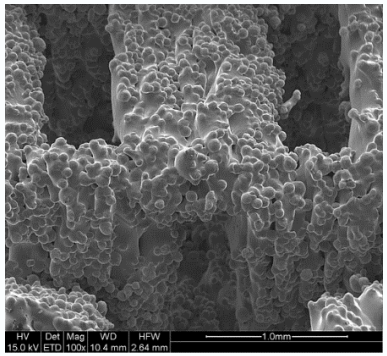


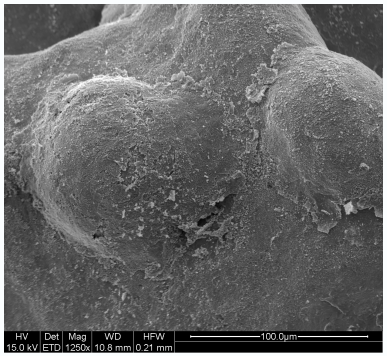




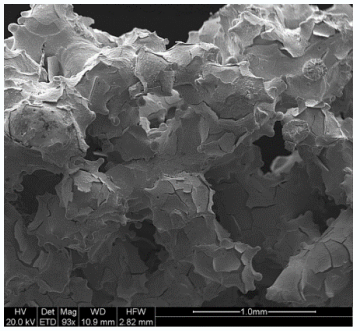


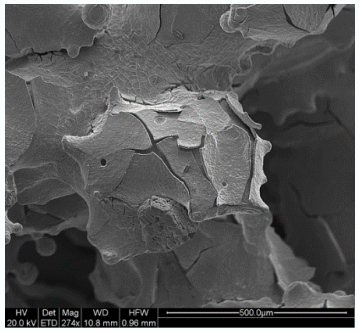
Nickel - Electroplating



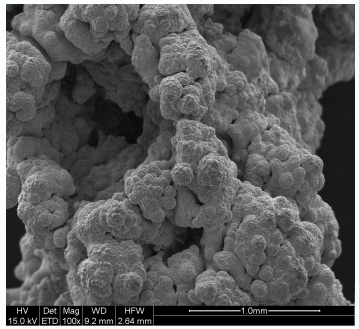


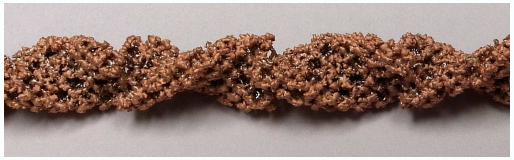
Platinum – Electroplating

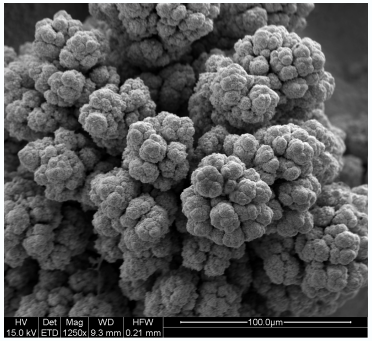




Copper – Electroplating







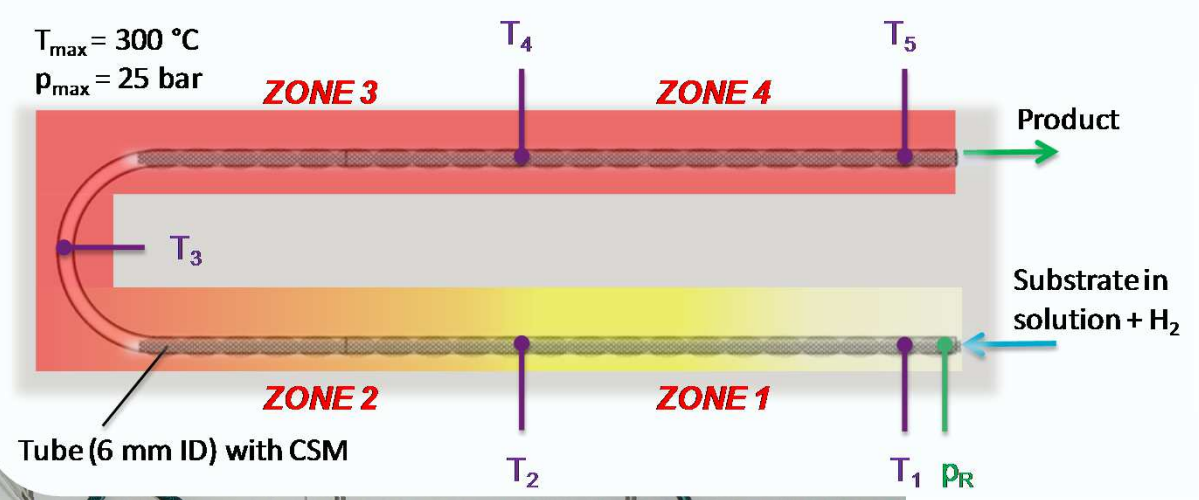
Palladium - Electroplating

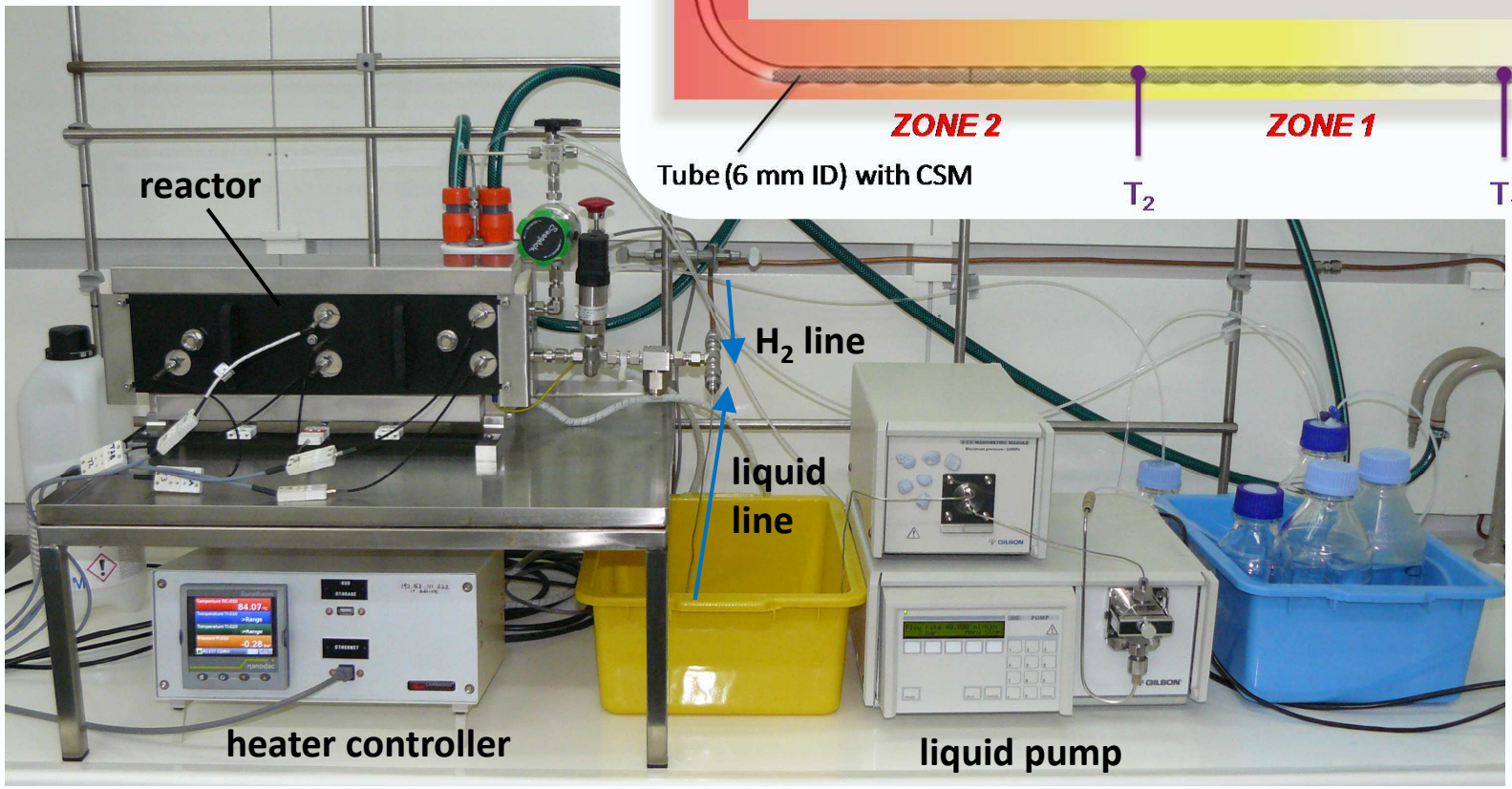
Hydrogenation Reactor – Experimental Rig, Part 1

Prototype Flow Chemistry Reactor:

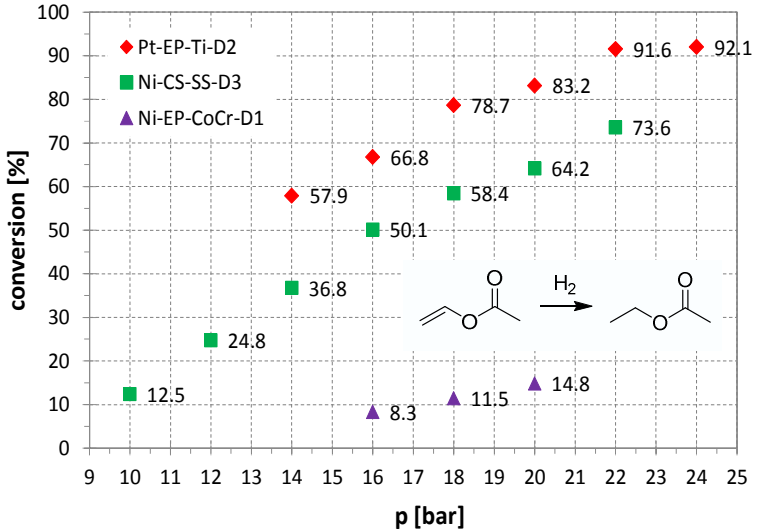
Mk 1: 4 catalyst zones, each 15 cm

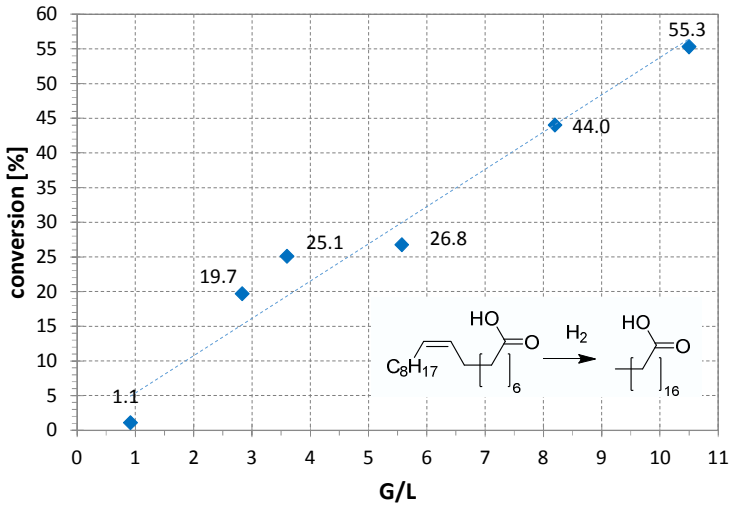
(designed & built by CRD and CSIRO)



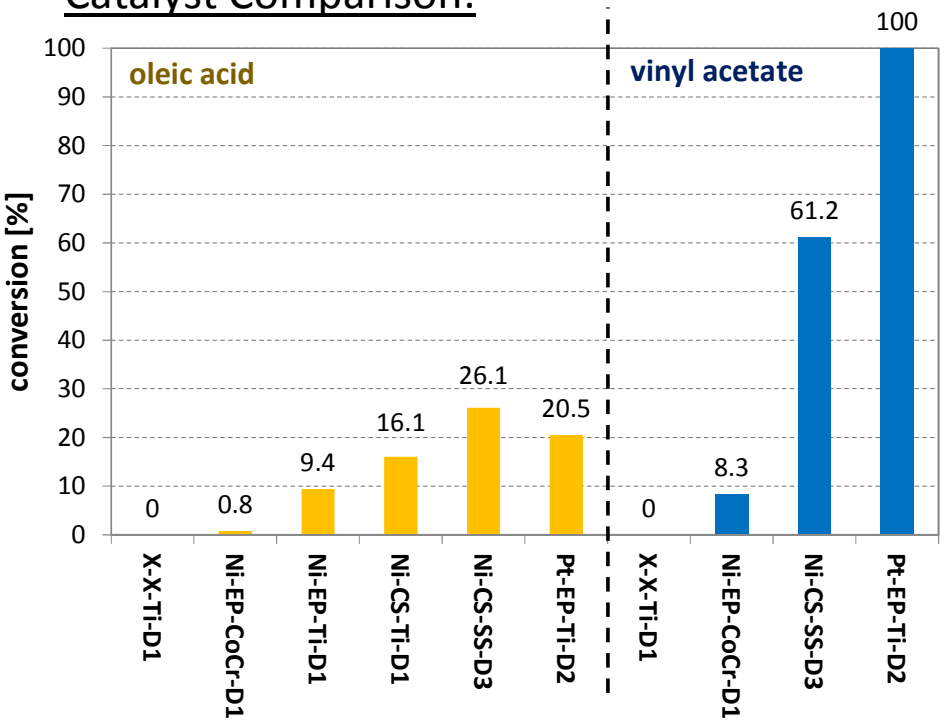


Proof of Concept – Hydrogenation using gaseous H_2

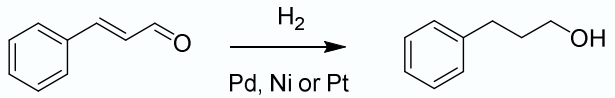




Catalyst Comparison:

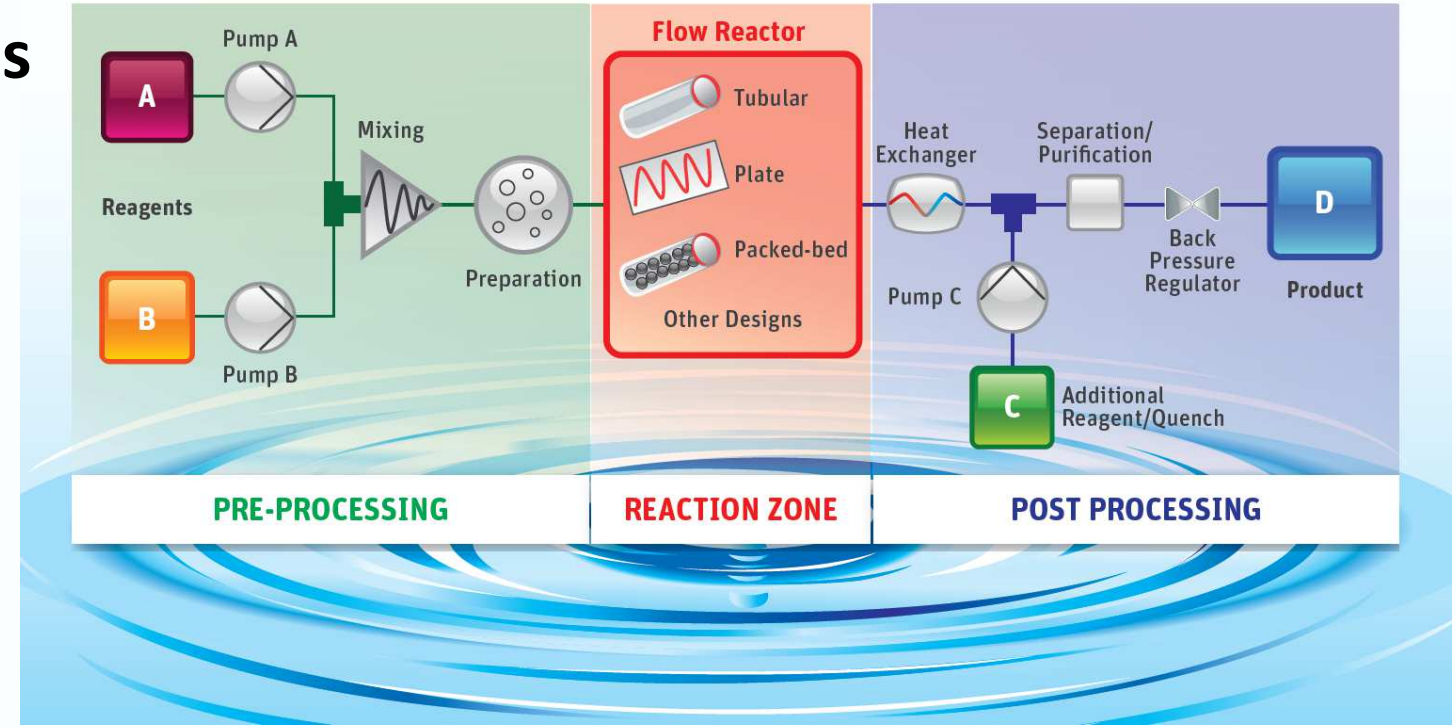


We successfully tested this prototype reactor for the hydrogenation of alkenes, alkynes, carbonyls, nitro- and diazo-compounds, nitriles, imines, and halides, as well as bifunctional molecules such as the following:



A. Avril *et al. Reaction Chemistry & Engineering* 2017, 2: 180–88. doi:10.1039/C6RE00188B.

Conclusions



- ***Continuous Flow Processing*** bridges the gap from laboratory / discovery scale to preparation / production scale, **mg** to **kg**, with minimum scale-up efforts.
- ***Integrated Processing*** allows for combination of several processing steps to form one continuous production line, e.g. purification, block co-polymers, …
- ***Efficient Processing*** is achieved by using micro- and mm scale flow geometries ➔ large surface to volume ratio, enhanced heat and mass transfer, higher STY

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Thank you

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