Development of Micro/Flow Reactor

Five key phases (Gartner)

- High publicity
- Viability unproven
- Better understanding required!
- Improved versions, better availability, and more flexibility
- Limited number of industrial applications

Better availability and more flexibility required!
Raf Reintjens (Principal Scientist @ InnoSyn): “Selective Laser Melting (SLM) or Additive Manufacturing - 3D printing of metal - is a very strong enabling technology and will have major impact on the production of future industrial flow reactors!”
Selective Laser Melting – 3D printing

Developed by IIT Fraunhofer Aachen (1995)

Selective laser melting process produces homogenous metal objects directly from 3D CAD data by selectively melting fine layers of metal powder with a laser beam.

- Max build envelop: 60x40x50 cm³
- Min feature size: 40-200 micron
- Min layer thickness: 30 micron
- Accuracy: 20-50 micron
- Surface finish: 4-10 micron RA
- Density: 99.9%

Materials:
- Aluminium
- Cobalt-chromium alloy
- Nickel based alloys
- Stainless steel
- Titanium
- Tantalum
- Tungsten
3D metal printing in other industries

e.g. Formula 1

Ferrari’s F1 team are ramping up preparations for the 2017 season by using 3D printing technology to create a new stronger piston for their new engine made from steel alloy. Ferrari were able to develop this piston quickly and efficiently, iterating the design and adjusting according to performance data. “3D metal printing enables the creation of complex geometrical structures that can provide more strength while reducing weight.”

Also McLaren recently signed a 4-year agreement with a 3D printing company.

EOS F1 brake pedal with hollow design made from EOS Titanium Ti64 at Formnext 2016. Photo by Michael Petch
“Output of 3D printer”
SLM for micro reactor manufacturing

3D printed flow reactors and static mixers
- Efficient in construction material consumption
- Intricate details possible in mm sized channels
- Full flexibility
Impact of zigzag & fluid velocity

CFD Calculations: At higher Re number, secondary flow occurs and gets more chaotic.
Hundreds of bars are reached with a few tenths of a mm wall thickness.

\[ V = 2.26 \text{ mm ID}; 0.5 \text{ mm wall: did not burst at 470 bars} \]

Recently, even at **1300 bars** the reaction channel survived.
Example
Cryogenic Organometallic Chemistry

**In batch mode** this fast and exothermic chemistry is “controlled” by lowering the temperature, dilution and/or slow dosing regimes. Often the cooling capacity determines the time demand. Byproduct formation due to local hot spots and/or wrong local stochiometries (slow mixing of reagents).

**In flow,** for these metalations the cooling/heat transfer is much better:
- Metalations in flow enable to operate in principle as fast as the chemistry allows (seconds only, or even shorter).
- Smaller cooling units required (limited capital expenses).
- Higher selectivities to the desired compounds.

Several successful low-temp flow processes developed and applied (up to plant scale)
Schematic set-up

Assay yield 80% (60% batch)
No clogging
Less by-products

Substrate 1

Substrate 2

HexLi

Cooling

Cooling

Cooling

Cooling

Cooling

R1

R2

product

I–N–N–O
S–Y–N

Tomorrow's chemistry. Today.
Lab set-up = pilot plant output

- Aryl-Br pre-cool reactor
- AlkylLi pre-cool reactor
- Keton pre-cool reactor

- Reactor 1: Aryl-Li formation (15 s)
- Reactor 2: Nucleophilic addition (11 s)

~1Kg Product/ hr

No clogging
> 16 hours
Ca 35 bar

Lab set-up = pilot plant output
3D Printing enables full flexibility

“One can now create the ideal asset for any type of demanding chemistry”

T-mixer + ‘flow part’

Additional inlet e.g. for thermo couple
16 mL T-mix + 2 thermo couple inlets
16 mL T-mix + 2 thermo couple inlets

See, touch & feel them: Hall A5, M170
Mixers
Organometallics = ‘Flash Chemistry’
Flash Chemistry

chemistry in this book can be defined as follows: *Flash chemistry is a field of chemical synthesis where extremely fast reactions are conducted in a highly controlled manner to produce desired compounds with high selectivity.* In flash chemistry, a substrate is activated to a reactive species

**Figure 3.2** Multi-step synthesis based on reactive intermediates

3D printing of metal
Mixers tested

Joint publication by Evonik, GSK and Imperial College London

Mixing Performance Evaluation for Commercially Available Micromixers using Villermaux-Dushman Reaction Scheme with IEM Model

Joseph M Reckamp, Ashira Bindels, Sophie Duffield, Yangmu Chloe Liu, Eric Bradford, Eric M. Ricci, Flavien Susanne, and Andrew Rutter

Org. Process Res. Dev., Just Accepted Manuscript • Publication Date (Web): 09 May 2017
Downloaded from http://pubs.acs.org on May 11, 2017

Unfortunately not including Kenics, SMX, SMXL, …
Static mixer - new design

CCM – Co-current mixing
CRM – Cross current mixing

Average turbulent kinetic energy in the cross section along the x-axis
Large static mixers - up to 10 L/min

3/8 inch Swagelok

CRM - “cross current”

8 SMX elements
5, 6, 7, and 8mm diameter
Next Version

10, 12, and 14 mm
½ inch Swagelok
~20 L/min
Catalytic Oxidation
Catalytic Oxidation of Alcohols

**Goal:**
- Set-up of a safe, continuous flow system for catalytic aerobic oxidations
- Using cheap oxidant (pure oxygen or air)
- Are zigzag’s beneficial?
- Implementation of online analysis (FT-IR)
- Substrate scope: Oxidation of primary and secondary alcohols to have safe access to industrially relevant aldehydes and ketones

See also: B Pieben, CO Kappe, Top. Organomet. Chem. 2016, 57, 97
Copper + TEMPO (or ABNO)

less hindered bicyclic nitroxyl radical e.g. ABNO, keto-ABNO
oxidation of sec. alcohols and steric hindered alcohols

Setup zigzag flow reactor

16 ml
2 * 4 ml
4 ml with T-mixer
Taylorflow - Coiled vs Zigzag

$\text{ratio (l/g)} \approx 1.0$

$\text{ratio (l/g)} \approx 0.25$

1.6 bar, RT

yield (Benzaldehyde) wt%

eq \text{O}_2
Solubility of $O_2$ in acetonitrile

Pictures taken at 20 bar, 20 °C, 1 eq.$O_2$

$O_2$ dissolved quickly, length of PTFE-tubing approx. 30 cm

Taylor-flow vs. ‘single phase’

Oxidation in zig-zag vs. coil reactor vs. single phase, RT

Productivity / mmol * ml (reactor volume)⁻¹ * min⁻¹

- Zig-zag reactor
- Coil reactor
- Single phase

Equivalents O₂: 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4

Chemical reaction:

[Cu], TEMPO, 2,2’-bipyridine, NMI, O₂

Product:

Productivity parametric representation.
**KetoABNO vs. TEMPO**

Oxidation of Geraniol, single phase, 1.0 eq

O$_2$, 80 °C, 20 bar O$_2$

- **Yield / wt%**
  - [Graph showing yield vs. residence time for TEMPO and KetoABNO]

- **Productivity / mmol * ml (reactor volume) $^{-1}$ * min$^{-1}$**
  - [Graph showing productivity vs. residence time for TEMPO and KetoABNO]

Tomorrow's chemistry. Today.
## Substrate scope

<table>
<thead>
<tr>
<th>Substrate</th>
<th>T/ °C</th>
<th>Residence time / min</th>
<th>p / bar</th>
<th>Eq. O₂</th>
<th>Yield / %</th>
<th>Productivity / ‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taylor benzyl alcohol* coil</td>
<td>20</td>
<td>4</td>
<td>1.6</td>
<td>1</td>
<td>22</td>
<td>0.0068</td>
</tr>
<tr>
<td>Taylor benzyl alcohol* zigzag</td>
<td>20</td>
<td>4</td>
<td>1.6</td>
<td>1</td>
<td>45</td>
<td>0.0140</td>
</tr>
<tr>
<td>Single phase benzyl alcohol*</td>
<td>20</td>
<td>4</td>
<td>20</td>
<td>1</td>
<td>100</td>
<td>0.0313</td>
</tr>
<tr>
<td>Octanol*</td>
<td>80</td>
<td>4</td>
<td>20</td>
<td>1</td>
<td>100</td>
<td>0.0313</td>
</tr>
<tr>
<td>Geraniol*</td>
<td>80</td>
<td>4</td>
<td>20</td>
<td>1</td>
<td>100</td>
<td>0.0313</td>
</tr>
<tr>
<td>Geraniol**</td>
<td>80</td>
<td>4</td>
<td>20</td>
<td>1</td>
<td>100</td>
<td>0.0313</td>
</tr>
<tr>
<td>Epoxol**</td>
<td>80</td>
<td>4</td>
<td>20</td>
<td>1</td>
<td>94</td>
<td>0.0293</td>
</tr>
</tbody>
</table>

* With 5 mol% TEMPO
** With 1 mol% KetoABNO
‡ mmol * ml (reactor volume)^-1 * min (residence time)^-1

![Chemical structures](image)
3D printed flow reactors for sale

- Available sizes: 1, 2, 4 and 8 mL
- Any combination available (also double jacketed T-mixers)


<table>
<thead>
<tr>
<th>MR module</th>
<th>Channel volume (ml)</th>
<th>Channel diameter (mm)</th>
<th>Channel length (cm)</th>
<th>Pressure drop (bar)</th>
<th>Heat transfer coeff. (W/m²K)</th>
<th>Output (ltr/h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flow 1</td>
<td>1.0</td>
<td>1.13</td>
<td>100</td>
<td>0.1 - 0.3</td>
<td>1000-2000</td>
<td>0.75 - 1.5</td>
</tr>
<tr>
<td>Flow 2</td>
<td>2.0</td>
<td>1.60</td>
<td>100</td>
<td>0.1 - 0.3</td>
<td>1000-2000</td>
<td>1.5 - 3.0</td>
</tr>
<tr>
<td>Flow 4</td>
<td>4.0</td>
<td>2.26</td>
<td>100</td>
<td>0.1 - 0.3</td>
<td>1000-2000</td>
<td>3.0 - 6.0</td>
</tr>
<tr>
<td>Flow 8</td>
<td>8.0</td>
<td>2.26</td>
<td>200</td>
<td>0.3 - 1.0</td>
<td>1000-2000</td>
<td>6.0 - 12.0</td>
</tr>
</tbody>
</table>

- Larger 3D printed flow reactors can be made available as well.
- Any customized configuration for your specific type of demanding chemistry at request. “One can now create the ideal asset for a specific type of chemistry”
Summary

- 3D printing has enabled cost-efficient manufacturing of flow reactors
- Full freedom of design: *Create the ideal asset for your demanding chemistry*
- Smooth integration in existing hardware (lab and plant)
- Wide diversity of applications:
  - Cryogenic organometallic chemistry
  - High Temperature (‘in the melt’)
  - Catalytic Oxidations
  - Catalytic Hydrogenation
  - Nitrations
  - Cyclopropanations (‘Ethyl diazoacetate’)
  - Polymerizations
  - Azide Chemistry
  - Fluorinations