Microchemical and Microphysical Systems

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http://iscamap.chem.polimi.it/citterio/education/course-topics/
Miniature reaction and other unit operations show *specific* advantages over conventional chemical systems.
Modern Trends in Chemistry & Chemical Engineering Crossing Discipline Boundaries

ENABLING TECHNOLOGIES

Microfabrication
- Microfluidics
  - Micro process engineering

Green / sustainable chemistry
- Process intensification
  - Small-scale conti-flow processing

Novel means of chemical process engineering

Catalyst & materials science
- Mathematical Modelling & simulation
  - Chemistry & Chemical engineering

FUNDAMENTAL SCIENCES
Microchemical Systems – Scale Down and Out

Attilio Citterio

Pilot

UP

~ 5 liter flow?

temperature?

~ 5 µliter

25°C

DOWN

OUT

~ 1 ml

Not to scale

~ 50 ml

SCALE

UP

MIT
Fine-Chemical Microreactors
Production Plant

Micromixer (1000 l/h)

Microtube reactor (100 l/h)

Micro heat exchanger (100 l/h)

Fine-chemical plant with 10 microstructured production devices: launch at ACHEMA, May 15, 2006

IChemE Chemistry Innovation KTN/Impact Award
award (Whitehall, London)

IMM Plant in NATURE
Nature 442, 27 July 2006
“Miniature version of the regular thing.”

- Same functionality per volume as macro
- Miniature size is distinguishing factor
- Portability often important
- Often highly integrated
- Microscale platforms for nanoscale structures/materials
What is Microfluidics?

Microfluidics enables precise control, manipulation and analysis of fluids in the microliter to picoliter range. Microfluidic devices are fabricated using techniques developed in the semiconductor industry and are often referred to as microfluidic chips. Today the main application areas for microfluidics include:

- Research and development chemistry
- DNA analysis and genomics
- Microreactors
- Cell based systems
- Microarrays
- Clinical diagnostics
- Liquid chromatography
- Bio-defence sensors

The benefits of using microfluidic devices for laboratory applications include:

- Reduction in sample volume and reagent usage
- Improved resolution of separations
- Ability to run reaction and analysis processes faster
- Ability to run processes in parallel
- Improved control of mixing and heating of fluids
- Rapid mass transfer as a result of high surface area to volume ratios
- Improved integration of process steps, for example reactions and separations
- Development of new and improved detection methods
- Simpler and cheaper disposable devices
- Access to a wide range of fluidic geometries
Microfluidic Literature

Nguyen, Wereley
Microfluidics
RC / 3.3 / 20
~110€; 500 pages

Oliver Geschke, Henning Klank, Pieter Tellemann
Microsystem Engineering of Lab-on-a-Chip Devices
EH / 9.0 / 31
~80€; 260 pages
ISBN-3527307338, 2004

Henrik Bruus: "Theoretical Microfluidics« (Oxford Master Series in Physics)
~40€; 346 pages;

Microchemical Journal
Microreactors Literature
Fluids

Pressure

Potential energy

Bernoulli Equation

Kinetic energy

Static Fluid Pressure

Hydraulic Press

Hydraulic Brakes

Other Examples

Pascal's Principle

Buoyancy

Archimedes Principle

Other Examples

Internal Energy

Turbulence Effects

non-Newtonian Fluids

Wall Tension

Poiseuille's Law

Blood flow Examples

Osmosis

Diffusion

Viscosity

Laplace's Law

Surface Tension

Membrane Transport

Capillary Action

Fluid Friction

Internal Energy

have

have

at rest

obey

In motion

leading to

leading to

as well as

summarized in

and

and

and

are characterized by
About Microfluidics

• „Micro“ means at least one of the following features
  ▪ small volumes ($\mu$l; nl; pl; fl)
  ▪ small size
  ▪ low energy consumption
  ▪ effects of the micro-domain
    • Laminar flow
  ▪ …

1 fl – 1 μl: 10 orders of magnitude
still far away from molecular level

### Chemical Reactor Scale

<table>
<thead>
<tr>
<th></th>
<th>Industry</th>
<th>Laboratory</th>
<th>Micro-system</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Volume</strong></td>
<td>30 $m^3$</td>
<td>$10^{-3} m^3$</td>
<td>$3 \times 10^{-11} m^3$</td>
</tr>
<tr>
<td><strong>Scale-down</strong></td>
<td>1</td>
<td>$1:3 \times 10^{-5}$</td>
<td>$1:10^{-12}$</td>
</tr>
<tr>
<td><strong>Diameter</strong></td>
<td>2 $m$</td>
<td>2 $cm$</td>
<td>20 $\mu m$</td>
</tr>
<tr>
<td><strong>Surface/Volume</strong></td>
<td>$2 \frac{m^2}{m^3}$</td>
<td>$200 \frac{m^2}{m^3}$</td>
<td>$200 000 \frac{m^2}{m^3}$</td>
</tr>
</tbody>
</table>
Key Benefit: Intensified Surface Phenomena by Higher Surface Area-to-Volume Ratios.

- **intensified mass transport** toward the smaller dimensions
- **Intensified heat transport** toward the smaller dimensions
- **Intensified mixing**
- **Explosion-Safety improvement**
Temporal Scale and Typical Length of Chemical Reactors

- Micro-structured apparatus
- Milli-structured apparatus
- Multi-tube reactor
- Tube reactor
- Stirred tank reactor

Lengths in μm, mm, m:

- 1 μm
- 10 μm
- 100 μm
- 1 mm
- 10 mm
- 100 mm
- 1 m
- 10 m

Mean residence time [s]
Micro-structured Components are Available

**Micro mixers**
Mixing from few ml/h up to 30 l/h

**Micro heat exchangers**
Maximum value of 700 W/m2K at an air flow rate of 75 l/min

**Micro reactors**
Combinaison of μHE and μmixers

**IMM:**
Interdigital micromixer

Heatric:
Cross Flow Heat Exchanger

Mikroglas:
Microreactor
MICRO CHEMICAL AND THERMAL SYSTEMS CONSIDERED AS A “PLATFORM” FOR NANOTECH

- Engineered structures with improved heat and mass transport
- Self-assembling surfaces
- Nano-fabricated structures
- Biological enzymes as highly functional catalysts
Micro-structured Multichannel Reactor

Flow conditions for typical fluids, Volume: $V_R = 5 \text{ cm}^3$; $L = 5 \text{ cm}$
Surface to Volume: Effective Transport

Example: overall heat transfer coefficient

<table>
<thead>
<tr>
<th>Type Hx</th>
<th>$U , (W \cdot m^{-2} \cdot K^{-1})$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tubular</td>
<td>150-1200</td>
</tr>
<tr>
<td>Spiral</td>
<td>700-2500</td>
</tr>
<tr>
<td>Laminar</td>
<td>1000-4000</td>
</tr>
</tbody>
</table>

Micro-channel: $3800-6800 \, (W \cdot m^{-2} \cdot K^{-1})$

$(500 \times 500 \, \mu m^2 \times 1.5 \, cm \, channels)$
Properties of Micro Devices

- **Behavior of fluids at this scale**
  - Wall effects dominate

- **Surfaces and interfaces**
  - Fouling
  - Multi-phase flow
  - Surface energy, tension, wettability
  - Dynamics -- start-up

- **Equipment**
  - Basic state measurements - $P$, $T$, phase, quality, composition
  - Density, thermal conductivity, electrical conductivity
  - Controls -- need to be integrated
  - Fluid flow and distribution
  - System homogeneity
About Microfluidics

• „Micro“ means at least one of the following features
  ▪ small volumes \((\mu L; nL; pL; fL)\)
  ▪ small size
  ▪ low energy consumption
  ▪ **effects of the micro-domain**
    • Laminar flow
    • Surface tension
About Microfluidics

• "Micro" means at least one of the following features
  - small volumes (μl; nl; pl; fl)
  - small size
  - low energy consumption
  - effects of the micro-domain
    - Laminar flow
    - Surface tension
    - electrical surface charges
    - diffusion

$$Re = \frac{u \rho L}{\eta}$$  

Reynolds Number < 2300  

velocity \( u \), density \( \rho \), traveled length \( L \), and viscosity \( \eta \) of the fluid
Market for Microfluidics

Printing

Industrial Automation

Flow sensors for air conditioning (HSG-IMIT)
50,000 units in 2005

Industrial dispenser

Chem Process Engineering/ Power systems
Market for Microfluidics

Life Sciences!!!!

- Capillary Electrophoresis
- Lab on chip
- Drug delivery
- Clinical analysis

![Diagram of microfluidic device with DNA molecule and labels for start reservoir, blood sample, transport zone, read-out windows, plastic housing, separation fleece, reaction fleece, detection zone for marker A, B & C, and actuation fleece.](image-url)
Flow Sensors

Working principle

- Thermal principles
- Heaters & temperature sensors
  - Anemometer
  - Calorimeter
  - Time of flight

Specifications

- Range: 15 \( \mu \text{m/s} \) – 1500 \( \mu \text{m/s} \)
- Power: < 15 \( \text{mW} \)
- Response time: < 1 \( \text{ms} \)
- Application specific configuration possible by adaption of flow channels
Lab-on-a-Chip: *Emulsion-Disk*

- Controlled droplet generation on rotating disk
- Water-plug is focused by two oil flows $\Phi_0$
- Production of water-droplets in oil (W/O emulsion)
  - Volume: 5…22 nL
  - Rate: 0…300 drops / s
- High Reproducibility
  - Droplet diameter: $CV < 2\%$
DNA Microarray Printing

Microarray

Fluorescent signal of one spot

Spots, aligned in an array
PipeJet Principle

• **Dispensing by direct volume deflection**
  - Polymer tube
  - Piezo-actuated piston
  - Fast displacement for jet ejection
  - Short plateau
  - Slow release for capillary refill

• **Unique strength of concept**
  - Contact-free delivery of fluid
  - Simplest possible fluidic geometry
  - Easiest packaging (mechanical clamping)
nL & pL Dosage: NanoJet

- Dosage volume: 5 nL to 1.000 nL
- Dosage rate: 1.000 nL/s
- Viscosity range: 1 – 100 mPas
- Precision: better 5 %
A New Class of Process Technology

- Typical Microchannel widths
- Micro Pumps and Valves
- Micromotor Rotors
- Microchannel Reactors and heat exchangers
- MicroThermal and Chemical Systems

- Single Transistor on IC
- IC Chip
- Personal Computer

- 1 Å
- 1 nm
- 1 μm
- 1 mm
- 1 m
- 1 km

- Smog
- Gas Molecules
- Tobacco smoke
- Atmospheric dust
- Bacteria
- Viruses
- Radius of Most Cells
- Human Hair
- Beach Sand
- Man

- Conventional Pumps and Valves
- Conventional Reactors and Heat Exchangers
- Conventional Thermal and Chemical Plant
Features of a Continuous Microreactor System

1. Precise control of temperature – easily set and changed – no temperature gradients
2. Precise control of time - easily set and changed – quick hot reactions for consistent particle size
3. Precise control of feeds/stoichiometry – rapidly investigate stoichiometry by changing feed rates
4. Consistent and rapid mixing – ensures nucleation not precipitation
5. No scale limitations – small scale for optimisation; or “leave tap running” to make kilograms per day (100 g/h readily achievable)
6. Reproducible – same temperature, same mixing, same reaction time, every time
7. Immediate aqueous work up – simple work up available if required

Tice, J.D. et al. Langmuir 2003 19, 9127-8133
Micro Chemical Equipments and Systems

- Microreactors
- Micro-channels
- Micro heat exchangers,
- Micromixers
- Separation Units and
- Micro analytical devices

Miniaturation:
- High capacity
- Light systems
- Mass manufacture
- Costly but versatile

MEMS, Mesoscopic Machine Micro/Nano Systems Microcats
Micro-Reactors

• New reactor types which offer high capacity and high productivity

• Microreactors are more versatile and less dependent on chemical-engineering operators
  ▪ Provide useful amount of products
  ▪ Are easy to use
### Micro-structured Multichannel Reactors

**Volume:** $V_R = 5 \text{ cm}^3$

**Pressure drop:** $\Delta p = 1 \text{ bar}$

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length</td>
<td>$L =$</td>
<td>5.</td>
</tr>
<tr>
<td>Diameter</td>
<td>$d =$</td>
<td>100.</td>
</tr>
<tr>
<td>Number of channels</td>
<td>$N =$</td>
<td>12,740</td>
</tr>
<tr>
<td>Specific surface</td>
<td>$a =$</td>
<td>40,000.</td>
</tr>
<tr>
<td>Flow velocity</td>
<td>$u =$</td>
<td>0.63</td>
</tr>
<tr>
<td></td>
<td></td>
<td>35.</td>
</tr>
<tr>
<td>Mass flow</td>
<td>$Q_m =$</td>
<td>225.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>15.</td>
</tr>
</tbody>
</table>
Injection of Multiple Microjets

1. The central element of the mixer is a sievelike structure with a large number of regular holes.
2. During operations, the mixing area is filled with one liquid, and the other liquid is injected into the mixing volume through a multitude of microholes.
3. Numerous microjets are generated and increase the contact surface between the two liquids.
4. The holes are positioned in rows 10-100 μm apart, which results in short diffusional paths between the jets.
5. Typical flowrates are in the μL/s, the hole diameter is 10 μm, and the height of the mixing chamber some 100 μm

Source: Quak Foo Lee
Multiple Flow Splitting and Recombination

1. Application: industrial chemical sensor
2. Flow range: 0.01 – 0.1 μL/s
3. Highly viscous flow with a Re < 1
4. The whole system consists of a silicon/glass sandwich connected by anodic bonding.
5. One channel structure is etched into glass and the other into silicon.
6. In the region where the channels overlap, they are separated by a structured plate defined by an etchstop layer.
7. Max. width = 300 μm
   max. depth = 30 μm
8. The thickness of the structured plate for separating the channels in the glass and the silicon wafer is 5 μm and the slit width 15 μm.

Source: Quak Foo Lee
**Micromixers**

### Multilamination of Fluid Layers

1. The fluid to be mixed are introduced into the mixing elements in counter-flow and stream into an interdigitated channels with corrugated walls.
2. Typical channel widths = 25 or 40 μm
3. The channel configuration leads to a periodical arrangement of flow lamellae of the two fluids.
4. The lamellar flow leaves the device perpendicular to the direction of the feed flows and, because of the thinness of the lamellae, fast mixing takes place by diffusion.
5. The corrugated channel walls increase the contact surface of the lamellar streams and improve the mechanical stability of the separating walls.

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Scanning electron micrographs of a mixing element based on multilamination of thin fluid layers. The device consists of 2 × 15 interdigitated microchannels with corrugated walls, fabricated by LIGA technology.

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Multilamination of streams in channels with corrugated walls, leading to fast mixing by diffusion.

Source: Quak Foo Lee
Gasoline Vaporizer

- 50 $kW_e$ capacity: Four cells each of microchannel reactors and heat exchangers
- Volume: 0.3 L
- Processes/combusts 1400 SLPM

1999 - R&D Award Winner
Cross-Flow Heat Exchange in Stacked Plate Devices

Channel diameter: ~50 – 500 μm
Channel length: 20 – 100 mm
No of channel: 200 – 1000
Specific surface: $10^4$–$10^5$ m$^2$/m$^3$

Micro heat exchanger with connections for fluid supply
(source: Forschungszentrum Karlsruhe)
Advantage: Rapid Heat and Mass Transport Microchannel Heat Exchangers

- Heat fluxes: 100+ watts/cm$^2$
- Low pressure drops: 1-2 psia
- High convective heat transfer coefficients
  - Liquid phase: 10,000 - 15,000 W·m$^{-2}$·K$^{-1}$
  - Evaporating phase: 30,000 - 35,000 W·m$^{-2}$·K$^{-1}$
Microseparators

Exchange between Immiscible Fluids

Schematic of solute exchange between immiscible fluids in partially overlapping microchannels (left) and scanning electron micrograph of the cross section of the partially overlapping microchannels (right)

Exchange between Immiscible Fluids

Scanning electron micrograph (left) and schematic (right) of an extraction unit with adjacent channels for two fluids with slits, oblique to the flow direction, for exchange between the two phases
Filtration, Diffusion, and Aerodynamic Separation

Scanning electron micrograph of a cross-flow filter consisting of lamellae arranged at an angle of attack to the flow direction

- In the macroscopic range, filtration and sieve structures are often carefully designed with regard to the shape and position of the openings.
- In the microscopic range usually porous materials with irregular pattern are applied.
- Microfabrication methods allow the production of completely isoporous microfilters (pore dimensions in the micrometer range) from a wide variety of materials, whereby the size, shape, and position of each pore can be designed.
- Special configurations for cross-flow filters for concentrating suspended particles/cells.
- In the case of membrane units, microfabricated devices are useful as carrier structures with integrated inlets and outlets for fluids.
Miniaturization of Analytical Systems

Traditional System

NeSSI system

UOP LLC
Mechanism Tools

- **Reactors Testing**: LAMIMS, MRX Atm., TSR, TEOM
- **Pulsed MRX**
- **Process Model**: Number of Intermediates lifetime
- **Characterization**: ZLC, Heat of Ads. Capacity, Calorimetry, Isotopic Labeling, SSITKA
- **UOP LLC**
CPM – H₂ Production
Paal Knorr Synthesis via Microreactors

FutureChemistry’s FlowSyn on Micronit Microfluidics microreactors
Miniaturization of Chemical Reaction: Synthesis of Carbamates

Experimental setup for carbamate synthesis.

- μR₁, micro-reactor for conversion of acyl chloride to organic azide;
- μS₁, quantitative separation of organic and aqueous streams;
- μR₂, microreactor loaded with solid acid catalyst for conversion of organic azide to isocyanate;
- μS₂, quantitative separation of gaseous N₂ from the liquid;
- μR₃, microreactor for reaction of isocyanate and alcohol to carbamate.

Acyl chloride + NaN₃ → Organic azide → Heat → Acyl isocyanate → R'OH → Carbamate

Sintesi di carbammati via azidi
Corning Glass Microreactors

Mixing
300 micron

Pressure drop
1 millimeter

Heat exchange layer

Heat transfer

700 microns

Reactants
Fluidic Modules: Concept and Library
Engineered Reactor Components

- Interfaces
- Frames
- Standard Fittings
- Connectors
- Tubing
- Sensors
- Fluidic Modules
- O-ring seals
- Labelling (insulation…)
- Add-on (Pressure relief valve…)
- Instrumentation
Phloroglucinol-Type Kolbe Schmitt - Synthesis in Microreactors

\[
\begin{align*}
\text{HO} & \quad \text{OH} \\
\text{OH} & \quad \text{OH} \\
\text{HO} & \quad \text{OH} \\
\text{KHCO}_3 (\text{aq}) & \quad \xrightarrow{\Delta, t} \quad \text{COOH}
\end{align*}
\]

\[
\begin{array}{c}
\text{HO} \\
\text{OH} \\
\text{COOH} \\
\text{HO} \\
\text{OH}
\end{array}
\]

Yield (%) vs. Temperature (°C)
Kolbe Schmitt-Synthesis: High P,T-Processing

V. Hessel, C. Hofmann, P. Löb, J. Löhndorf, H. Löwe, A. Ziogas

High p,T

- Pressure: 40-70 bar
- Temperature: 100-220°C
- Reaction time: 4 – 390 s

- Reduction of reaction time by ~2000
- Increase in space-time yield by factor 440
- Increase in productivity by factor 4
Modelling Study on Styrene Solution Polymerization

Thermal phenomenon
convection/conduction

Kinetics constant depend on temperature

Heat released by polymerization

Reaction, convection and diffusion of chemicals

Convection

Viscosity affected by Reaction temperature

Hydrodynamics
Navier-Stokes equations

Viscosity affected by Reaction yield

Microstructured Epoxidation Reactor

Model Synthesis:

\[
\text{H}_3\text{C} = \text{CH} = \text{CH}_2 + \text{H}_2\text{O}_2(\text{vap}) / -\text{H}_2\text{O} \rightarrow \text{H}_3\text{C} - \text{HC} -- \text{CH}_2
\]

Features:

- Modular (unit operations, capacity)
- Multi-purpose (catalyst and reaction)
- Reaction under pressure
- Reactions in the explosive regime

Degussa
Radical Polymerization Reactor

Plant running at industrial site of Idemitsu Kosan

Dr. Takeshi Iwasaki (MCPT)
Proceedings IMRET 8, Atlanta, April 2005.
Where to Apply Microchemical Technology?

- Direct routes from hazardous systems
- Routes at increased concentration or even solvent-free
- Routes at elevated temperature and/or pressure
- Routes mixing the reactants ‘all at once’
- Routes using unstable intermediates
- Routes in the explosive or thermal runaway regime
- Routes omitting the need of catalysts and auxiliary agents

DEVELOPMENT OF REACTORS TO ENABLE CHEMISTRY RATHER THAN SUBDUEING CHEMISTRY AROUND THE REACTOR

Scientific and Technological Drivers in Surface-Nano Applications

FROM SURFACE TO NANO

TECHNOLOGICAL DRIVERS

- transistors/electronics
- aerospace
- catalysis
- tribology (friction/adhesion)
- surfactants
- optoelectronics
- photochemistry
- environment
- polymers
- sensors/actuators
- embrittlement
- membranes
- nanomechanics
- quantum dots/nanowires
- biocompatibility
- spintronics
- molecular electronics
- environmental sciences
- biochemistry
- biology
- medicine
- informatics
- electrical engineering
- chemical engineering
- mechanical engineering
- applied physics
- material science
- chemistry
- physics
- bionano
- nanostructures
- superlattices
- coatings
- thin films
- clusters
- interfaces
- surfaces

SCIENTIFIC DISCIPLINES

- physics
- chemistry
- material science
- applied physics
- environmental sciences
- biochemistry
- biology
- medicine
- informatics
- electrical engineering
- chemical engineering
- mechanical engineering
- applied physics
- material science
- chemistry
- physics
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4. Nam-Trung Nguyen, Micromixers, 2008, 293


12. Li-Hua Du, Xi-Ping Luo, Lipase-catalyzed regioselective acylation of sugar in microreactors, RSC Advances, 2012, 2, 7, 2663