Microreactors

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Intro and objectives

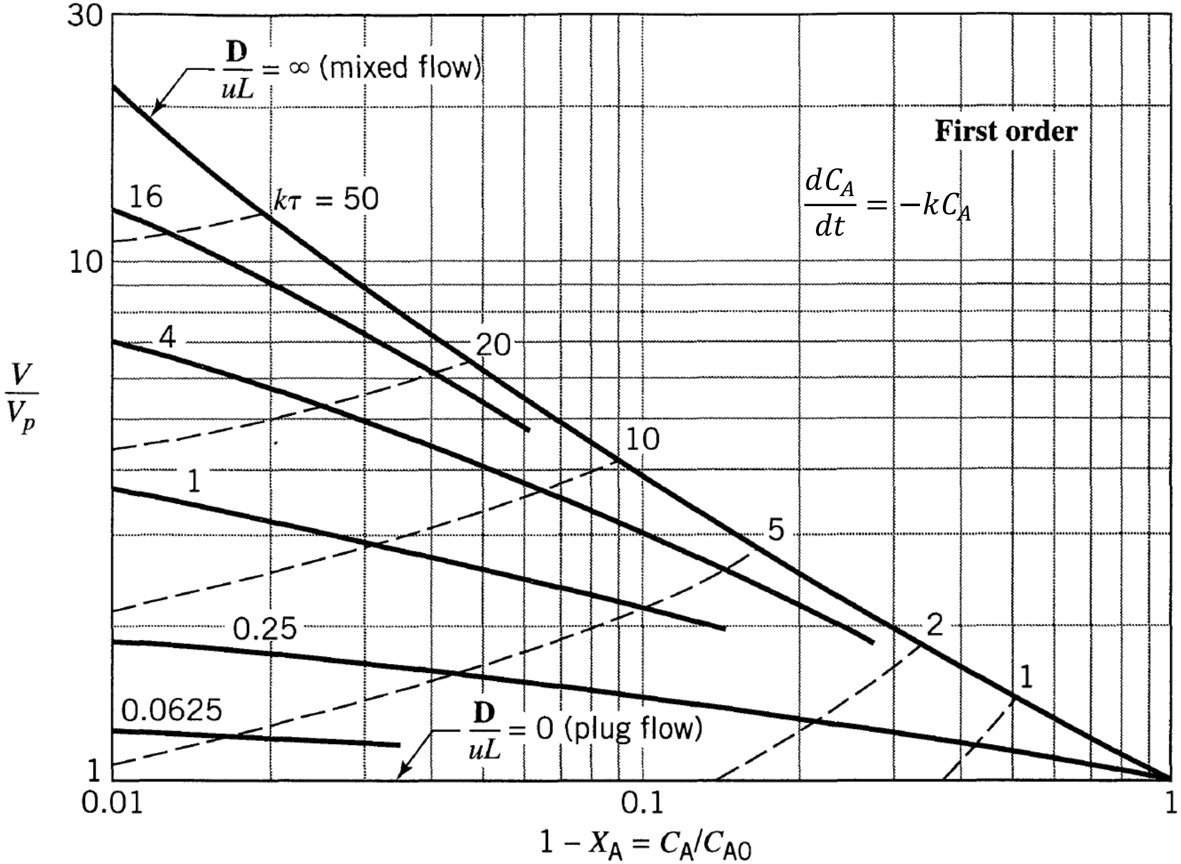
- Bio(reactors):
  - Production of/by ‘particles’
  - Handling and separation of particles
  - Operate at high concentrations
- Low Re numbers advantageous?
- Throughput?
- Particle handling: small versus large particles
- Plug flow?
- Dispersion?

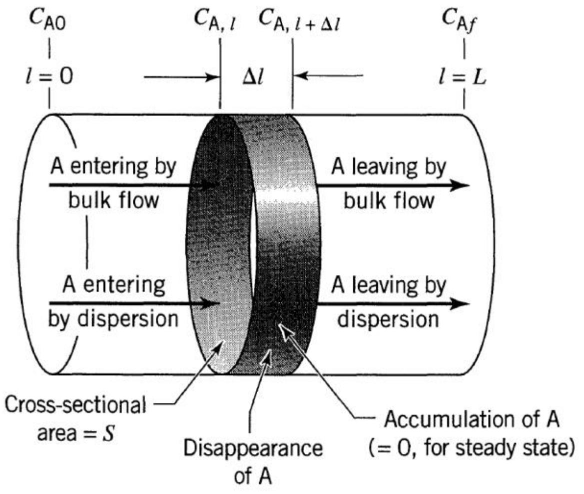
Outline

- Intro
  - Background
  - Fabrication
- Applications
  - Contactor: L-L-extraction
  - Heavy duty liquids crystallization
- Droplet/particle manipulation

Dispersion + reaction→ higher V, t

- V: Bo=uL/D



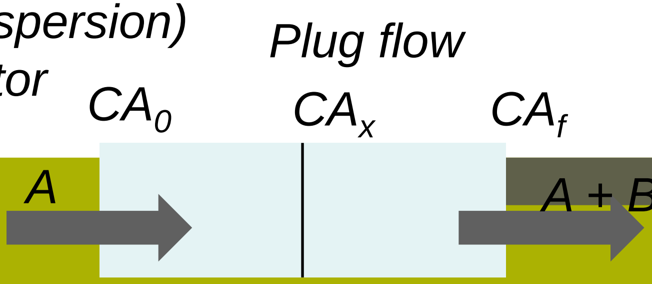


$$A \rightarrow \text{products}, \qquad -r_A = kC_A^n$$

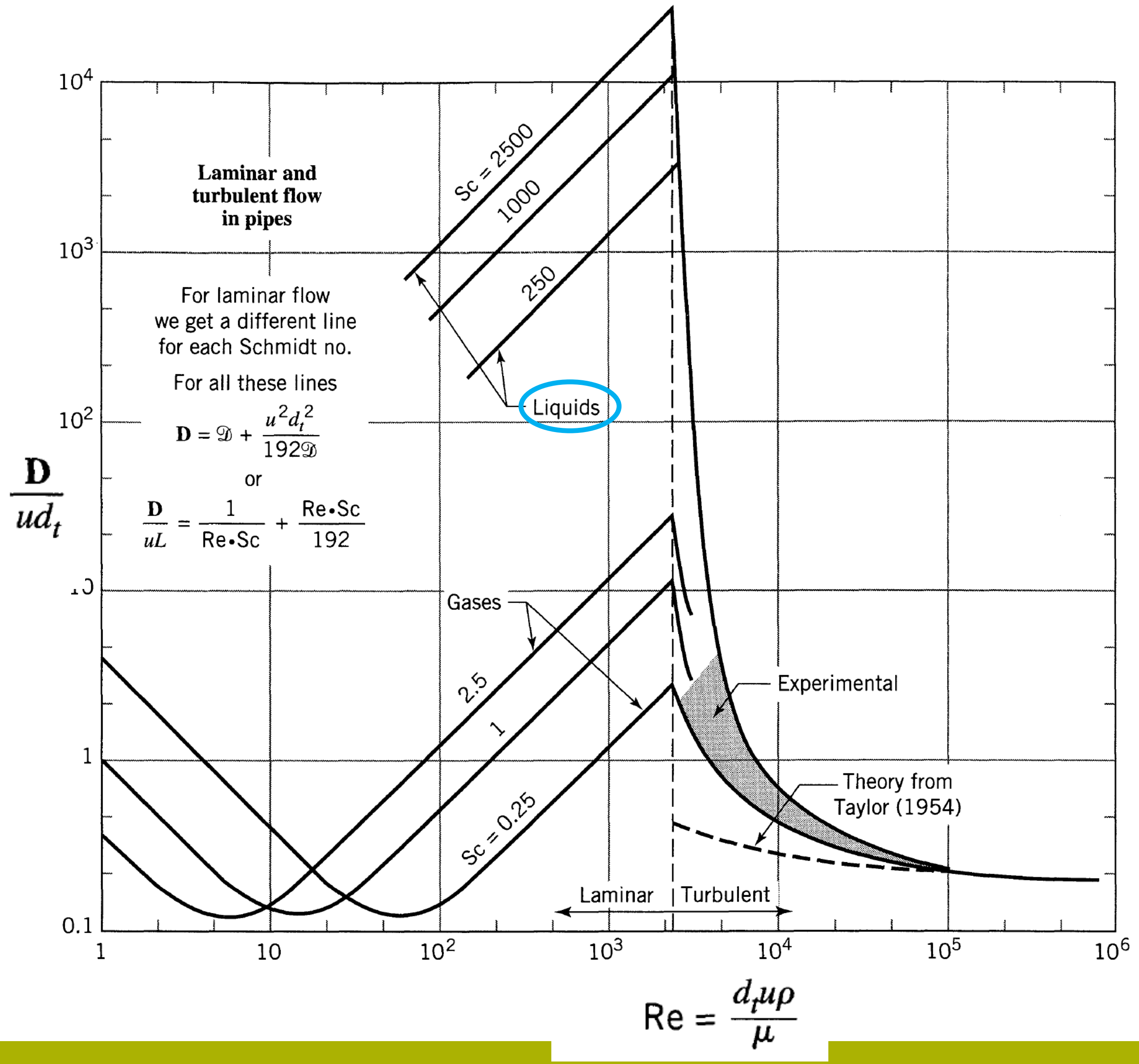
V: volume reactor (with dispersion)

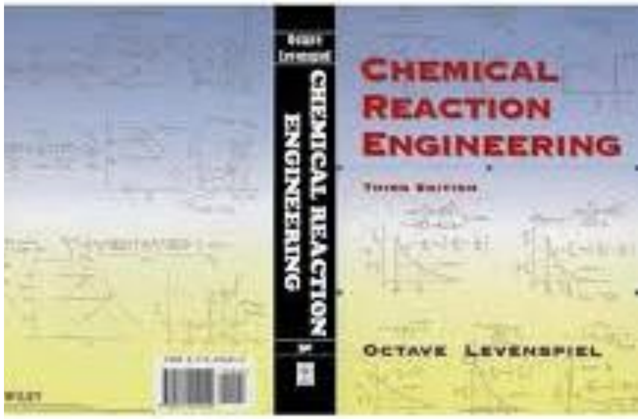
V_p: volume plug flow reactor

Chemical Reactor Engineering, Levenspiel, 1972, Wiley



Laminar flow – turbulence in reactors





Chemical Reactor Engineering, Levenspiel, 1972, Wiley

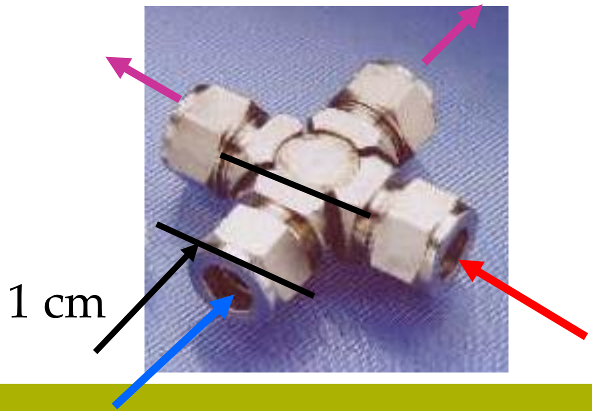
Fundamental advantages

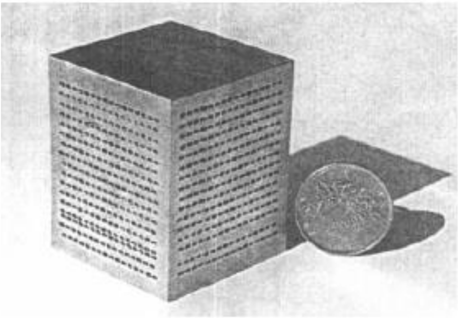
- **Nano-scale** reactors : supra-molecular assemblies
  - Unique molecular forces due to confinement
  - Specific catalysts, zeolites, micelles

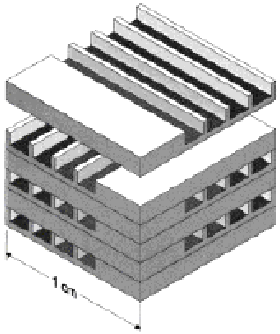
- **Micro-scale** reactions
  - Increase of gradients (T, Conc., density, pressure)
  - Mixing times: can be ms-ns
  - Short residence times
  - Plug-flow: narrow residence time distribution
  - High P-T processing: operation at liquid pressures above boiling point
  - High troughput screening of reaction kinetics
  - Safety
  - Scaling out

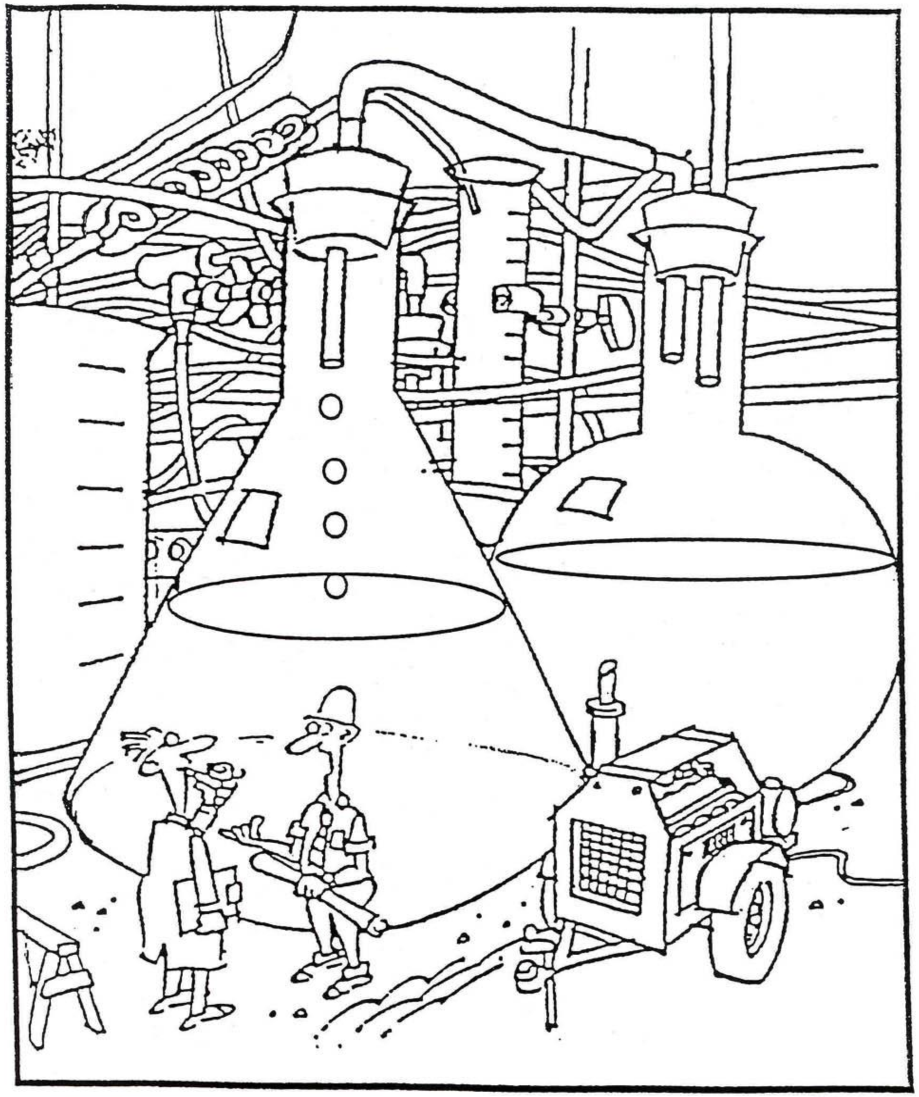
Heat aspect: Important asset of µreactors

- More efficient and faster (**endothermic reactions**)
- No hot spots
- Controlled **exothermic reactions**: safety!
  - *Solvent free* processes: higher efficiency
  - Routes *in explosive regime* (actual shift: quenching of radicals by collisions with surface due to high S/V)
  - Only *small quantities* of toxic or explosives required (<-> batch reactors)







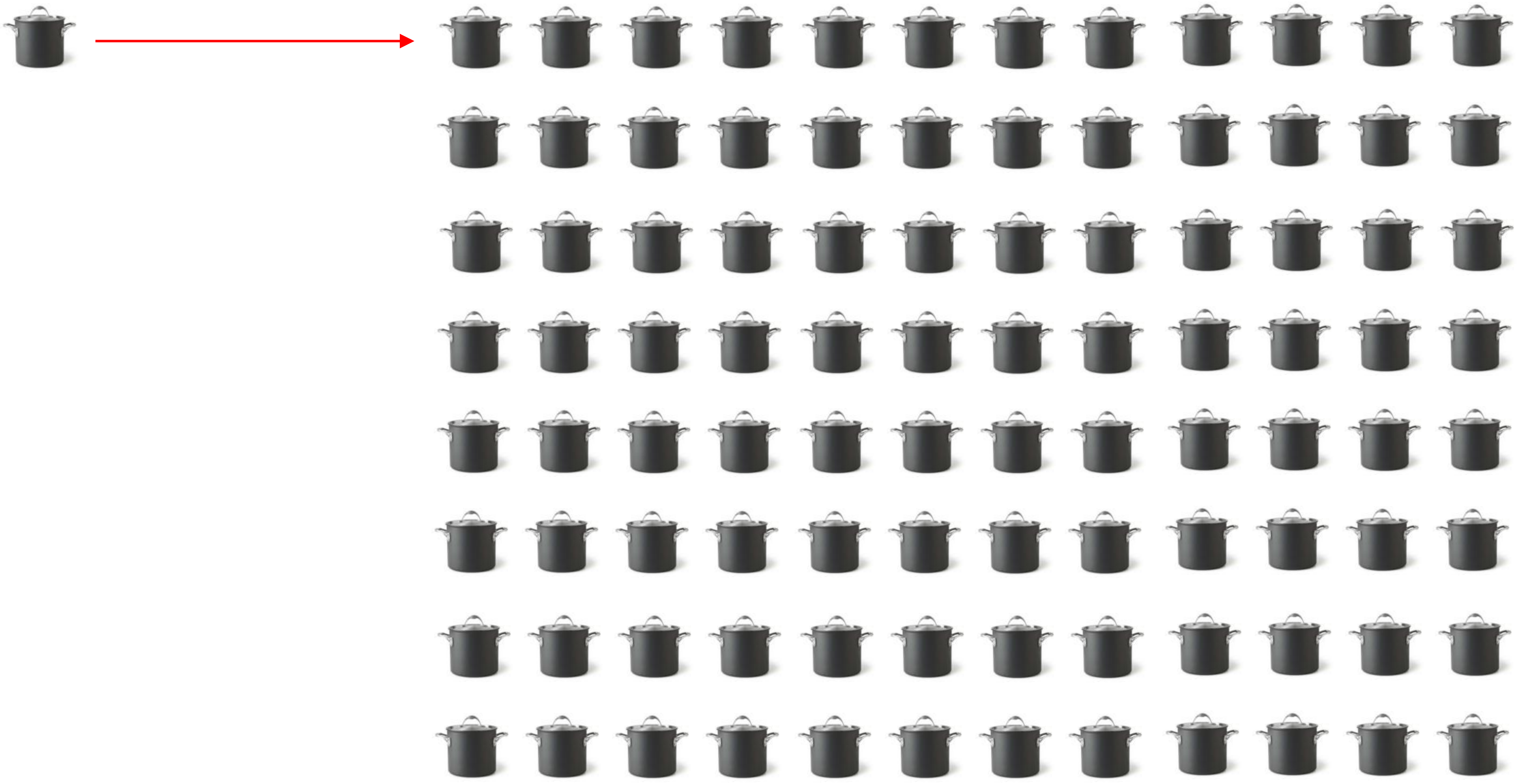


“It worked fine in the lab !"

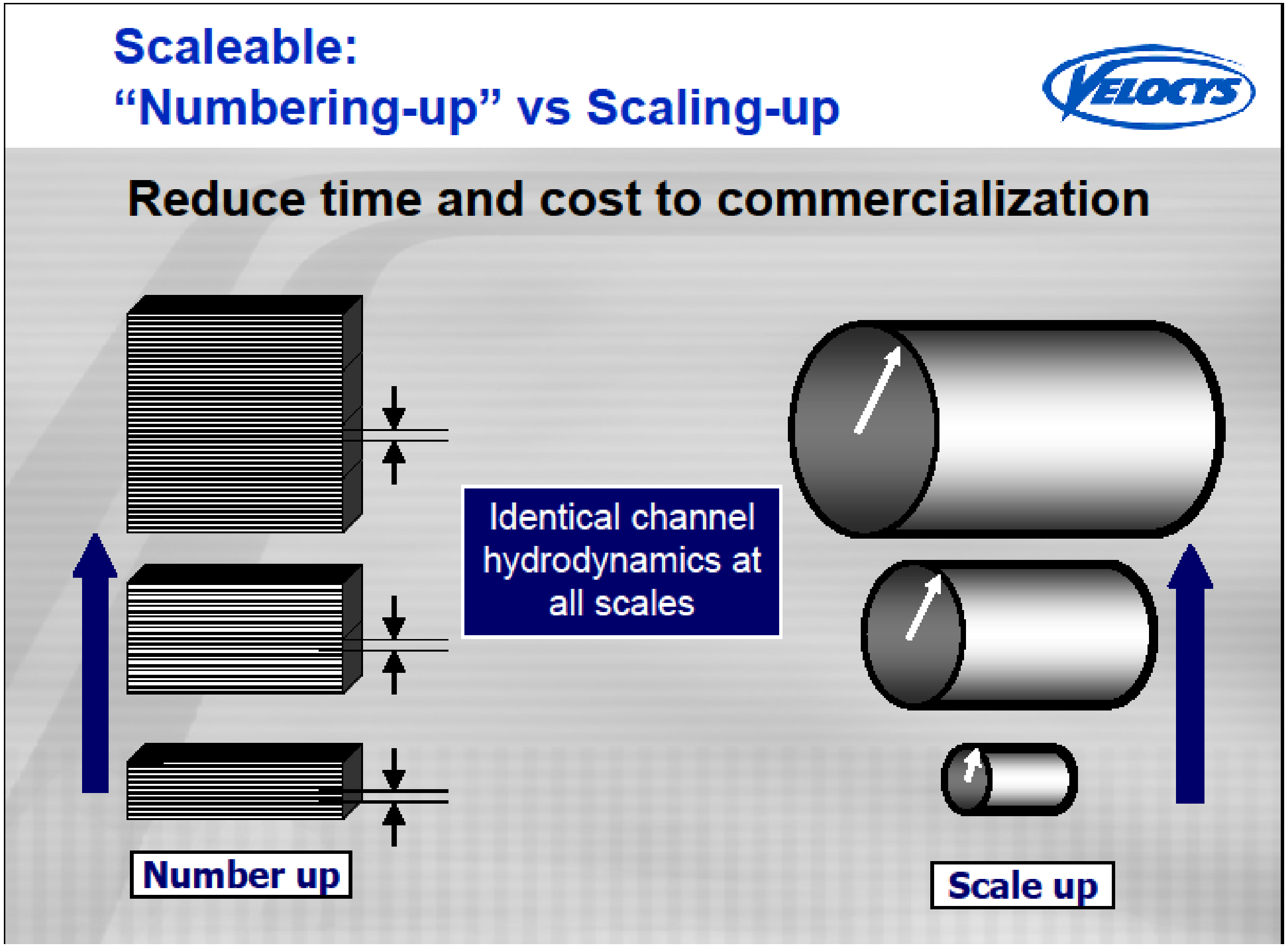
Upscaling is not always straightforward

Reactor upscaling

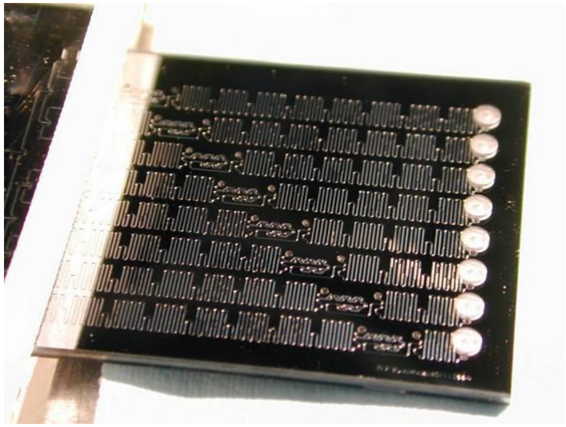
Reactor replication ("numbering up")



Numbering up vs. scaling-up

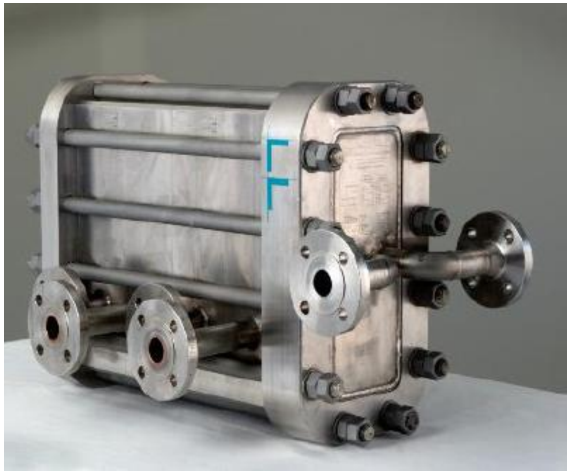


Micro-reactor scales



1 mg/hr

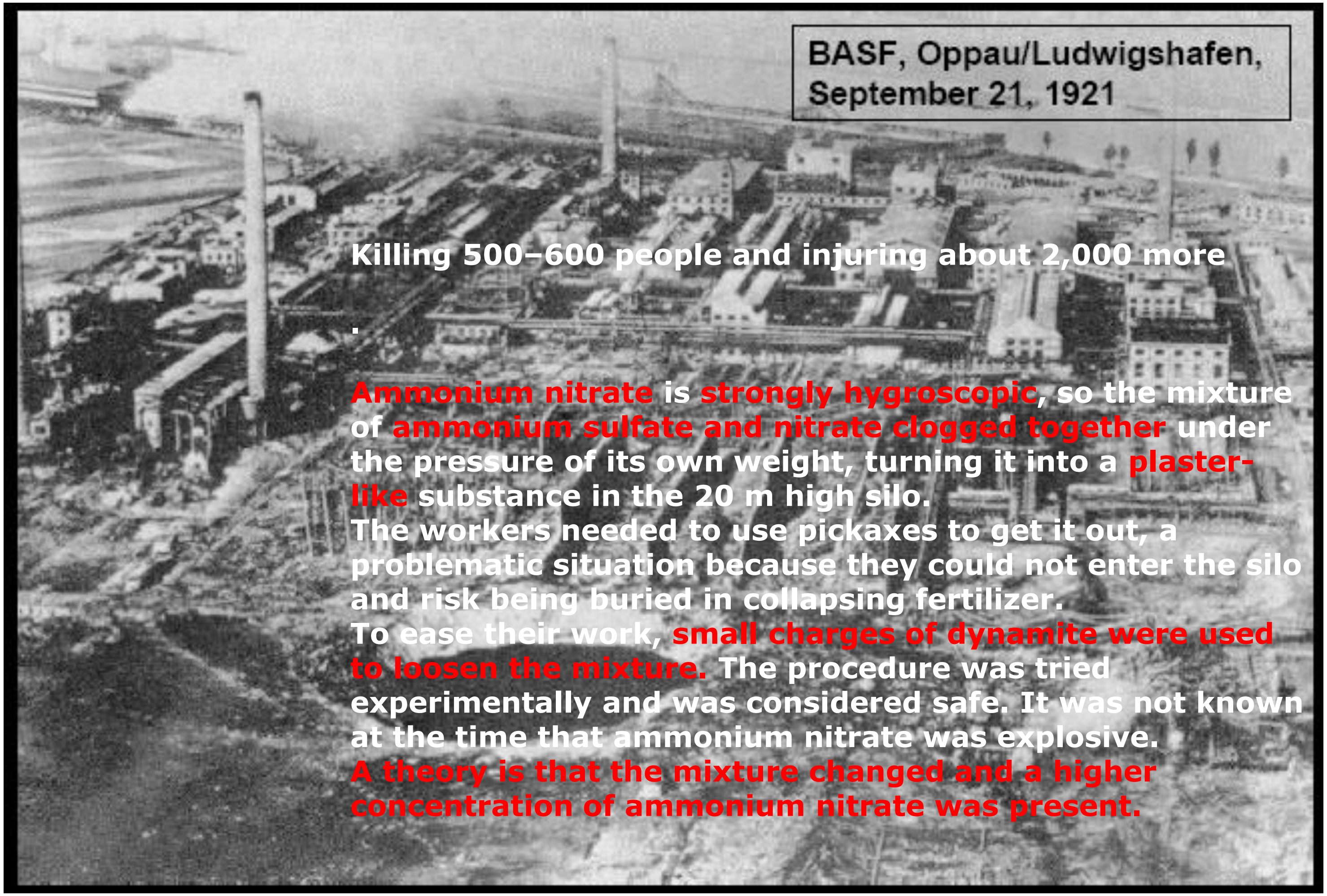
1 kg/hr



1700 kg/hr

Safety

Ammonium nitrate - 1921



Killing 500–600 people and injuring about 2,000 more

.

Ammonium nitrate is **strongly hygroscopic**, so the mixture of **ammonium sulfate and nitrate clogged together** under the pressure of its own weight, turning it into a **plaster-like** substance in the 20 m high silo.
The workers needed to use pickaxes to get it out, a problematic situation because they could not enter the silo and risk being buried in collapsing fertilizer.
To ease their work, **small charges of dynamite were used to loosen the mixture.** The procedure was tried experimentally and was considered safe. It was not known at the time that ammonium nitrate was explosive.
A theory is that the mixture changed and a higher concentration of ammonium nitrate was present.

Ammonium nitrate - 2001

Ammonium nitrate decomposes in temperatures above 210 °C. **Pure AN is stable and will stop decomposing once the heat source is removed**, but **when catalysts are present** (combustible materials, acids, metal ions, chlorides. ..) **the reaction can become self-sustaining** (known as self-sustaining decomposition, SSD).

The exact cause of this disaster remains unknown.

AZF, Toulouse, September 21, 2001

Minifactories: “smaller=safer"

<u>An expensive lesson</u>:

Accident at Bhopal, 1984

To produce the pesticide Sevin

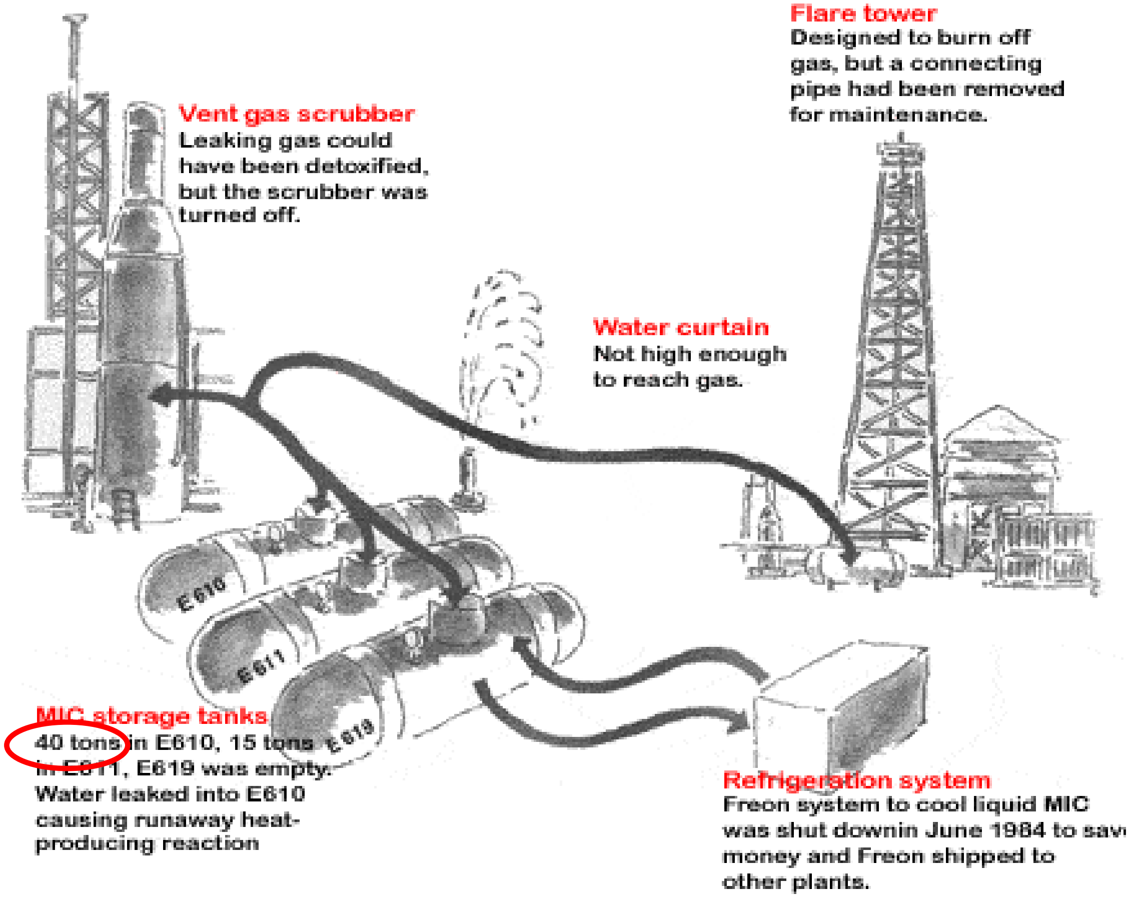
>50,000 injured (>2000 casualties, long-term 10,000) run-away reaction and escaped toxic gas

<u>Proces-intensified</u> continuous reactors could have processed MIC* directly with less than 10 kg MIC present

*methyl isocyanate

D.C. Hendershot, Chem. Eng. Progr, Jan. 2000, p. 35

Sevin (carbaryl)



Water entered a tank containing 42 tons of MIC.
The resulting exothermic reaction increased the temperature inside the tank to over 200 °C (392 °F) and raised the pressure. The tank vented releasing toxic gases into the atmosphere

Amm. nitr. accidents during transport

Port Neal, Iowa, 1994 [edit]

- At about 6:13am on December 13, 1994, two explosions rocked the Port Neal, Iowa ammonium nitrate processing plant operated by Terra Industries. Four people were killed and 18 injured. Approximately 5,700 tons of anhydrous ammonia were released and releases of ammonia continued for six days after the explosions. Groundwater under the processing plant was contaminated by chemicals released as a result of the blast. The timing of the explosion occurred prior to the start of the arrival of the 8:00am shift personnel, or the death toll may have been larger.[10][11]

Toulouse, France, 2001 [edit]

Main article: AZF_(factory)

- On September 21, 2001, at 10:15 AM, in the AZF_(factory) (Azote de France) fertiliser factory in Toulouse, France, an explosion occurred in a warehouse where the off-specification granular AN was stored flat, separated by partitions. About 200–300 tons is said to be involved in the explosion, resulting in 31 people dead and 2,442 injured, 34 of them seriously. The blast wave shattered windows up to 3 kilometres away and the resulting crater was 10 metres deep and 50 metres wide. The exact cause remains unknown. The material damage was estimated at 2.3 billion euros.

Cartagena, Murcia, Spain, 2003 [edit]

- The fertilizer storage facility of Fertiberia held a self sustained decomposition (SSD) fire in January 2003. The fire was controlled after most of the material was removed by mechanical means.

Barracas, Spain, 2004 [edit]

- A truck carrying 25 tonnes of ammonium nitrate fertilizer exploded half an hour after a traffic accident on March 9, 2004, killing two people and injuring three others. The explosion, which could be heard at a distance of 10 km (6.2 mi) caused a crater five metres deep.

Mihăileşti, Buzău, Romania, 2004 [edit]

Main article: Mihăileşti explosion

- A truck carrying 20 tones of ammonium nitrate tipped o… e started in the cabin. Two reporters got to the site of the accident and started filming while firemen were trying to stop the fire. Arou… 42 meters in diameter was formed by the explosion.

Distributed production !!!

Ryongchŏn, North Korea, 2004 [edit]

Main article: Ryongchon disaster

- A freight train carrying ammonium nitrate exploded in th… ng over 3000 others. The station was destroyed, as were most buildings within 500 metres, and nearly 8000 homes were destroyed or damaged. Two craters of about ten metres in depth were seen at the site of the explosion. The authorities blamed "human error" for the explosion, although rumours persist that it was in fact an attempt to assassinate the Korean leader Kim Jong-Il, who was due to be passing through the station at the time.

Estaca de Bares, Spain, 2007 [edit]

- The NPK fertilizer cargo of the ship Ostedijk sustained a self sustained decomposition (SSD) fire for 11 days. The fire plume reached 10 m in diameter and several hundred meters in length. Special water spears were inserted inside the cargo to extinguish the fire.

Monclova, Coahuila, Mexico, 2007 [edit]

- On September 10, 2007 near Monclova, Coahuila, México, a trailer loaded with 22 tons of ammonium nitrate crashed into a truck leaving three dead in the crash. A fire then started in the trailer's cabin and approximately 40 minutes after that, a huge explosion occurred, resulting in around 150 people injured and 37 more dead. A crater 30 ft (9.1 m) wide and 6 ft (1.8 m) deep was created due to the explosion.[12]

Bryan, TX, United States, 2009 [edit]

- A plant in Bryan, TX (El Dorado Chemical Company) which processes ammonium nitrate into fertilizer, caught fire at about 11:40 am on July 30, 2009. Over 80,000 residents in the Bryan/College Station area were asked to

Central or distributed ?

1965

2000

2000

2018 ?

"The natural course of every technology leads to fragmentation and smallness."

George Gilder, Harvard Business Review, April 1988

"We are blocking our roads with trucks..... Decentralization burdens the environment much less"

interview with Jos Put, CTO DSM, in C_2W, 15 Sept. 2007

Industrial µreactor, DSM Linz, 2005

65 cm, 290 kilo

1700 kg liquid/h
Removes a few 100 kW reaction heat

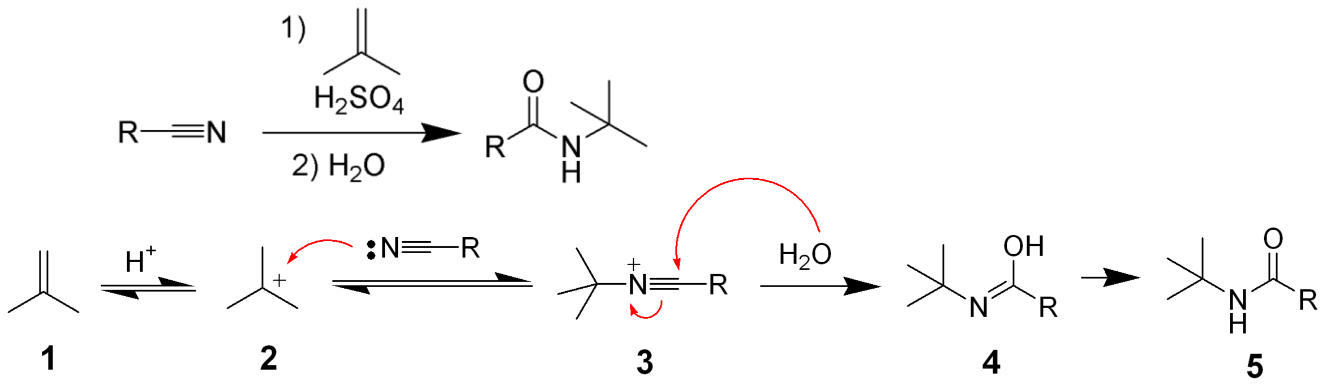
Contains mixers and a few thousand of microchannels

production: 300 ton in 10 weeks

Developed by Forschungszentrum Karlsruhe (FZK) and DSM

Specific aspects reaction

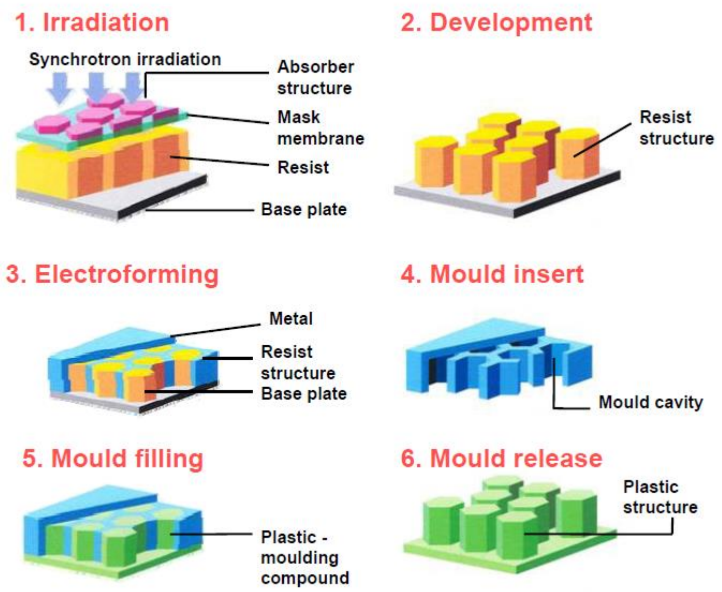
Goal was: synthesis organic intermediate via "Ritter" reaction:



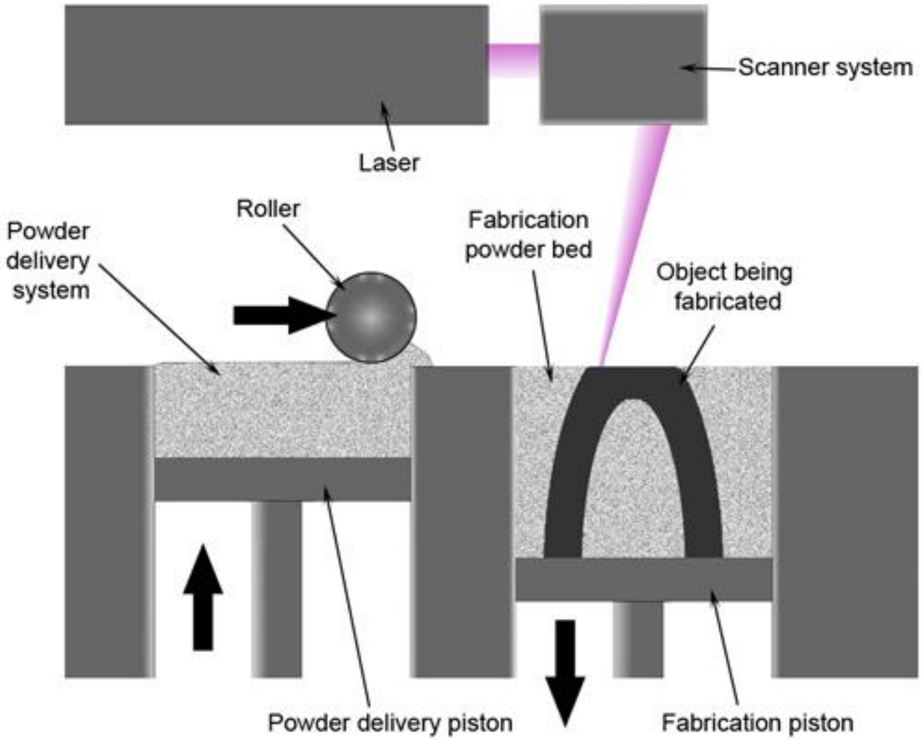
- Very fast reaction
- Highly exotherm
- Toxic products, concentrated sulfuric acid
- Large differences in and fast increase of viscosity

LIGA (Lithography, Galvanoformung, Abformung)

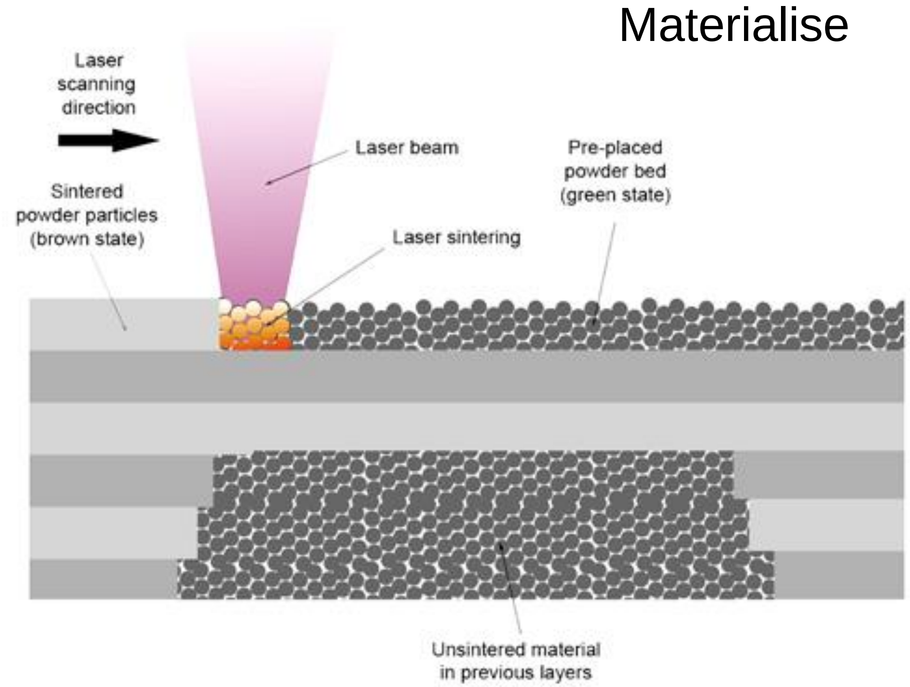
- Lithographic step (laser, electron- or ion beam, UV, X-ray: large AR's)
- Electroplating
- Mold insert or embossing: replication
  → mass production of plastics
- High precision, high surface quality, high AR's
- Based on broad material palette:
  - Metals:direct
  - Ceramics: cast
  - Polymers: cast



Laser melting deposition



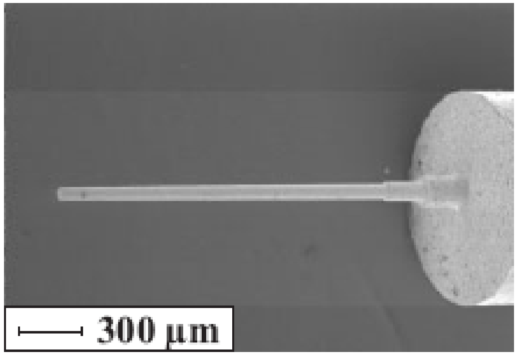
Materialise

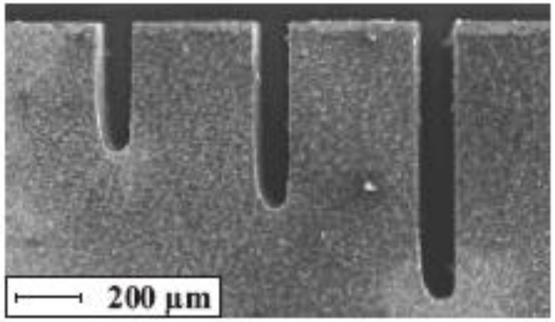


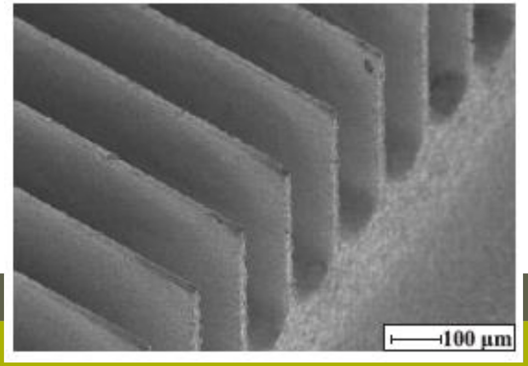
	SLM 250	SLM 125
Build volume	250mm x 250mm x 300mm (x,y,z) z extendable to 400mm	125mm x 125mm x 125mm (x,y,z)
Fiber laser power	200 – 400 W	100 – 200 W
Layer thickness	20 to 100µm	20 to 100µm
Standard laser spot size	50 microns diameter at powder surface	30 microns diameter at powder surface
Available materials	Stainless Steel 316L and 17-4PH, H13 Tool Steel, Aluminium Al-Si-12Mg and Al-Si-10Mg, Titanium CP, Ti-6Al-4V and Ti-6Al-7Nb, Cobalt-Chrome (ASTM75), Inconell 718 and 625	

Electro-discharge machining

- Especially appropriate for hard or chemically resistive materials
- Can be applied on all kinds of conductive materials
- Voltage generator, electrode
- Technology based on erosion process: discharge between electrode and workpiece
- Advantages
  - No mechanical contact: no contamination
  - 3D machining possible (vs. 2.5 D)







CONTACTING LIQUIDS

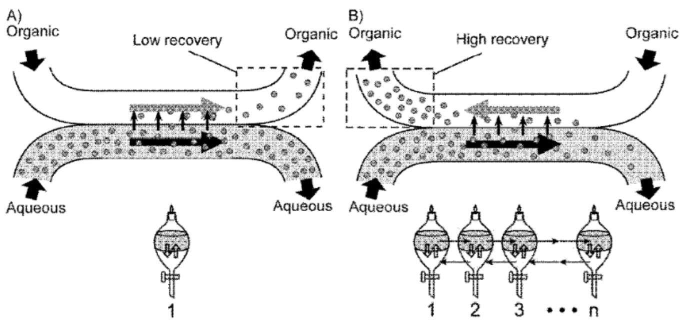
On-chip contactor/extractor

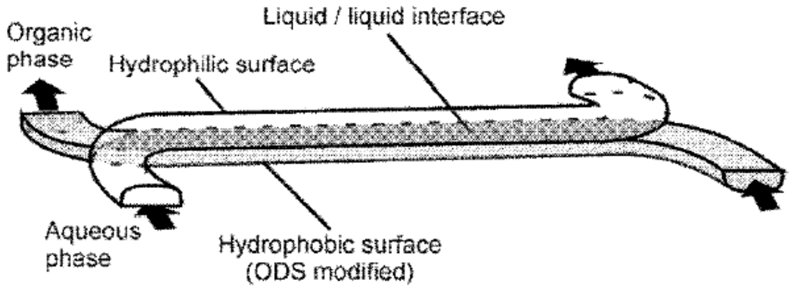
- Need for small scale extraction units
  - sample preparation
  - small scale production of pharmaceuticals
  - process development

- Increasing demand to combine extraction with reaction, heat transfer, (photo)catalysis, etc.

- Phase separation often slowest step: demand for alternative configurations

Interface stabilization

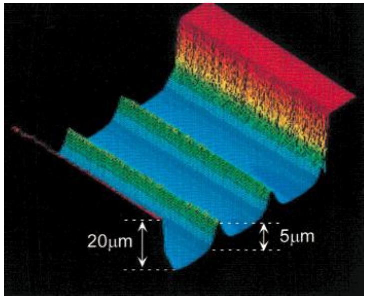


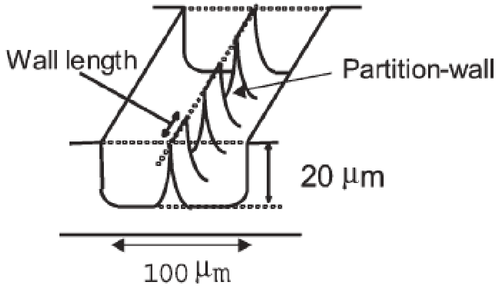


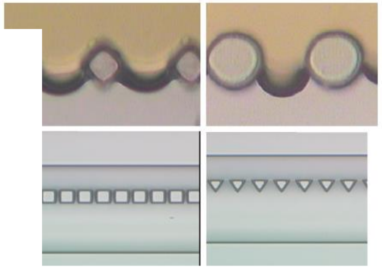
MICRO COUNTER-CURRENT FLOW SYSTEM FOR HIGHLY EFFICIENT EXTRACTION

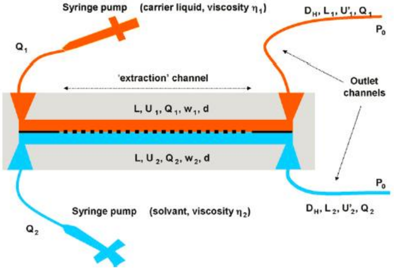
A. Aota[1], M. Nonaka[1], A. Hibara[1] and T. Kitamori[1, 2]
[1]*Department of Applied Chemistry, School of Engineering, The University of Tokyo*
[2]*Kanagawa Academy of Science and Technology (KAST)*

7th International Conference on Miniaturized Chemical and Biochemical Analysis Systems
October 5–9, 2003, Squaw Valley, California USA









Anal. Chem. **2002**, *74*, 1565−1571

Continuous-Flow Chemical Processing on a Microchip by Combining Microunit Operations and a Multiphase Flow Network

Manabu Tokeshi,† Tomoko Minagawa,‡ Kenji Uchiyama,† Akihide Hibara,‡ Kiichi Sato,‡ Hideaki Hisamoto,‡ and Takehiko Kitamori*,†,‡

Intermittent partition walls promote solvent extraction of metal ions in a microfluidic device

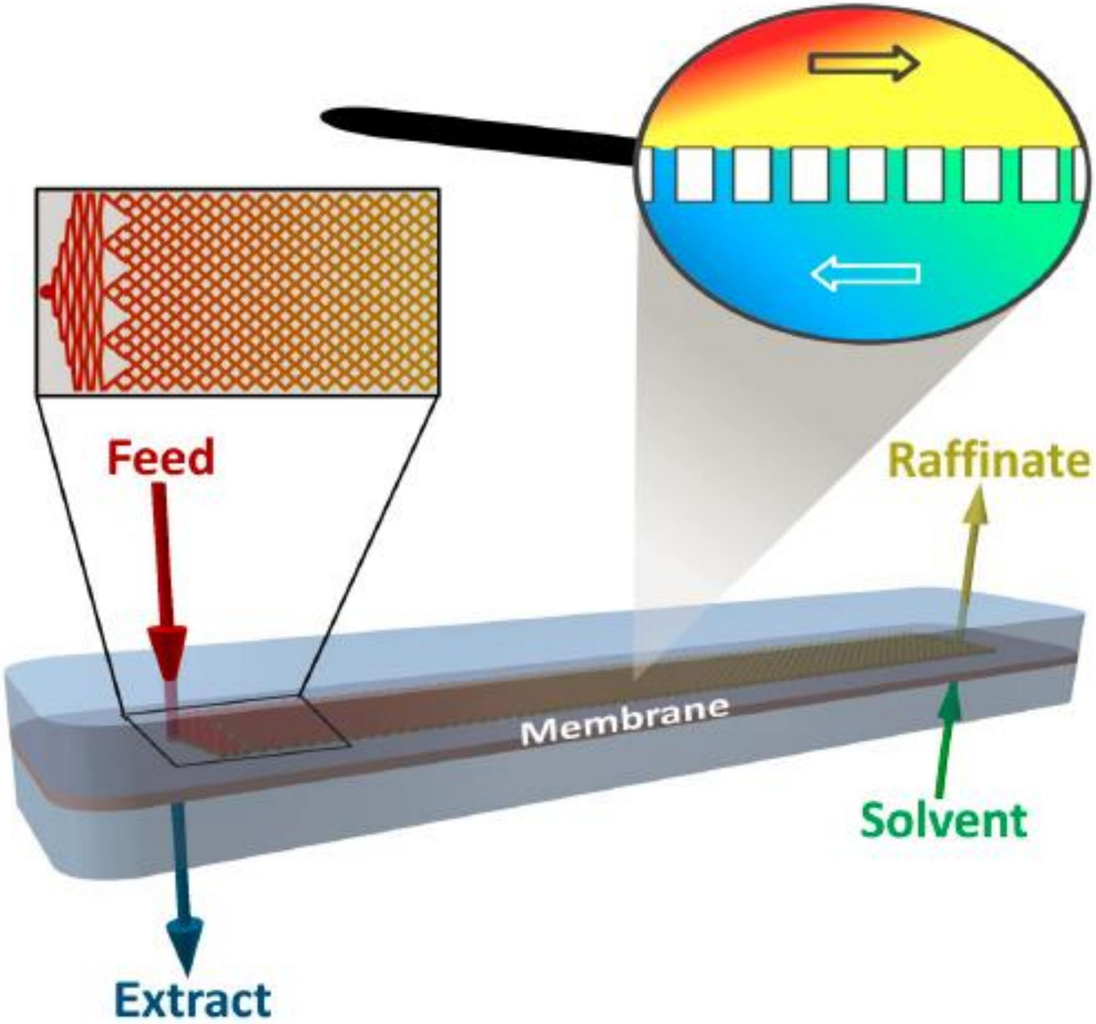
Tatsuo Maruyama,[a] Tomoaki Kaji,[a] Tomohiro Ohkawa,[b] Ken-ichiro Sotowa,[a] Hironari Matsushita,[a] Fukiko Kubota,[a] Noriho Kamiya,[a] Katsuki Kusakabe[a] and Masahiro Goto*[a]

The physics of a coflow micro-extractor: Interface stability and optimal extraction length

J. Berthier*, Van-Man Tran, F. Mittler, N. Sarrut

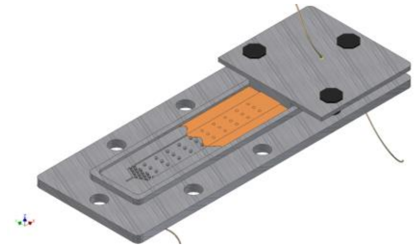
Sensors and Actuators A 149 (2009) 56–64

Membrane contactor



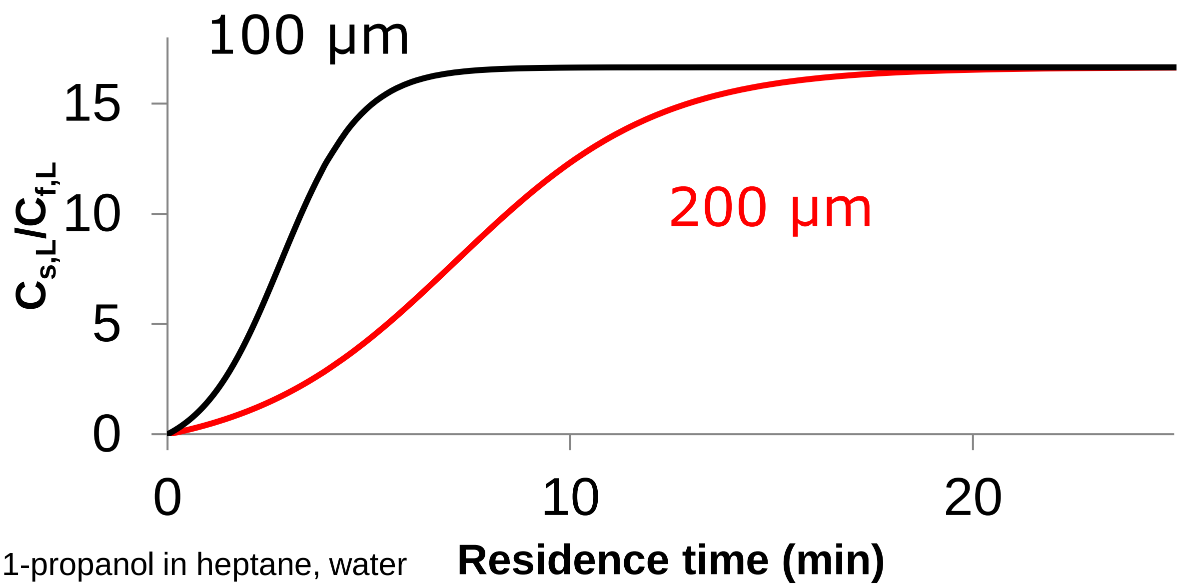
Membrane contactor (co-current)

- 1.3 cm wide channel
  - Flow distribution
  - Support structures
  - 100 µm deep channels
  - 70 µm thick membrane



$$\Delta P_{Laplace} = -\frac{2\gamma\beta\cos\theta}{r}$$

γ = Interfacial tension
β = Pore shape factor ($0 < \beta < 1$)
θ = Contact angle
(Membrane/Liquid 1/ Liquid 2)
r = pore radius

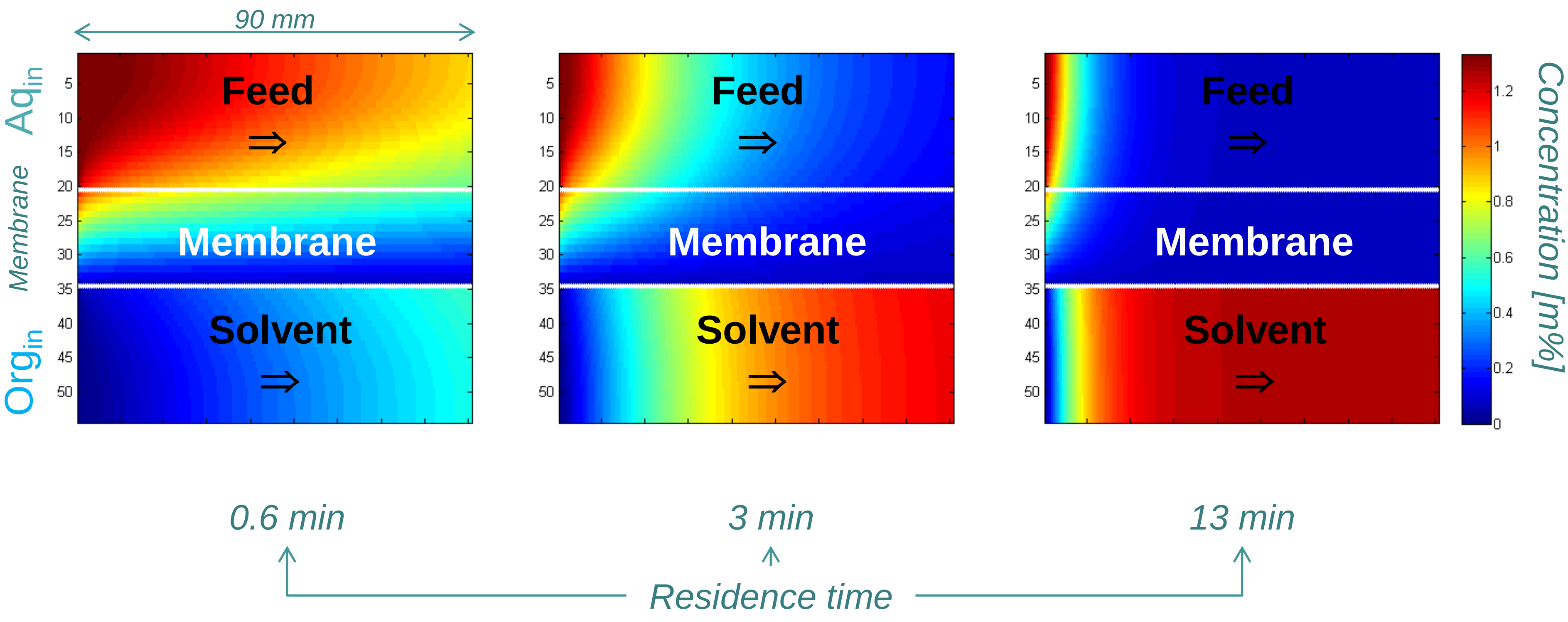


$$\frac{C_{S,L}}{C_{f,L}} = \frac{1 - e^{-\frac{KL}{u_f h_f}\left(1+\frac{\alpha_f}{\alpha_s}\right)}}{\frac{\alpha_s}{H\alpha_f} e^{-\frac{KL}{u_f h_f}\left(1+\frac{\alpha_f}{\alpha_s}\right)} + \frac{1}{H}}$$

$$\alpha_f = \frac{u_f h_f}{KL} \qquad \alpha_s = \frac{u_s h_s H}{KL}$$

J. Hereijgers, M. Callewaert, X. Lin, H. Verelst, T. Breugelmans, H. Ottevaere, G. Desmet, W. De Malsche, Journal of Membrane Science 436 (2013), 154-162.

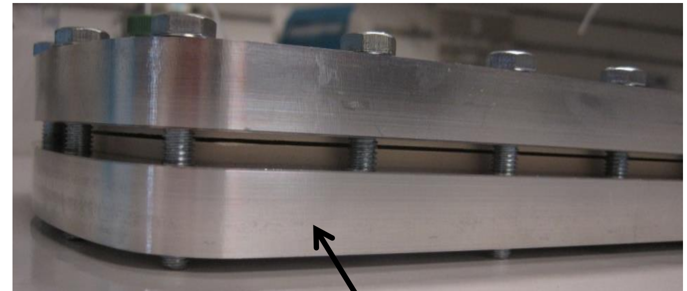
Kinetics



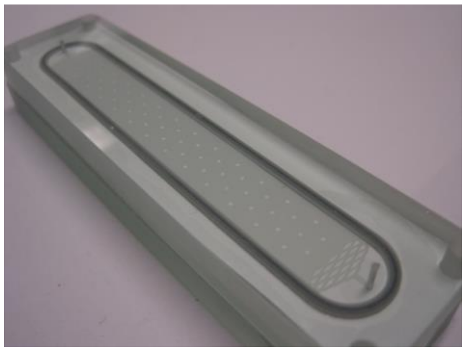
90 mm
Aq_{in}
Membrane
Org_{in}
Feed
Membrane
Solvent
Concentration [m%]
0.6 min
3 min
13 min
Residence time

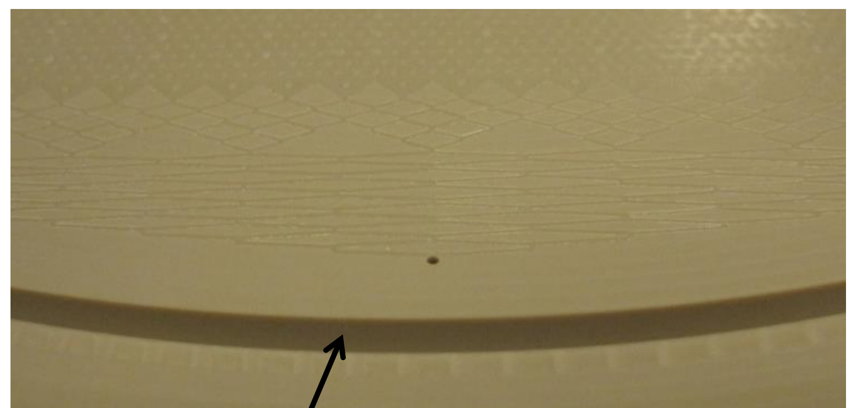
Contactor configuration

Glass, PMMA, PEEK, POM, Alu



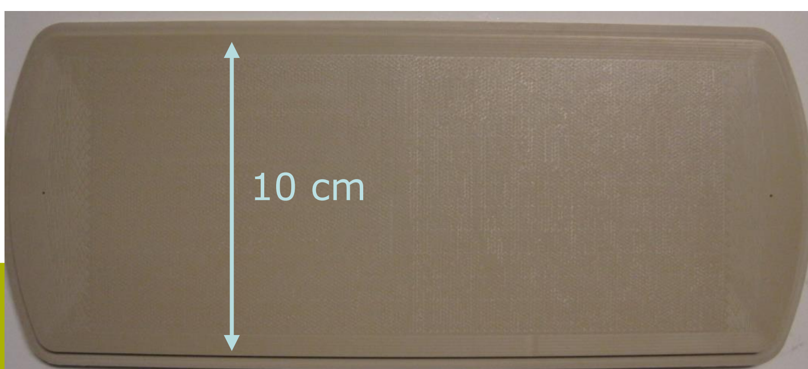
rigid casing for plastic substrates





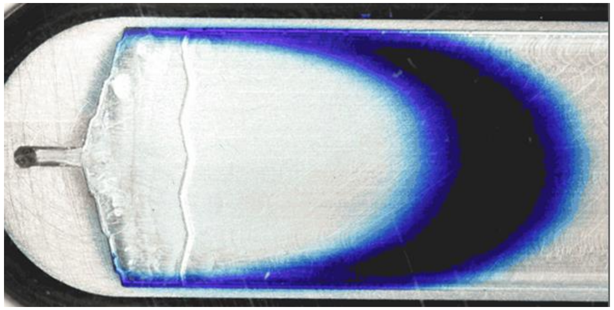
1 cm

sealing



Membrane contactor: increasing throughput

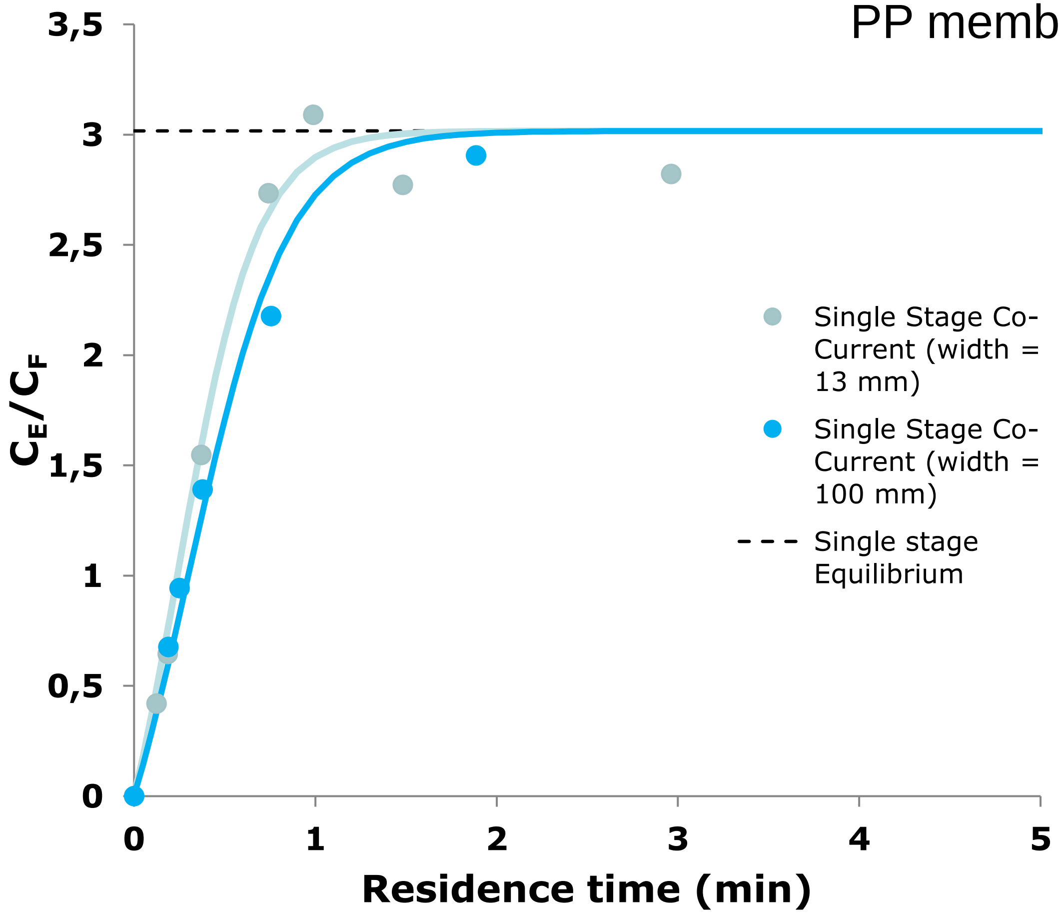
- Distributor
- Straightforward increase in width



20 cm wide

From 1.3 cm to 10 cm

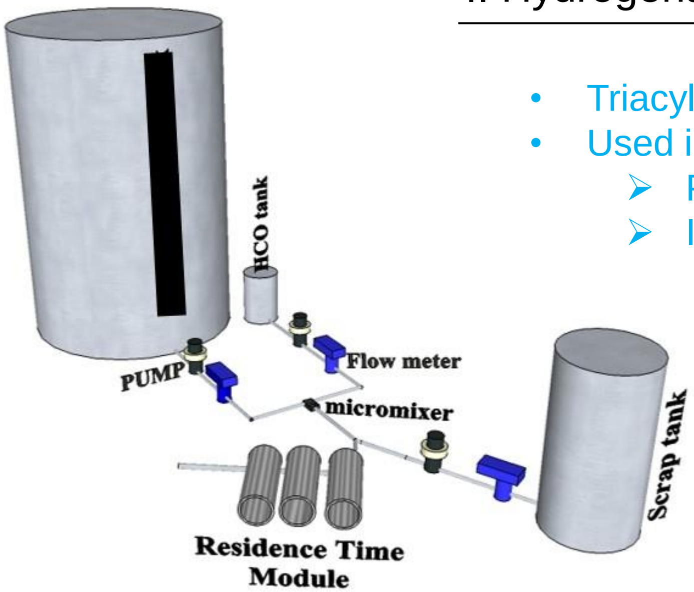
Feed: Heptane+3% benzylalcohol
Solvent: water
PP membrane 20 µm thick



10 cm wide channel
V=1 ml
F: 1 ml/min

CRYSTALLIZATION

Emulsion crystallization of HCO



I. Hydrogenated castor oil (HCO)

- Triacylglycerol (fat)
- Used in heavy duty liquids
  - Prevents phase split
  - Increases the viscosity

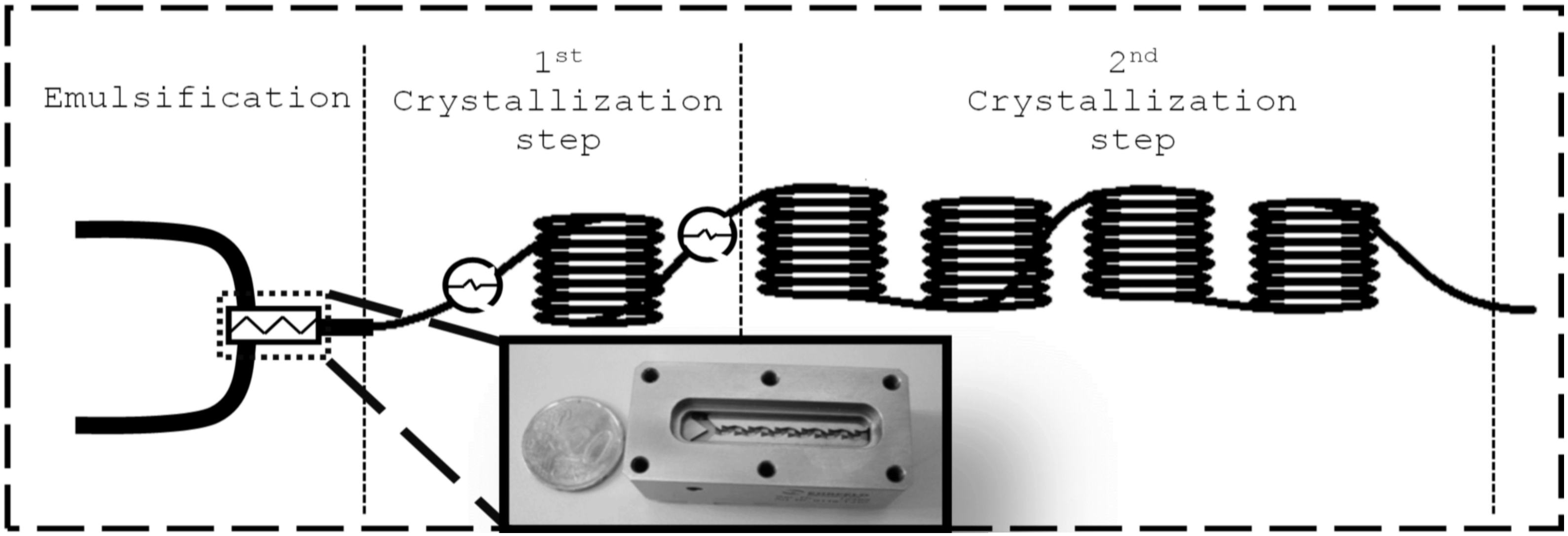
II. Meso-micro continuous process designed for the crystallization of Hydrogenated Castor oil (HCO)

- Ehrfeld microreactors & Swagelok tubing
- Total flow **5 – 20 kg/h**

III. Main objectives

- Increasing performance by controlling the crystal shape
- Characterization of the emulsion crystallization

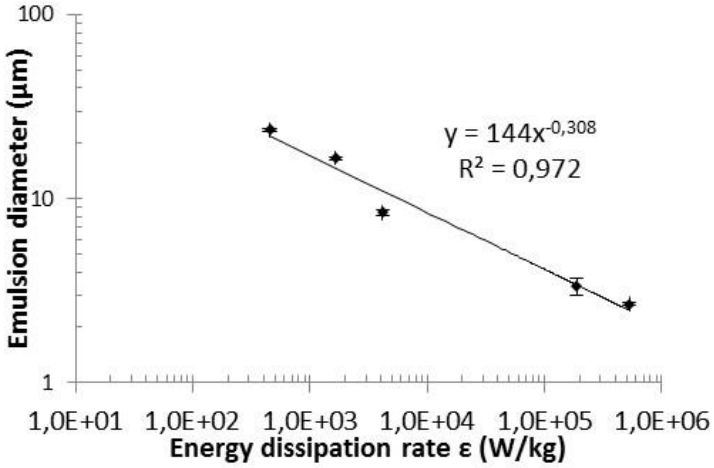
Emulsion crystallization of HCO



III. The emulsion crystallization of HCO

Contains two transformation steps

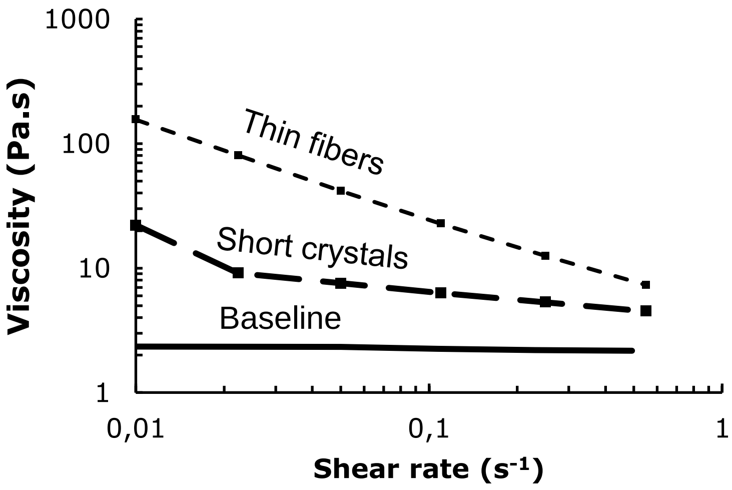
- Part I: **Emulsification**
- Part II: **Crystallization**

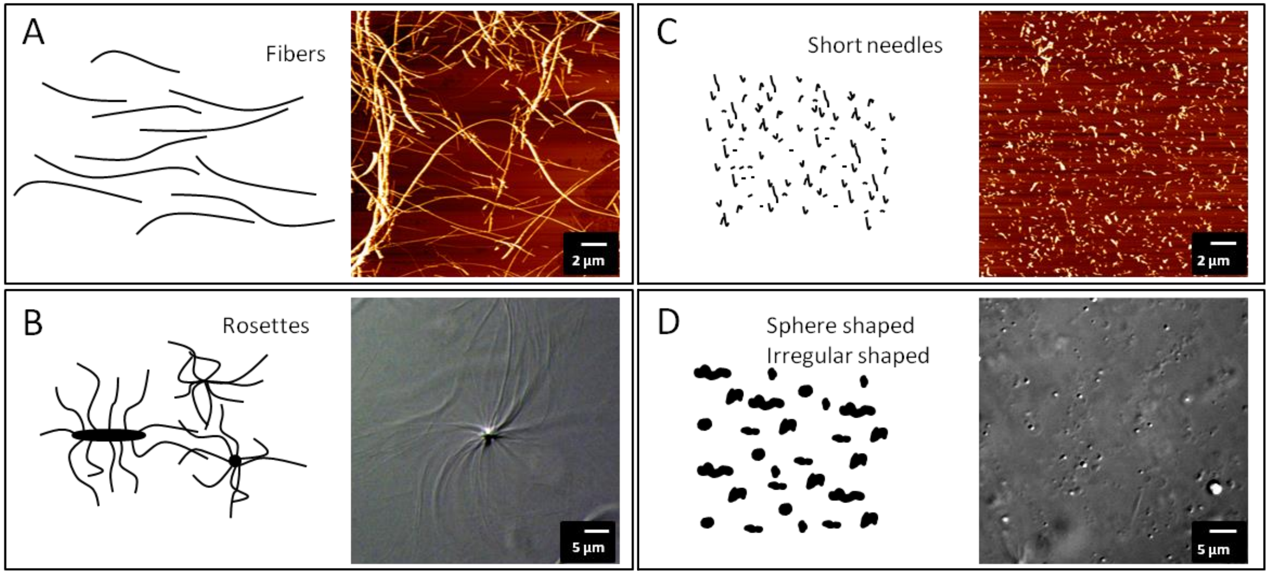


Emulsion crystallization of HCO

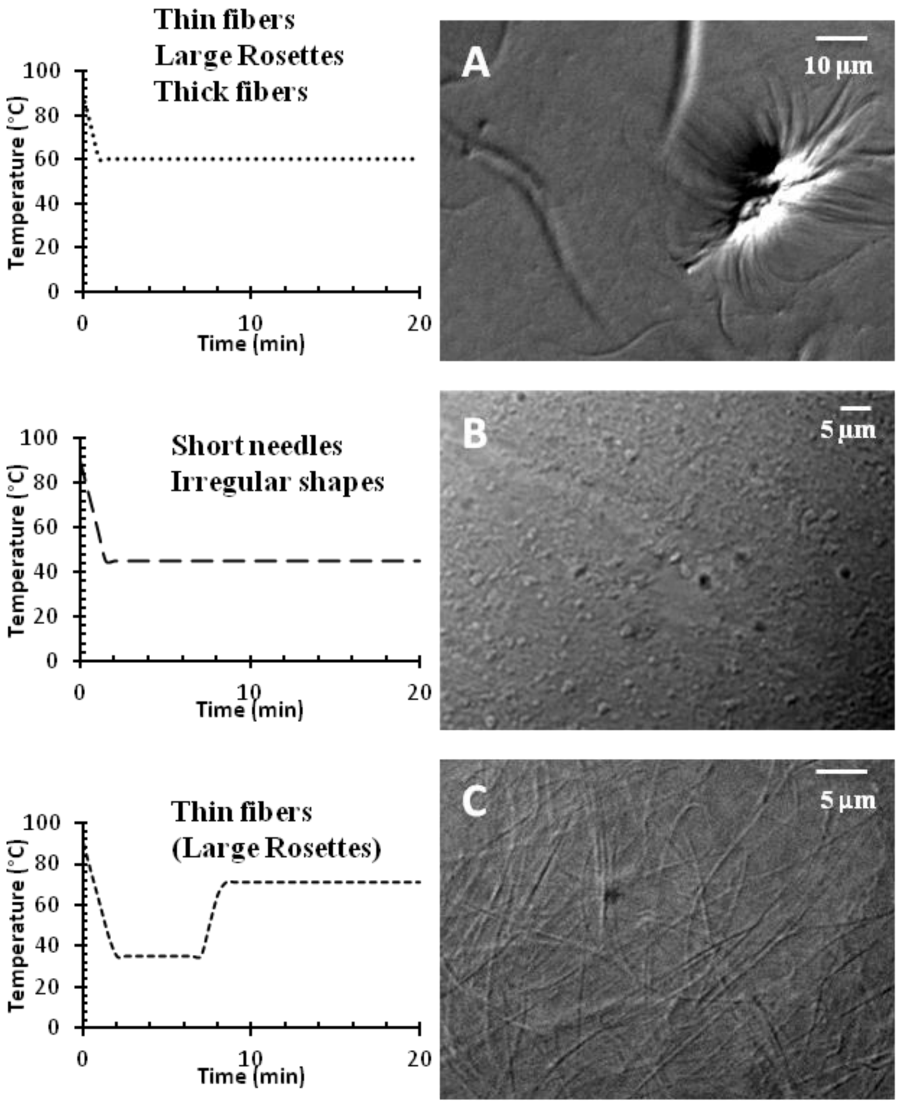
Crystallization - Crystal shape

Which crystal shape do we want?
➔ Thin fibers
Why?
➔ The highest low-shear viscosity increase





Emulsion crystallization of HCO



Identifying the optimal process parameters

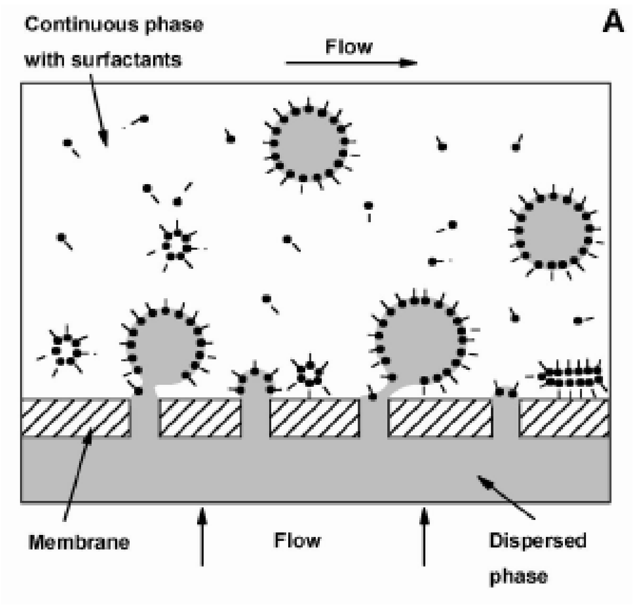
Temperature

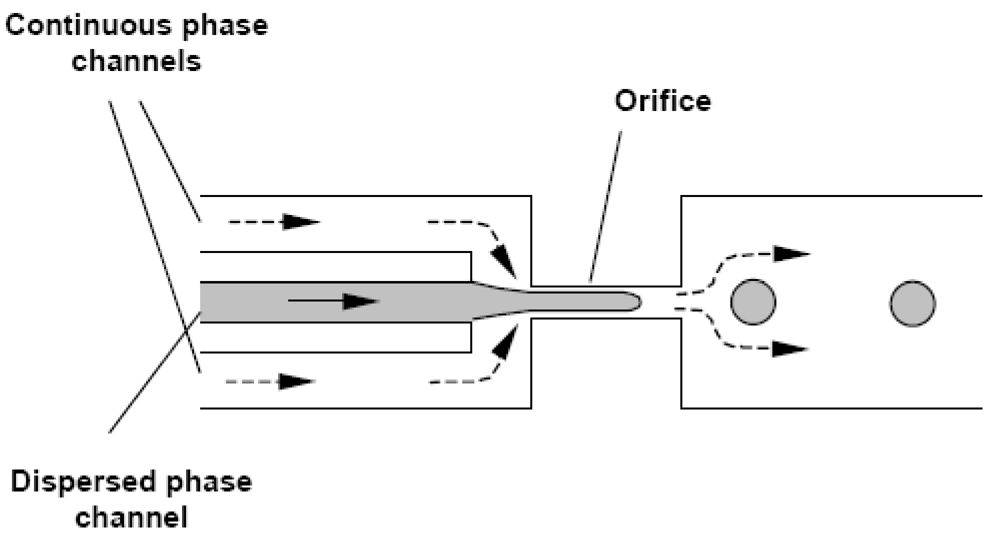
- T > 60 °C
  Large rosettes and fibers
- T < 60 °C
  Short needles and irregular shapes
- T_1 33 °C - 45 °C // T_2 71 °C
  Thin fibers

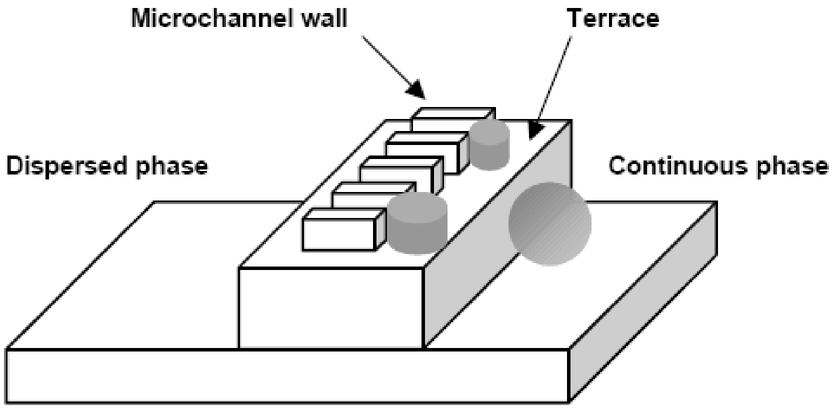
Emulsion size
Shear rate
[Surfactant]
[HCO]
Etc…

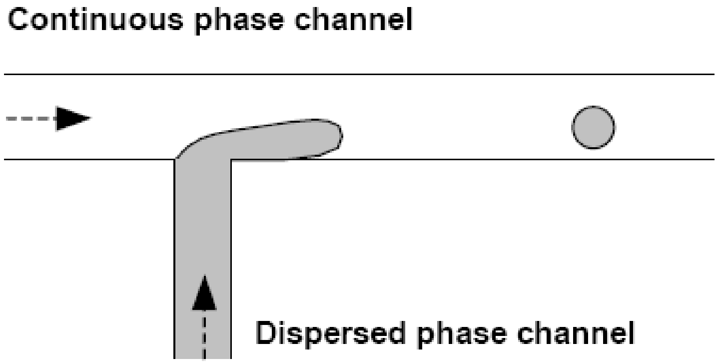
DROPLET GENERATION AND MANIPULATION

Emulsification using specific channel geometries





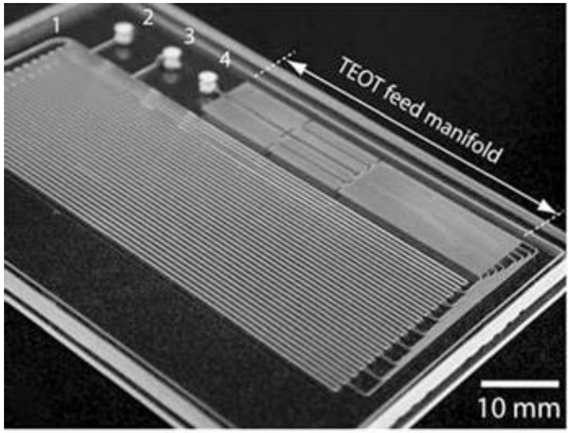


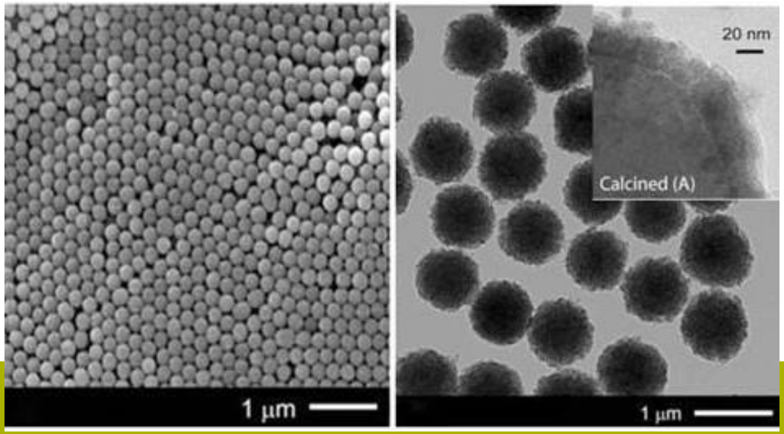


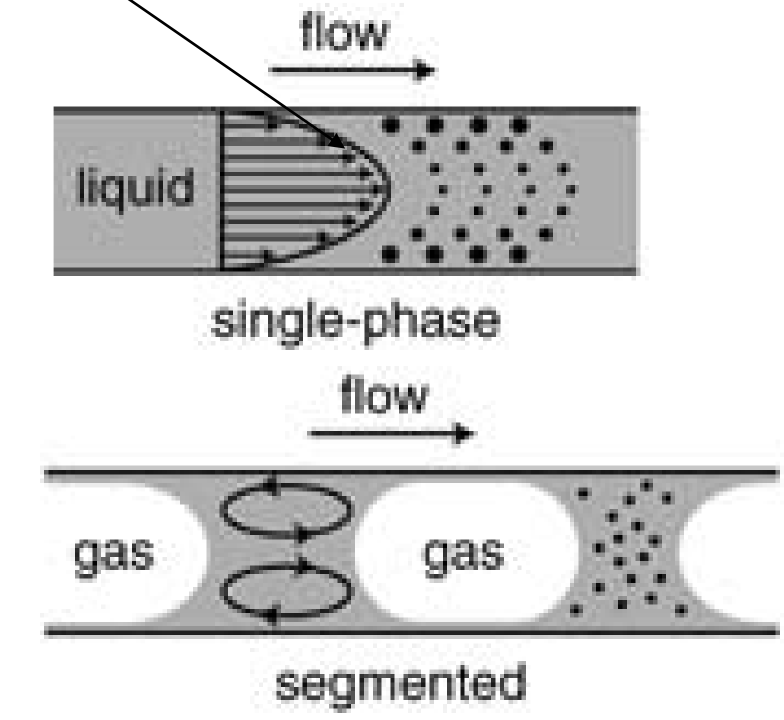
Segmented flow:gas-liquid

Gas divides liquid into small batch reactors

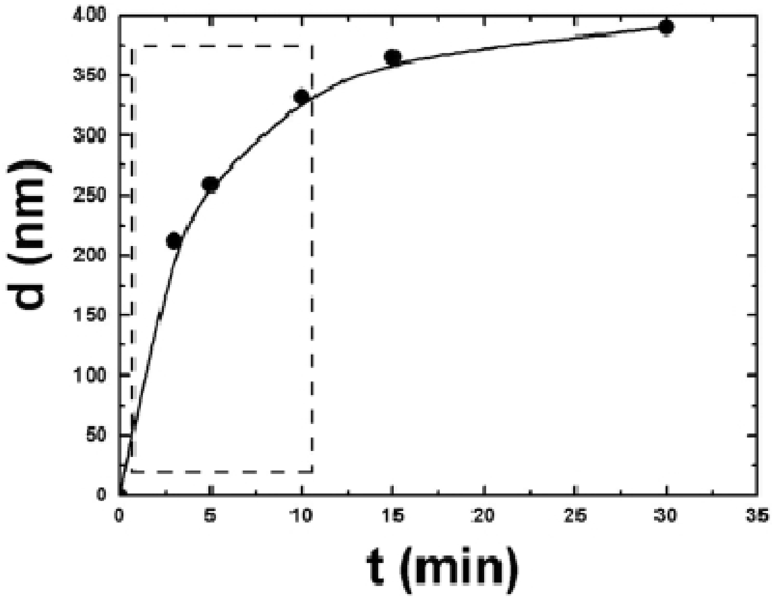
In case of (e.g. Silica or TiO_2) particle growth:
particles close to wall grow longer

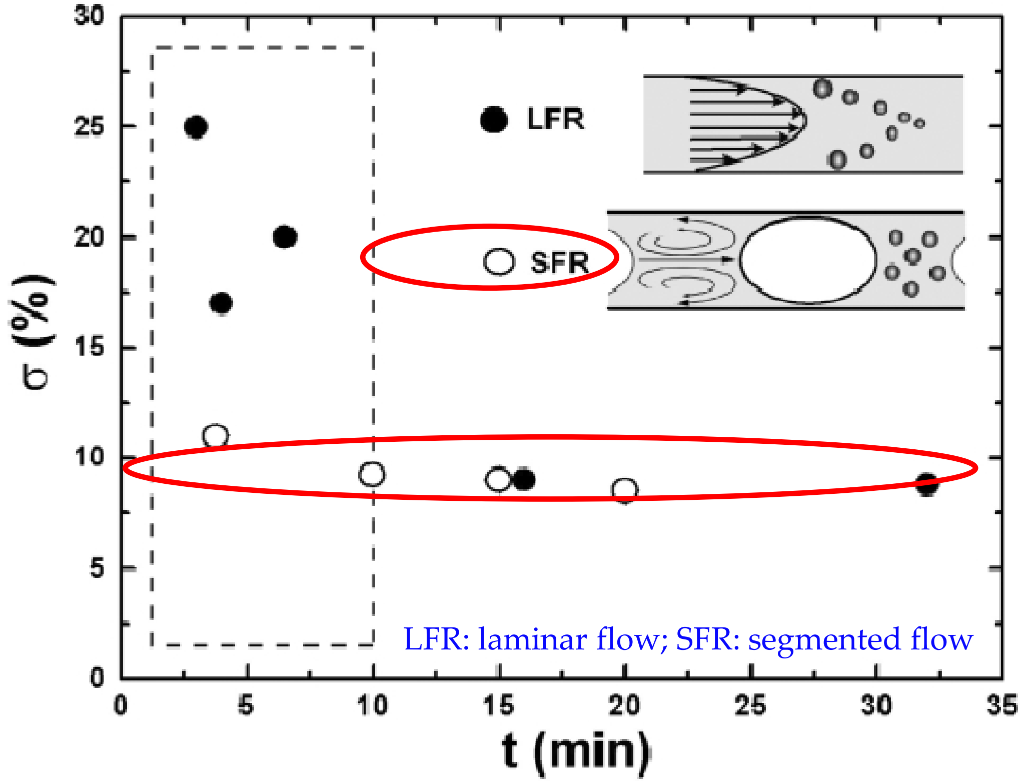


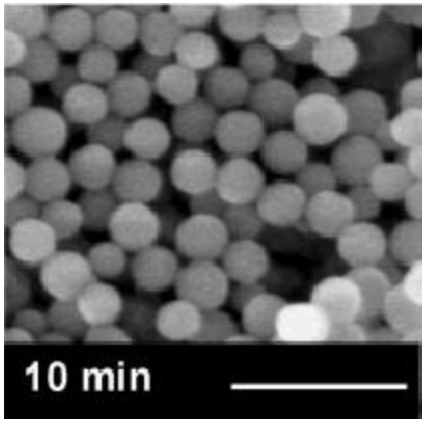




Segmented flow:gas-liquid







Silica nanoparticles. Scalebar 1 μm

A. Günther e.a., Lab Chip 4, 2004, 278

In-line demixing

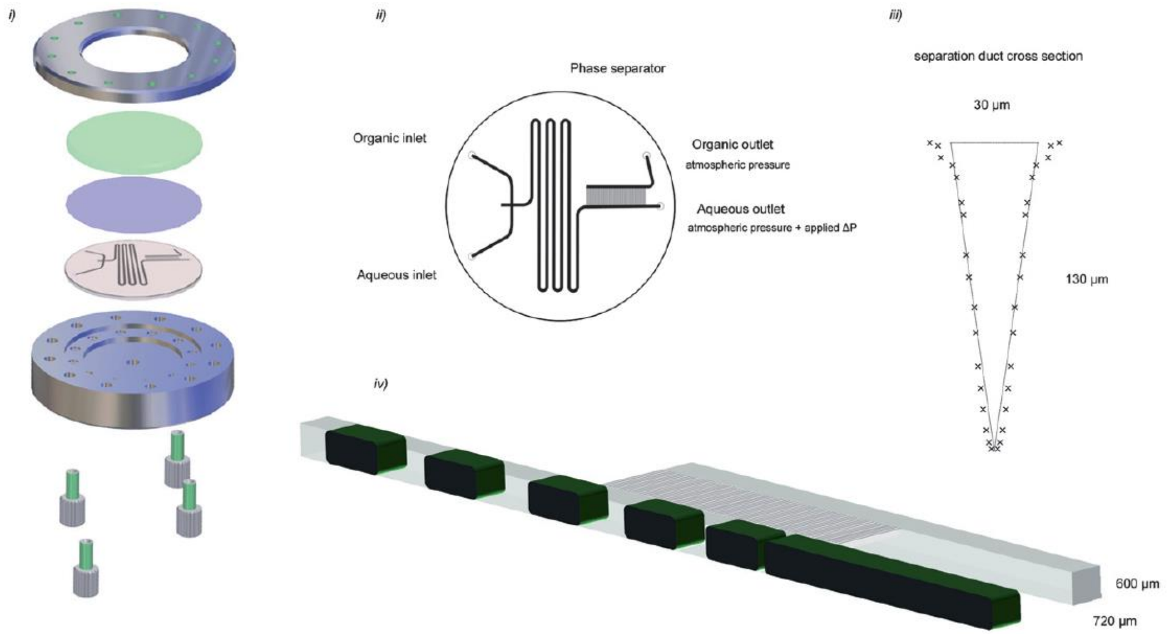


Fig. 2 Series of schematic diagrams illustrating (*i*) device construction. (*ii*) Microfluidic channel layout, including aqueous and organic inlets, T-junction for generation of segmented flow, phase separator region of the device consisting of a series of 140 parallel narrow side channels branching form the main fluidic duct leading to a designated organic outlet, with the main fluidic duct continuing to the designated aqueous outlet. (*iii*) Cross-sectional Gaussian profile of a single laser machined separation duct as measured by serial z-axis optical microscopy and the approximated triangular geometry used for modelling calculations. (*iv*) Cartoon illustration of the separator in operation, the organic phase (light) wets the PTFE channel walls and exits through the separation ducts, driven by the applied pressure differential between the two channel outlets. The non-wetting, aqueous fluid segments (dark) do not enter the narrow separation ducts but continue to flow in the main fluidic channel, coalescing into one continuous stream as the organic phase exits the channel.

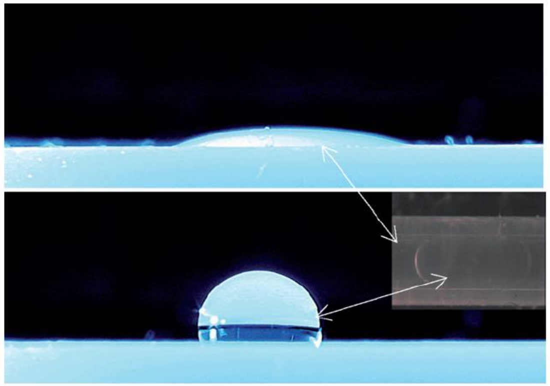


Fig. 3 PTFE wettability by chloroform (upper image) and water (lower image), drop volume 10 µl. Co-elution of the two liquids into a PTFE channel results in a segmented flow regime with chloroform wetting the channel walls as the continuous phase and water the disperse, droplet phase (inset image).

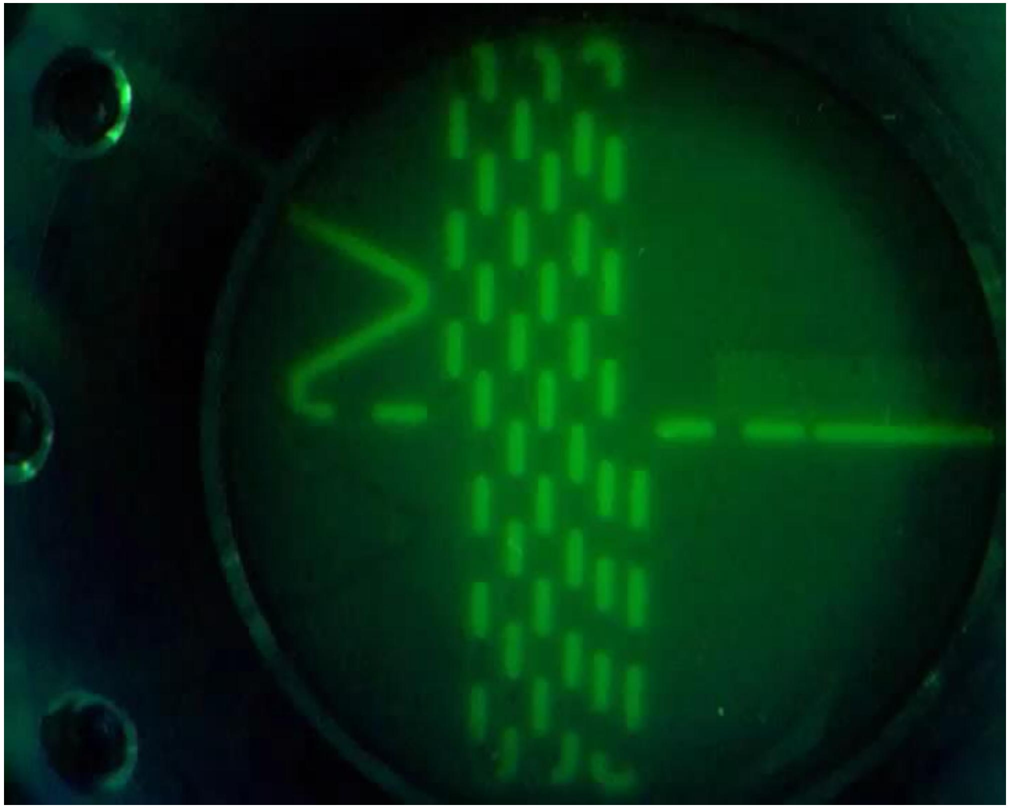
100 % efficiency separation

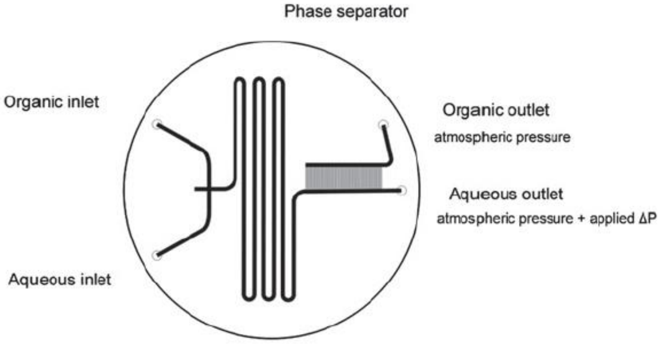
Non-coloured organic phase (chloroform) is wetting the teflon and flows in the narrow channels

720 µm wide, 600 µm deep

140 Side channels at phase separator: 36 µm wide, 130 µm deep

Segmented flow: liquid-liquid





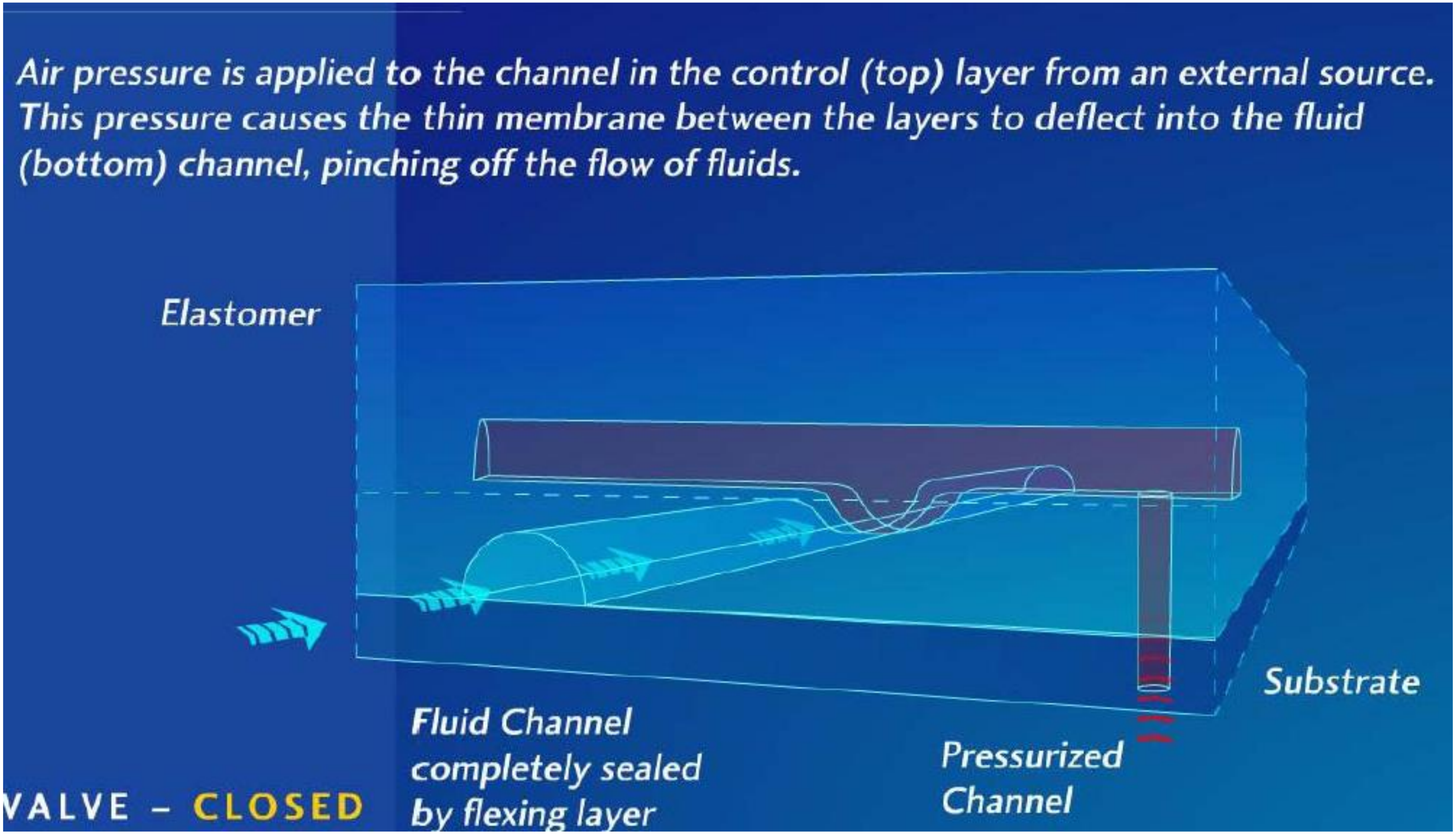
Laser machined PTFE (polyfluoroethylene)
720 µm wide, 600 µm deep
140 Side channels at phase separator:
36 µm wide, 130 µm deep

λ=780 nm, 0.55 W,
Machining speed: 50 mm/min

Barrow et al, lab chip, 9, 388, 2009

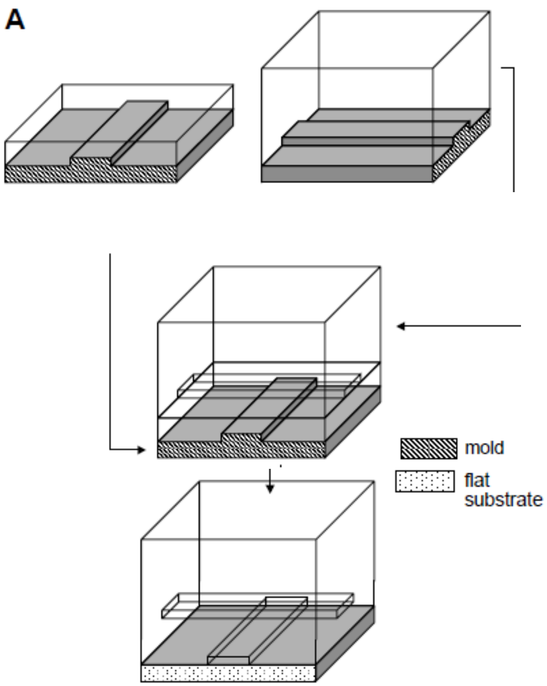
chloroform/water

Valving

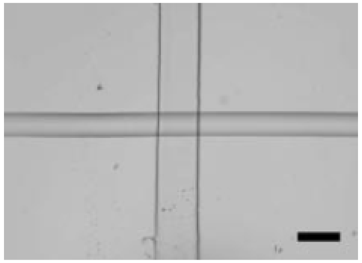


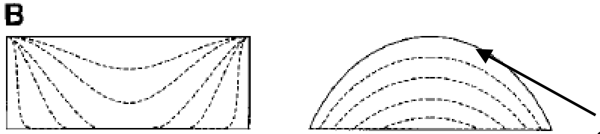
Air pressure is applied to the channel in the control (top) layer from an external source. This pressure causes the thin membrane between the layers to deflect into the fluid (bottom) channel, pinching off the flow of fluids.
Elastomer
Substrate
Fluid Channel completely sealed by flexing layer
Pressurized Channel
VALVE – CLOSED

Valving/pumping

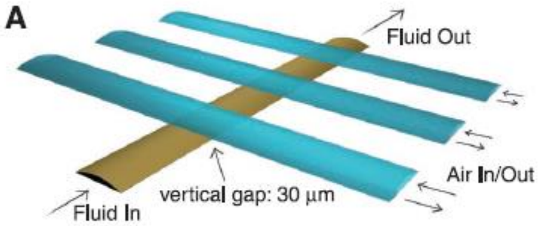


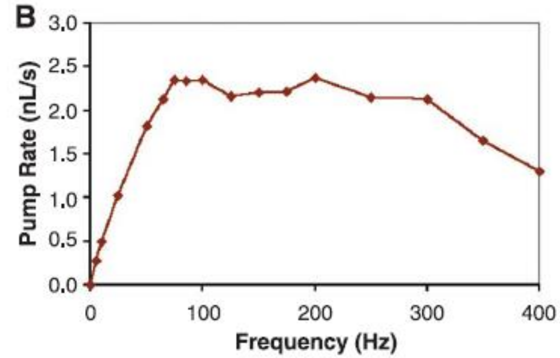
PDMS to PDMS
Air actuated
Membrane of 30 µm
10 µm deep channel





Complete sealing!
(Only up to a few bar)





Valves sequentially on-off: pumping

Stephen Quake et al, Science 288, 113, 2000

Multiple contents - screening

Emulsion polymerization

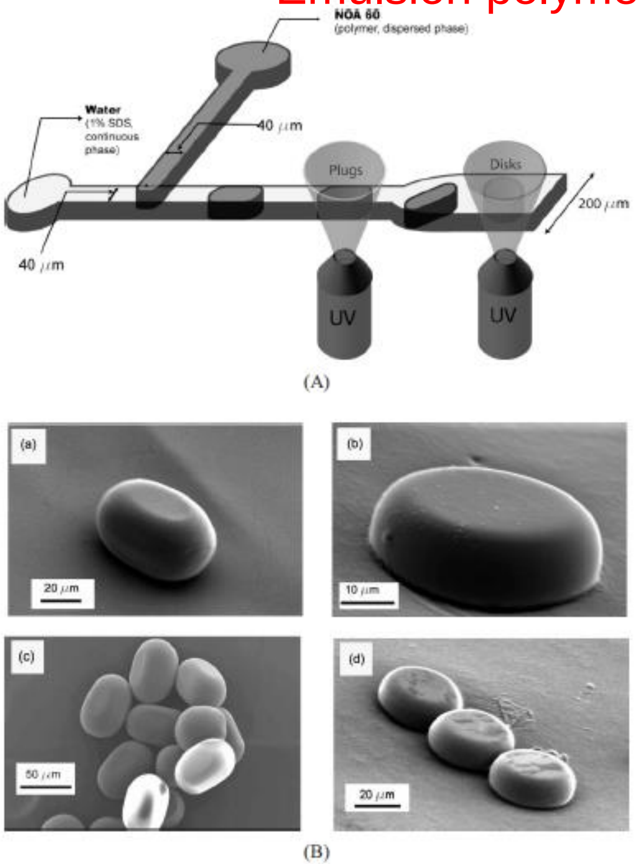


Figure 5. (A) Schematic depicting the T-junction microchannel device for production of non-spherical polymer particles. (B) SEM images of plug-shaped particles (a, c) and disk-like particles (b, d) (from ref. [10]).

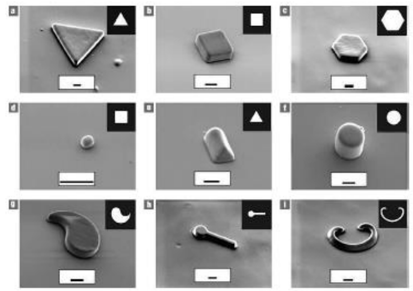


Figure 14. SEM images of the different particles synthesized; the inset represents the mask pattern used for that particle; the scale bar is 10 µm (from ref. [34])

Lock release

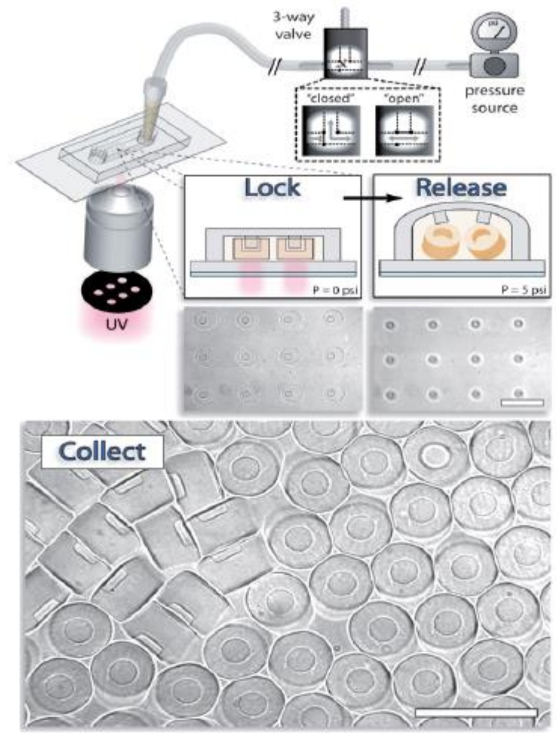
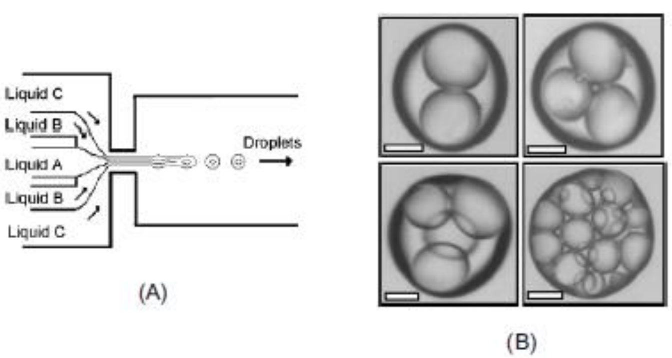
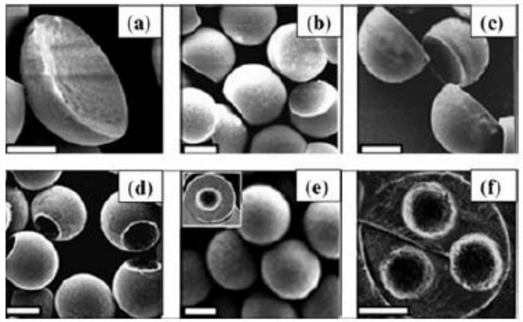
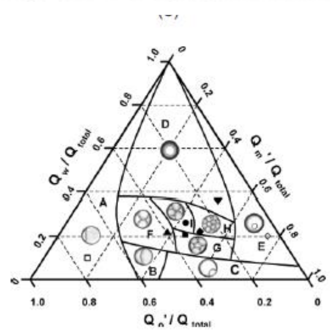


Fig. 1 Process of lock release lithography. First, structures are polymerized by shining bursts of UV light through a transparency mask and a microscope objective. The particles with shapes determined by the mask and channel topography, are "locked" by relief structures in the channel topographies. Particles are "released" with channel deflection after a relatively high pressure (~ 5 psi) is applied to initiate flow. Shown is a differential interference contrast (DIC) image of a collection of 3D particles with micro-cavity in the channel reservoir. Scale bars are 100 µm.

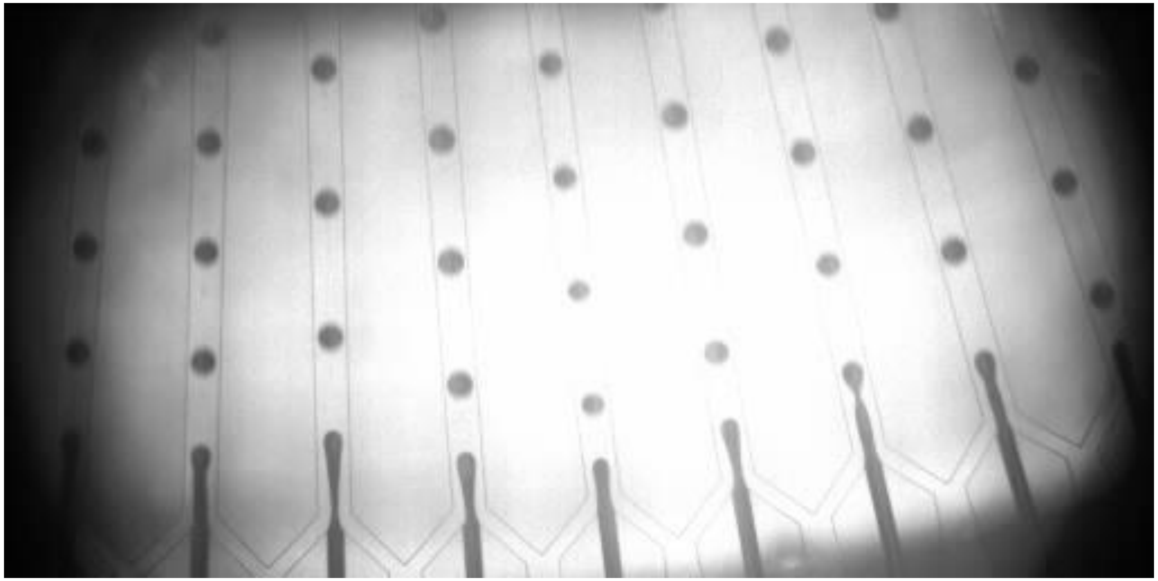
Complex emulsion particles







Parallellization



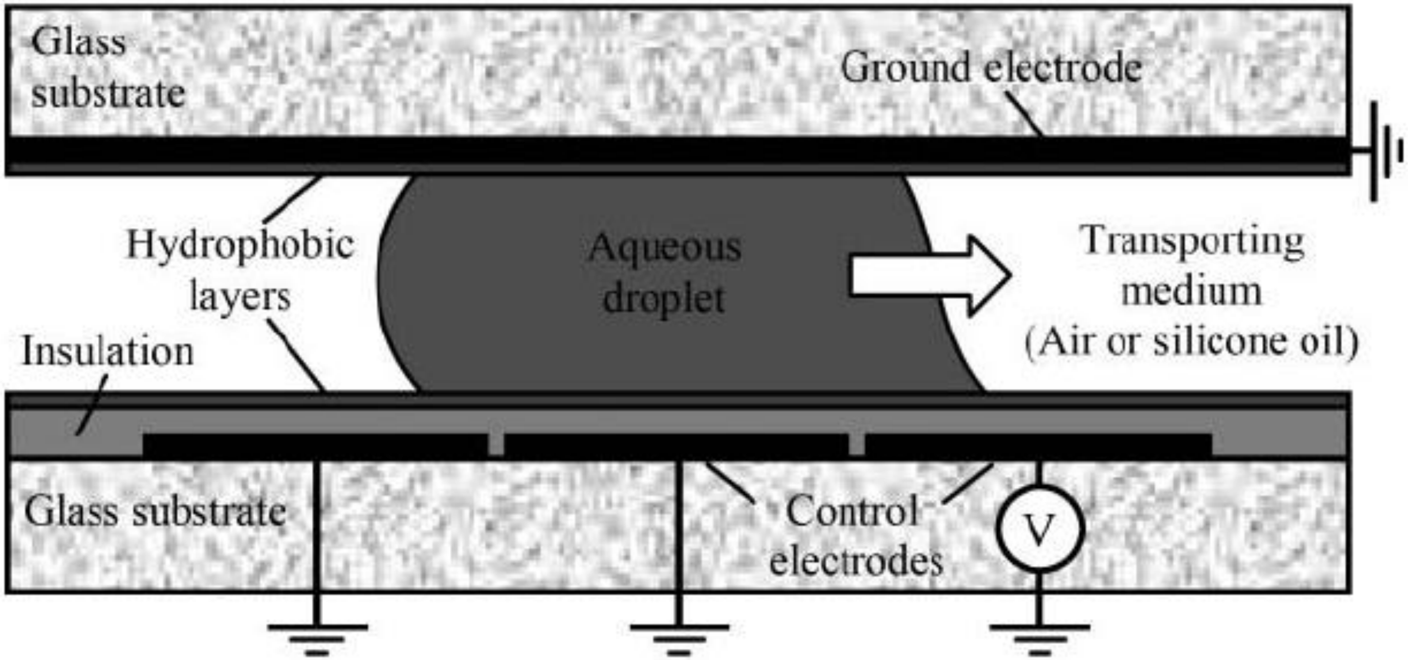
Glass chips (fusion bonded)
depth 100 µm
Width 100 & 200 µm

to be disp. Phase: 1,6 hexanediol diacrylate with photoinitiator

Aqeous phase: polyvinylalcohol (2%) in H_20

In this study, we report the mass production of monodisperse emulsion droplets and particles using microfluidic large-scale integration on a chip. The production module comprises a glass microfluidic chip with planar microfabricated 16–256 droplet-formation units (DFUs) and a palm-sized stainless steel holder having several layers for supplying liquids into the inlets of the mounted chip. By using a module having 128 cross-junctions (*i.e.*, 256 DFUs) arranged circularly on a 4 cm × 4 cm chip, we could produce droplets of photopolymerizable acrylate monomer at a throughput of 320.0 mL h^{-1}. The product was monodisperse, having a mean diameter of 96.4 µm, with a coefficient of variation (CV) of 1.3%. Subsequent UV polymerization off the module yielded monodisperse acrylic microspheres at a throughput of ~0.3 kg h^{-1}.

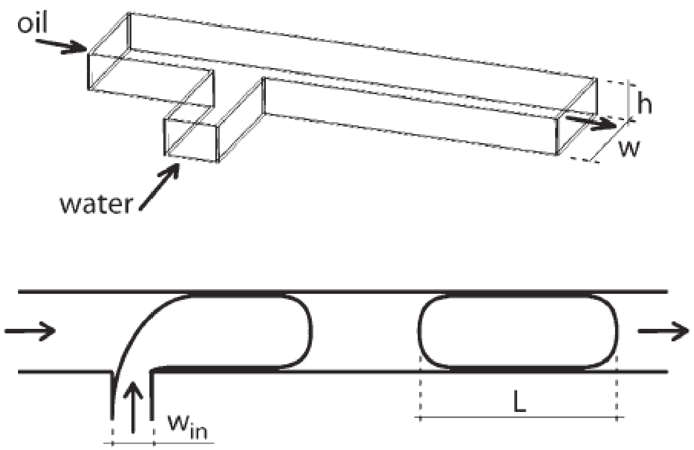
Contact angle manipulation



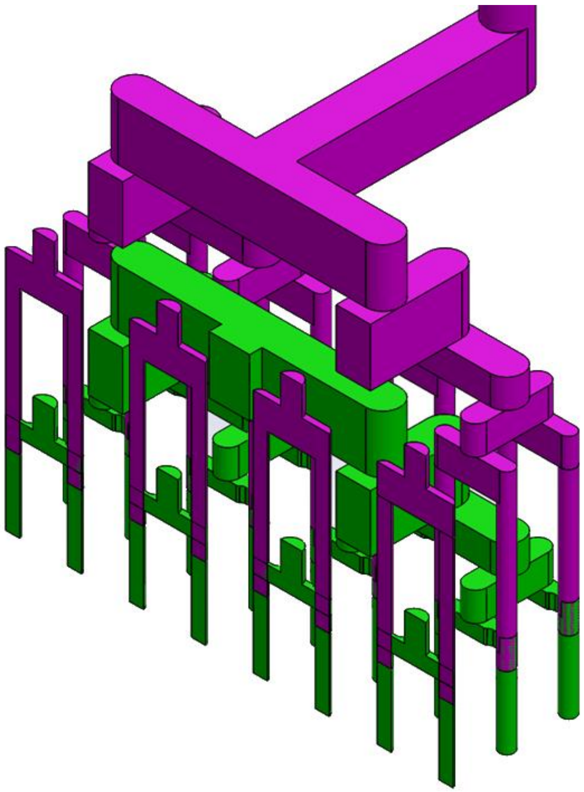
Brassard et al, Lab Chip, 2008, **8**, 1342–1349

Digital µFluidics

Emulsion approach: other opportunity for microreactor format



$$L/w = 1 + \alpha Q_{in}/Q_{out}$$



CV: <7% vs. 25-80 % (smx and batch)

Formation of droplets and bubbles in a microfluidic T-junction—scal and mechanism of break-up†

Piotr Garstecki,*[ab] Michael J. Fuerstman,[a] Howard A. Stone[c] and George M. Whitesides*[a]

Received 29th July 2005, Accepted 5th January 2006

Lab Chip, 2006, **6**, 437–446 | 437

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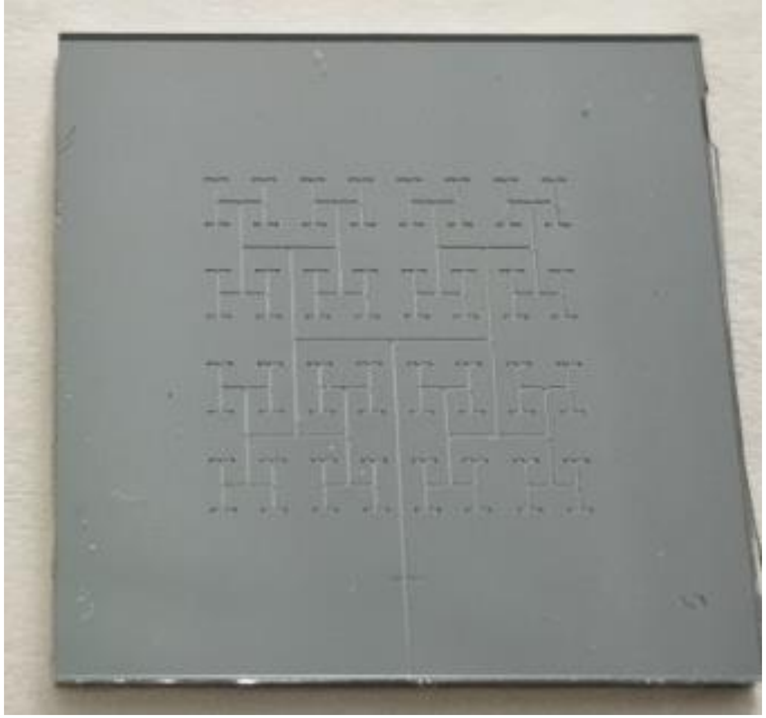
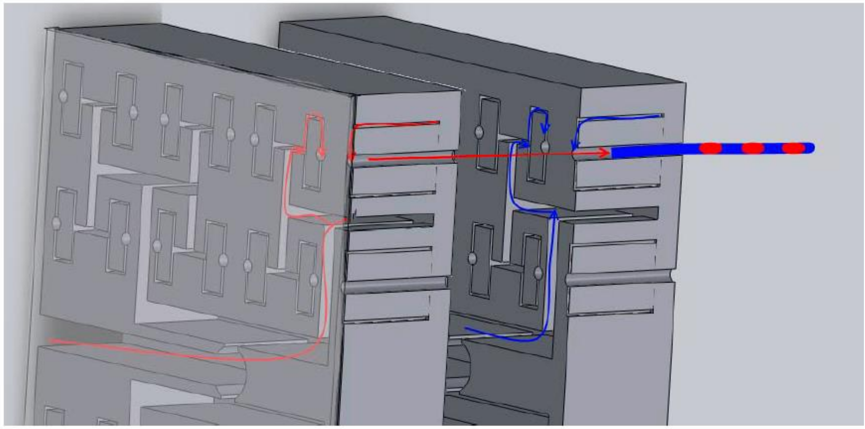
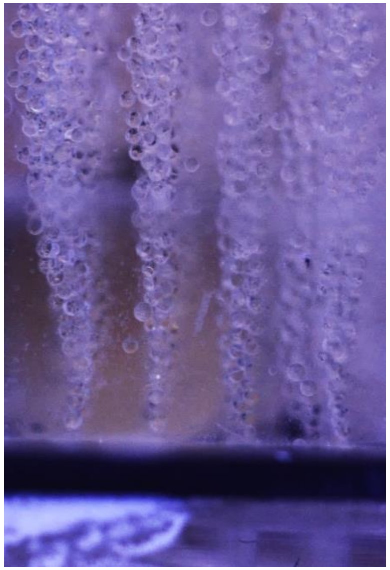
materials for a better life

Industrial scale emulsification





400 µm hexane droplets in water
+ SDS (CV ~10 %)
5 bar: 10 ml/min (64 nozzles)



Patent pending

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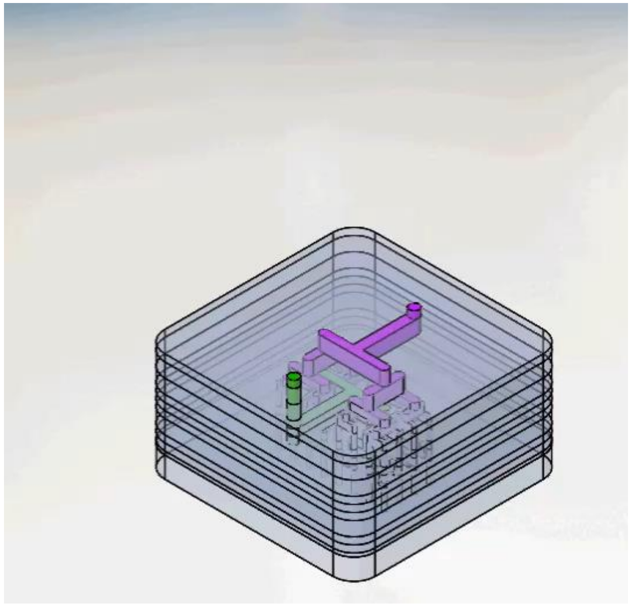
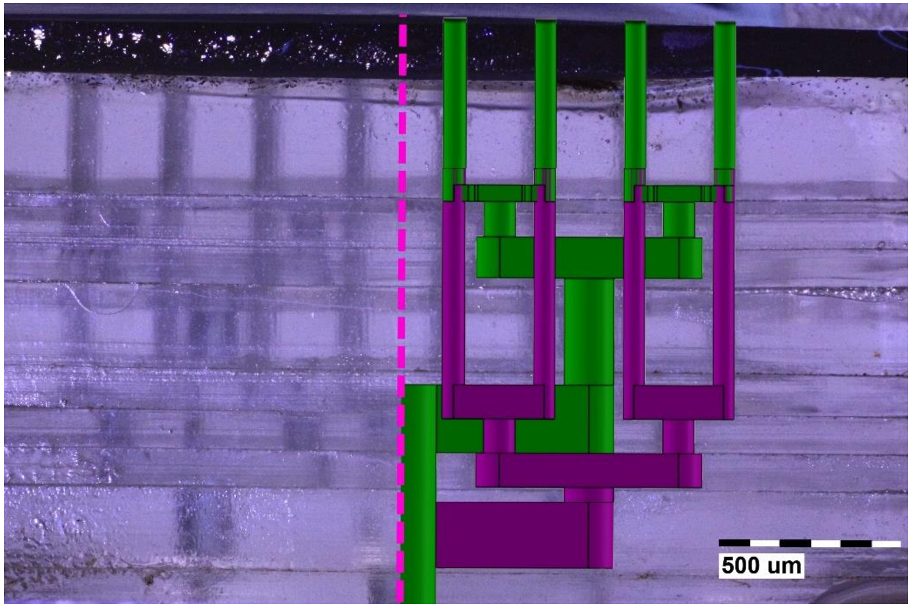
Chip assembly





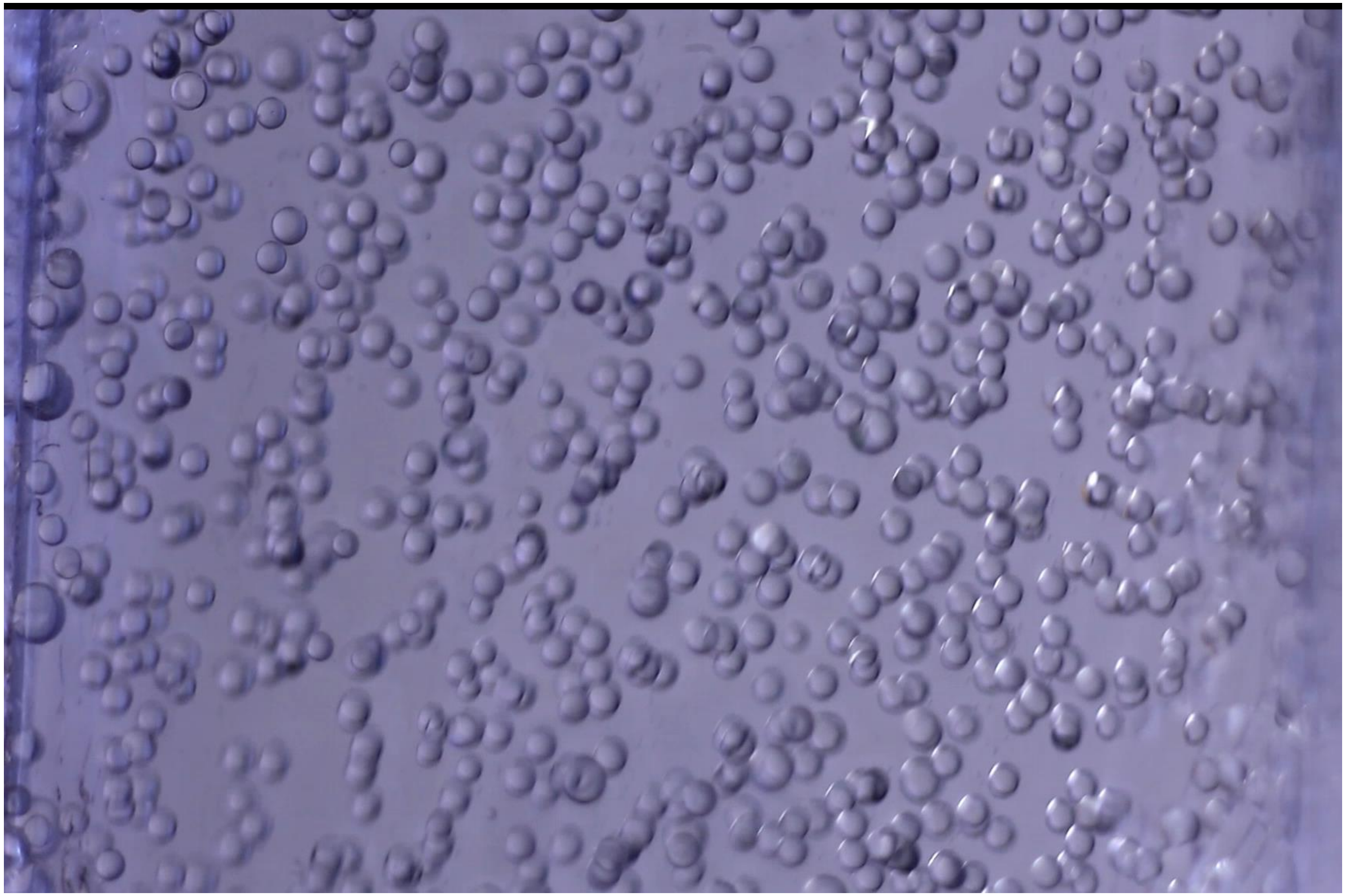
Several layers (11) are stacked and thermally bonded @ 155 C for 50 min under 5 kg weight (PMMA)

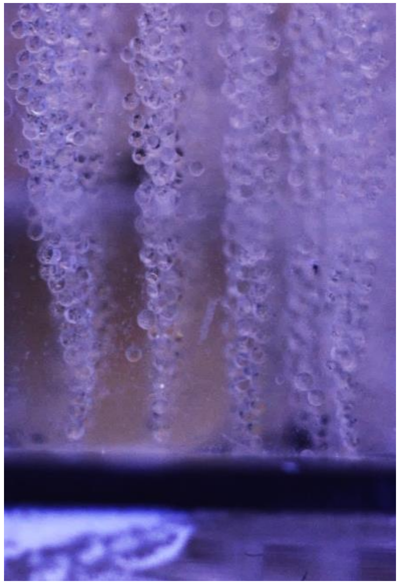
Reversible procedure with fluoroelastomer

On-chip characterization

0. 4 mm droplets
(CV ~10 %)

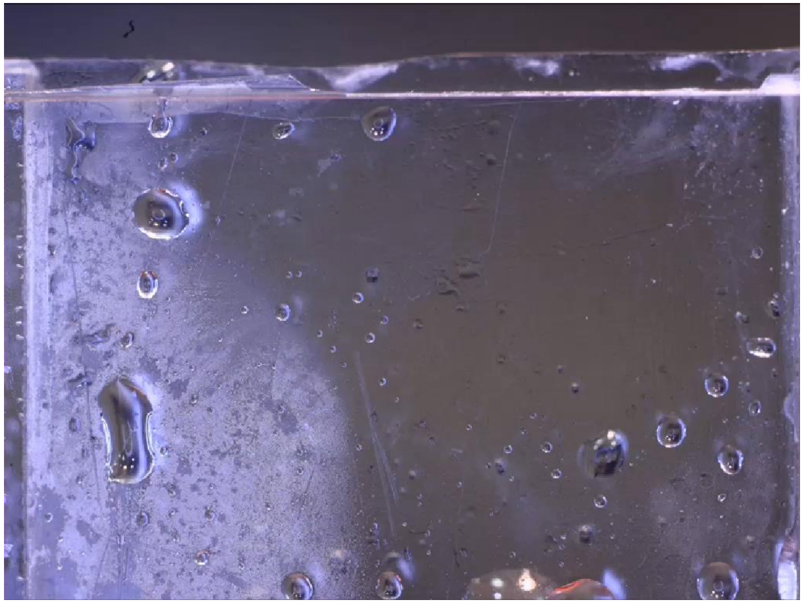
Hexane droplets in water+SDS
5 bar: 10 ml/min (64 nozzles)



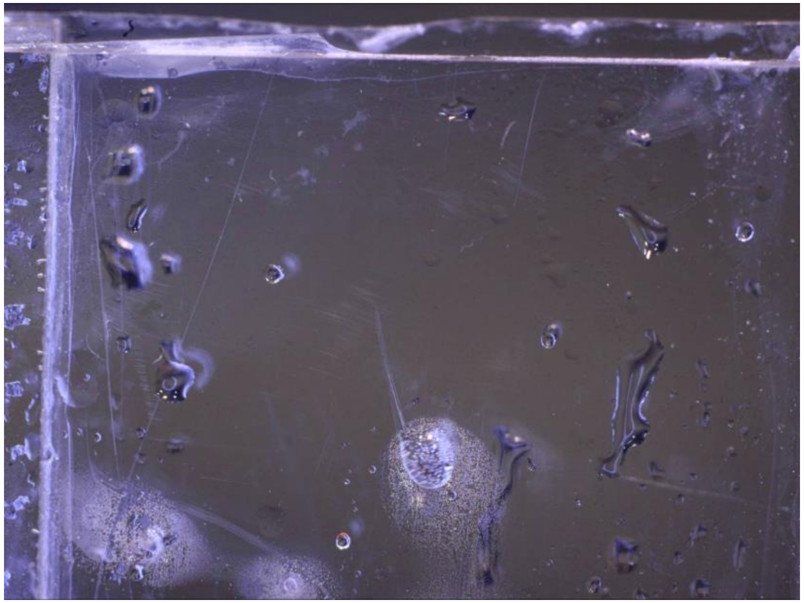


Enhanced phase separation

Multi-nozzle array (CV ~10 %)



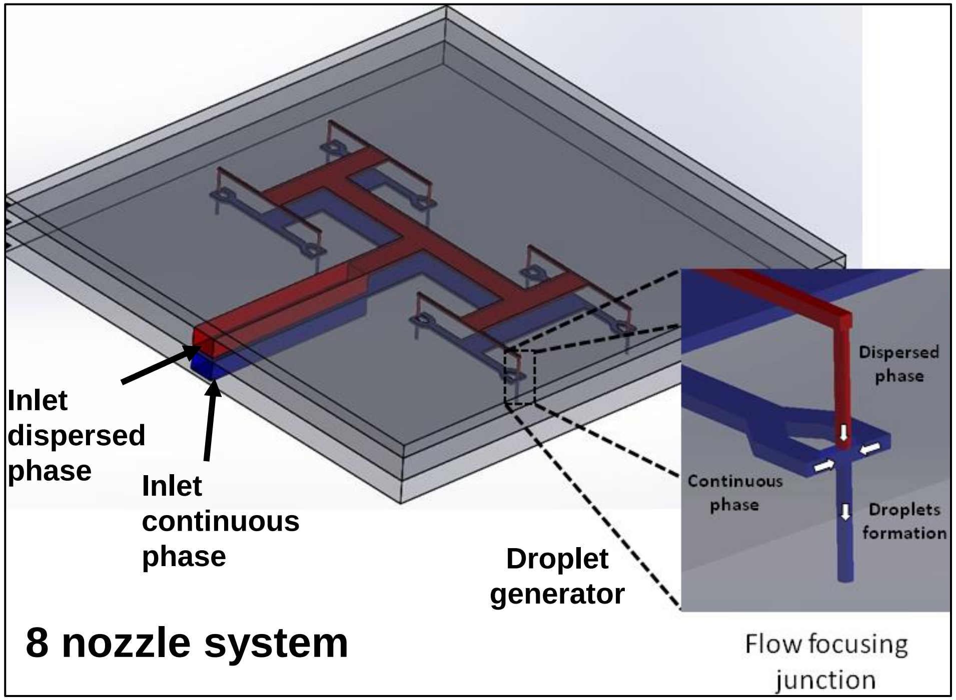
Mixer (CV ~ 35 %)

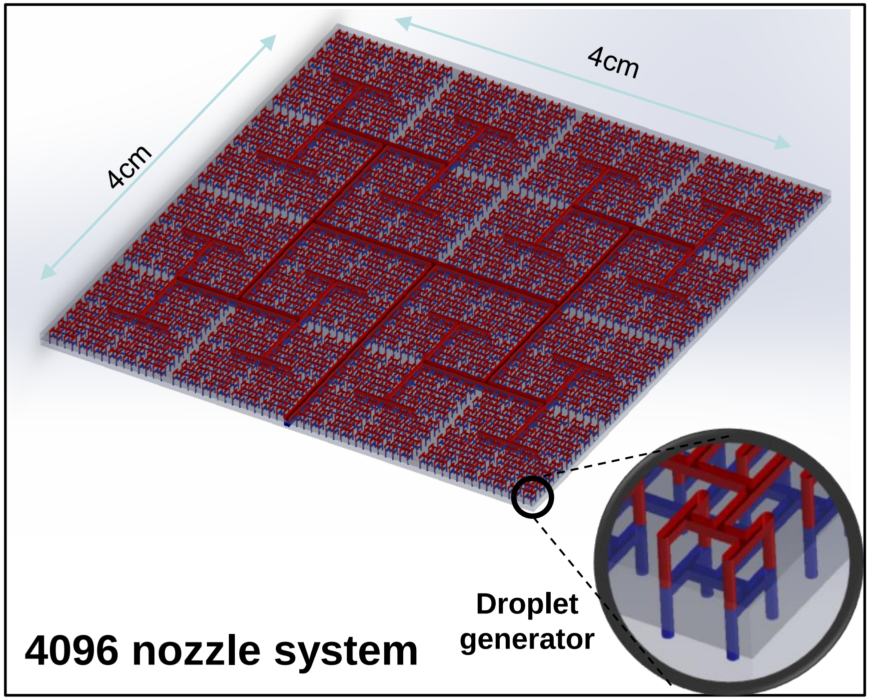


3D flow distribution

maximizing number of nozzles / surface

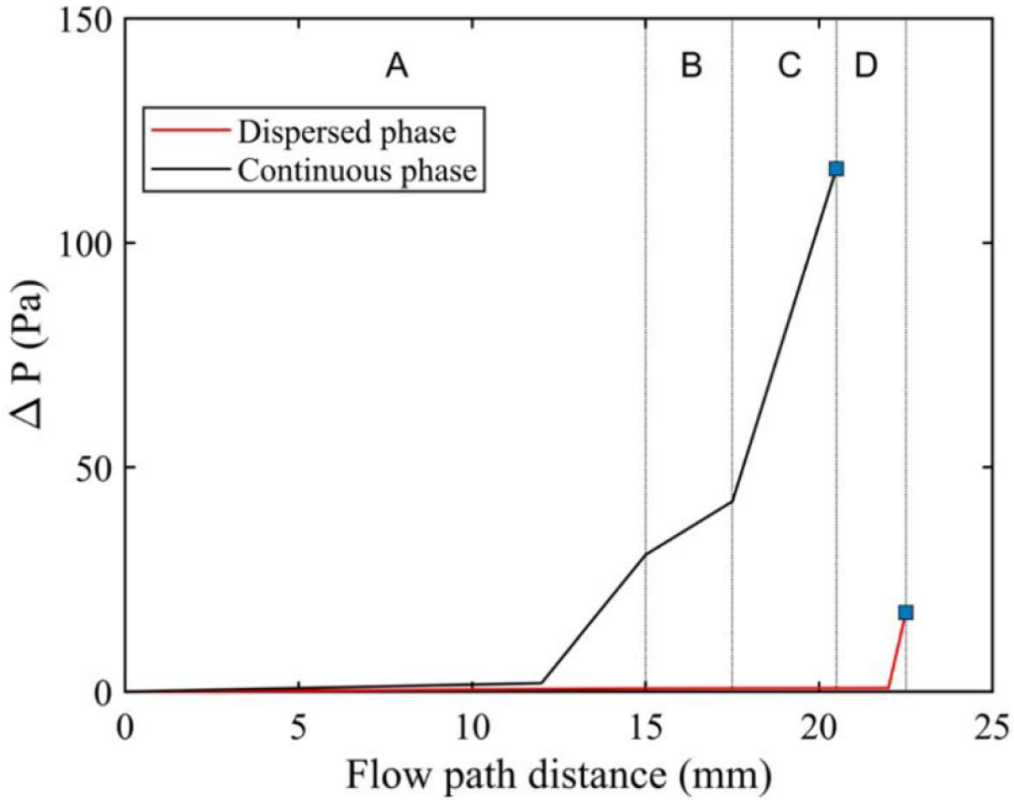
3D emulsifier:
microfluidic design for a high throughput droplet production

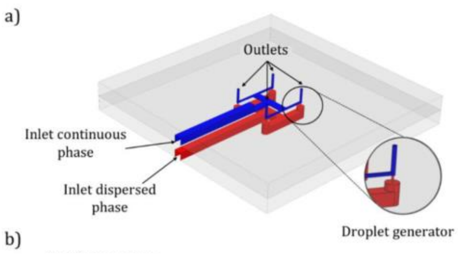




Pressure drop at branches

A (first layer)….D (nozzle)





Nozzle diameter 150 µm
Channel depths: 200 µm
Width: 1 mm to 300 µm

5 ml/h/nozzle

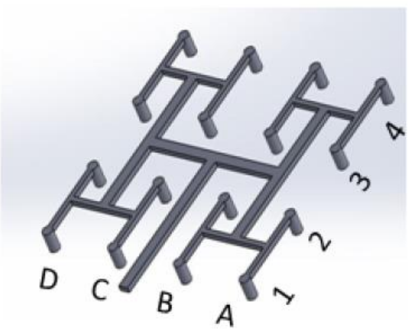
(Reducing) sensitivity to fouling

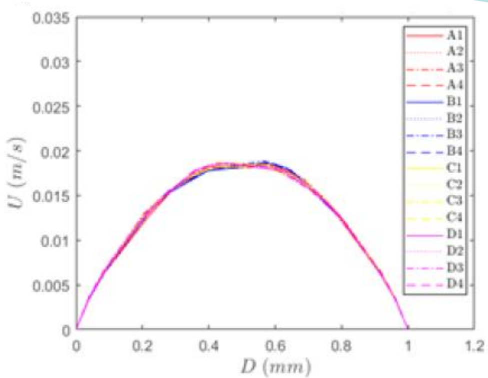
h=500 µm

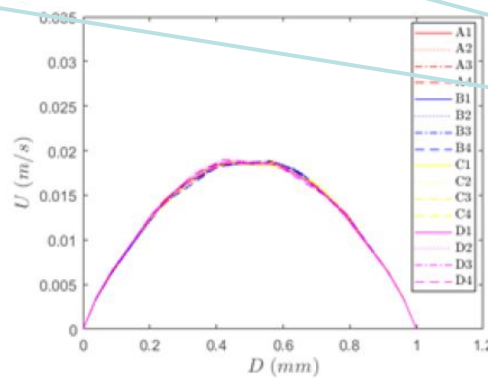
Channel depths

1 mm – 1 mm
-1 mm – 0.5 mm
- 0.5 mm

1 mm – 1 mm -
1 mm – 0.5 mm
- 0.1 mm

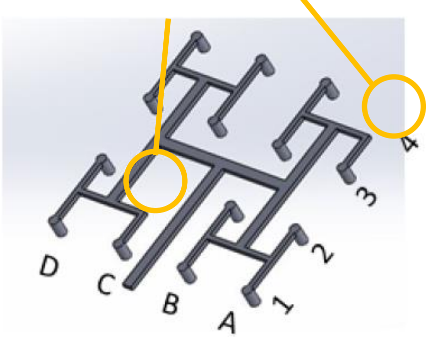


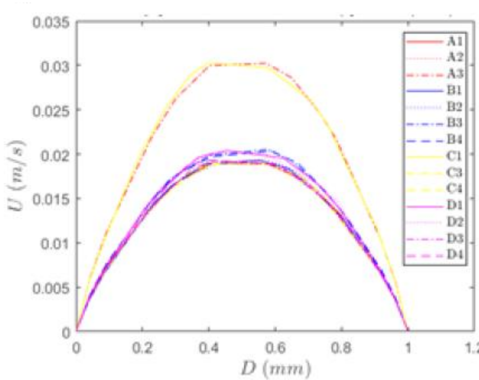


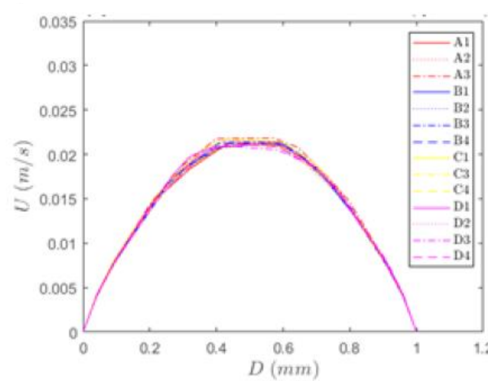


Last channel before through-hole

defects

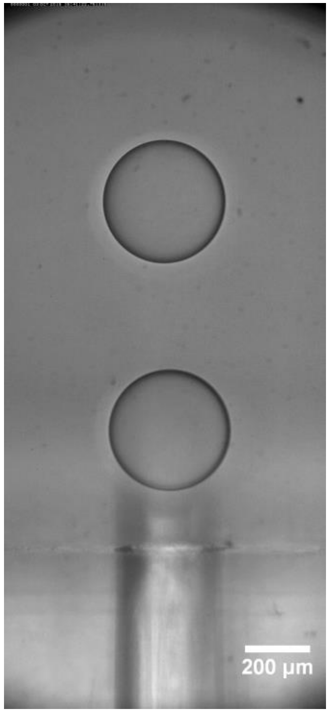




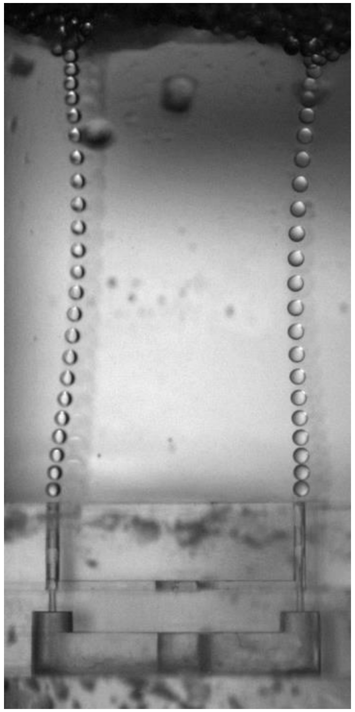


Throughput considerations

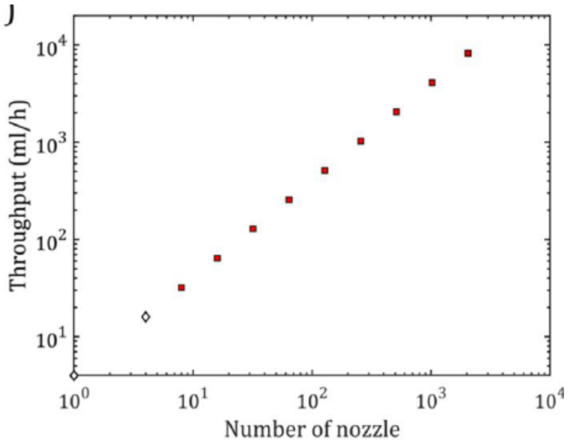
PMMA chips



Outlet



Overview



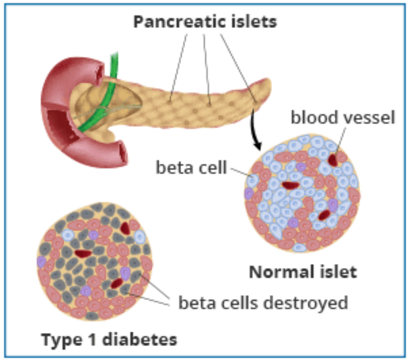
100 µm channels

2048 nozzles on 1 cm^2 :
8.2 l/h

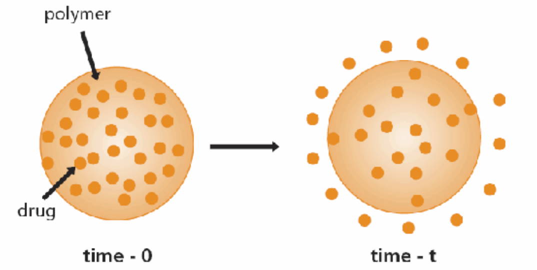
P. Gelin et al, Ind & Eng Chem Res (2020)

PLGA

- Biodegradable polymer



- Drug release
  - Cancer treatment
  - …
  - **Cell therapy for diabetes**



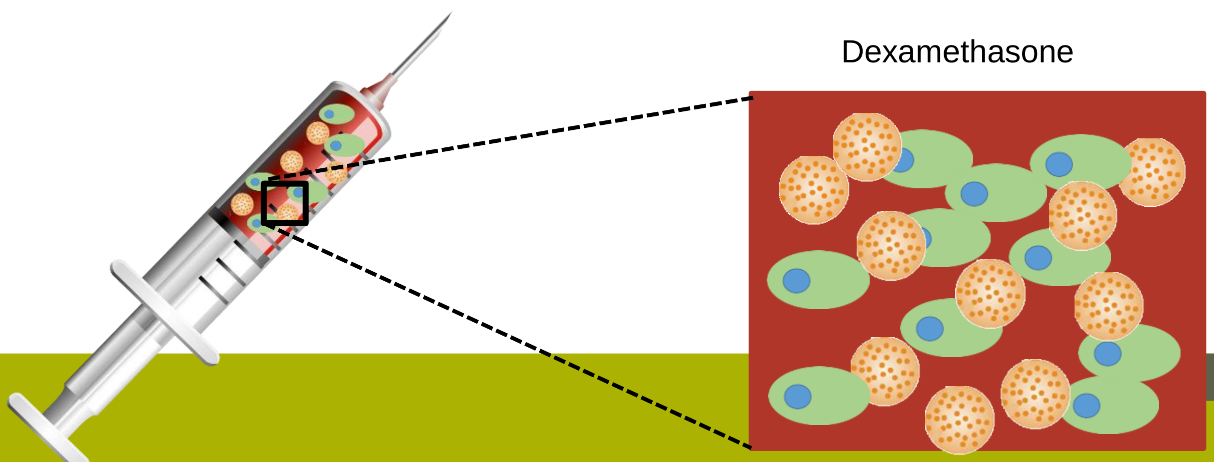
- Basic Mechanism
  - Slow degradation of the polymer, releasing the drug into the environment

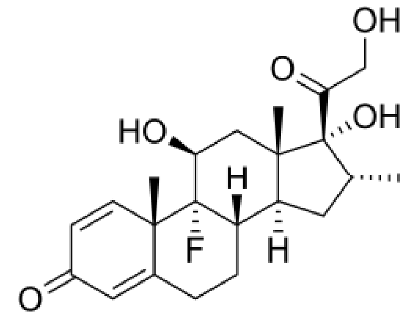
PLGA: motivation

Collaboration with Prof. Karine Hellemans (Diabetes Research Center, Brussels)

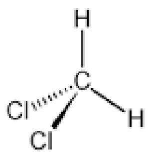
- Motivation
  - Inject alongside implant (β-cells)
  - Diameter: 10-50 µm
  - Dexamethasone loaded particles
    - →Prevent inflammation
    - →Induce β-cell proliferation

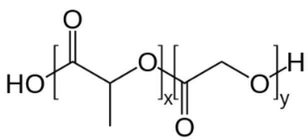
Dexamethasone





PLGA particles – cell therapy





PLGA: poly(lactic-co-glycolic acid)

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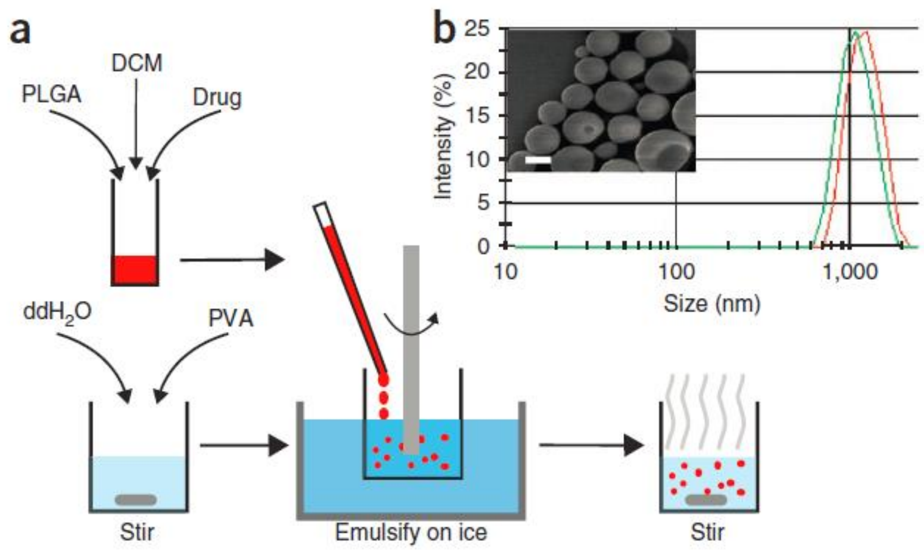
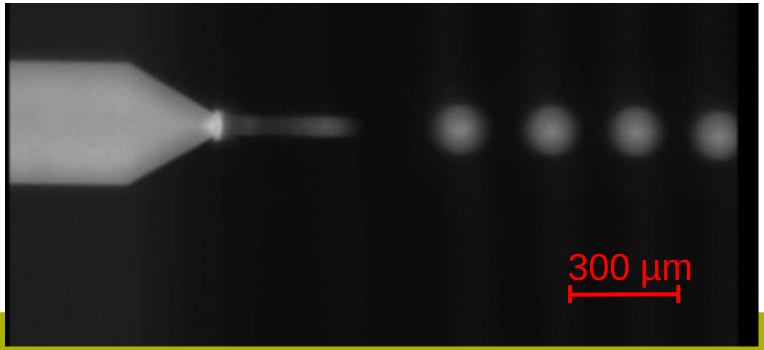
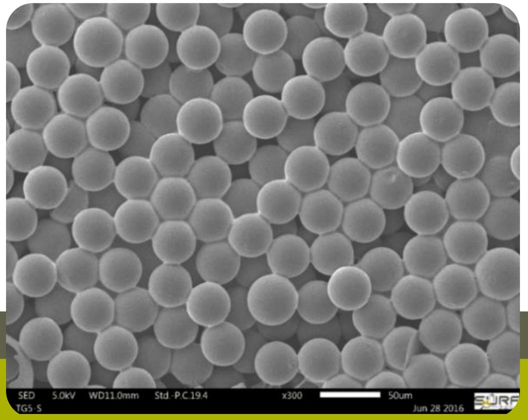


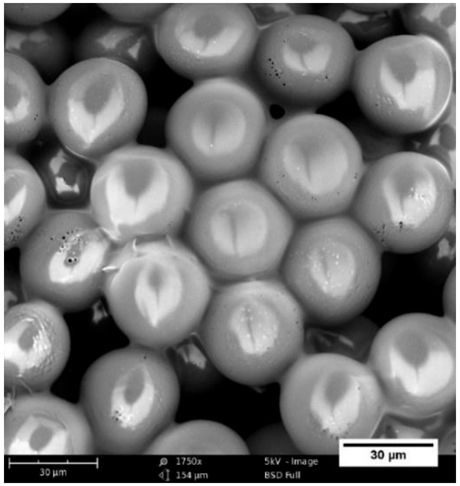
Type 1 diabetes: β cell therapy

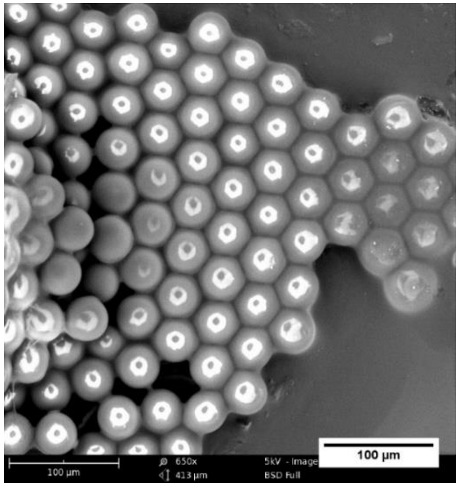
Promotion of favorable factors

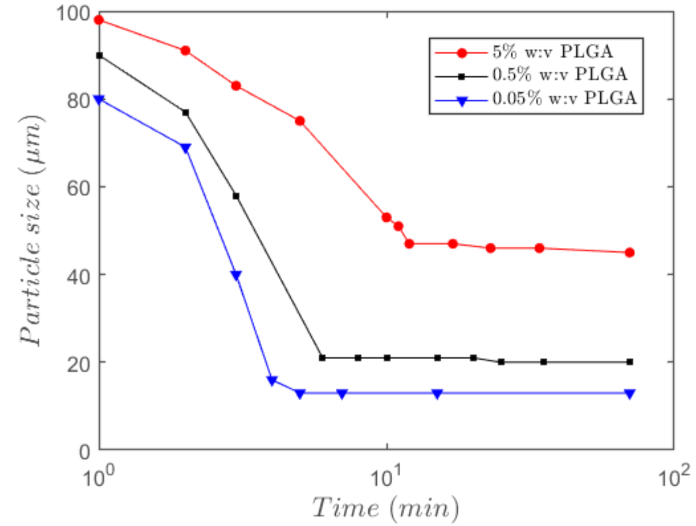


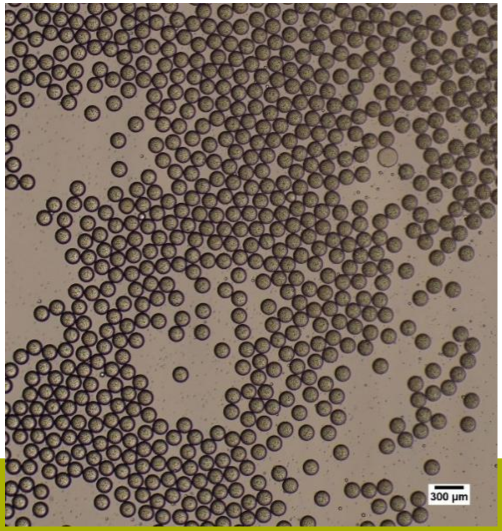


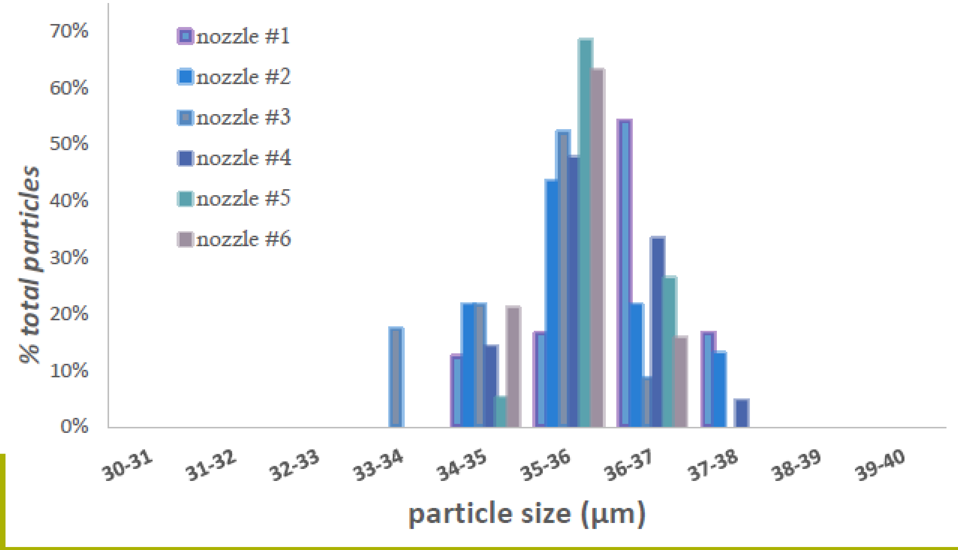
PLGA particles, loaded with dexamethasone



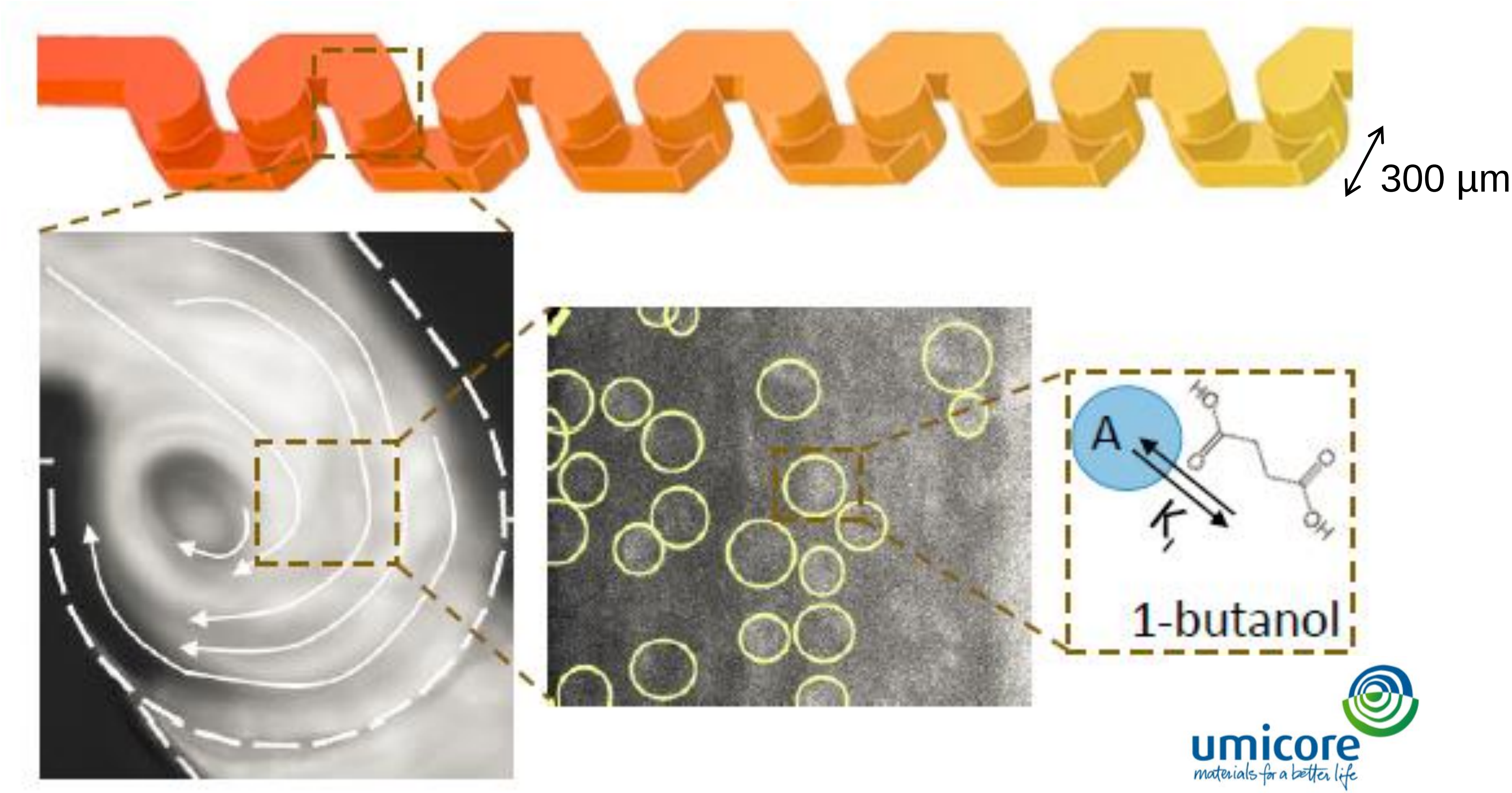








Vortex contact – geometrical approach

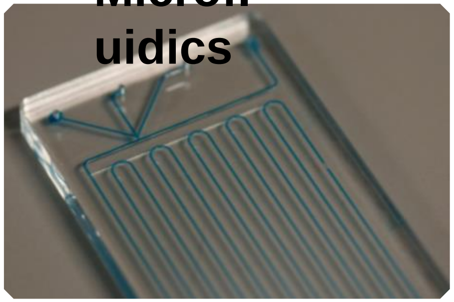


Vandermeersch, T., Goovaerts, R., Luyten, J., Denayer, J., De Malsche, W. (2015), Chemical Engineering Journal

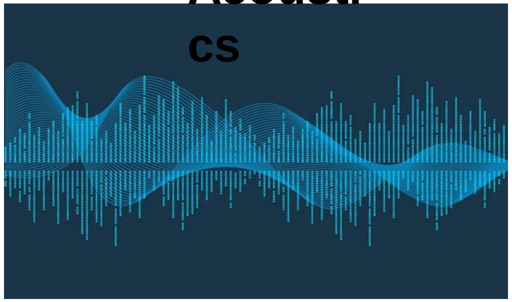
ACOUSTICS

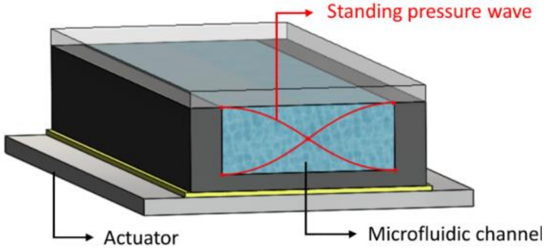
Acoustofluidics

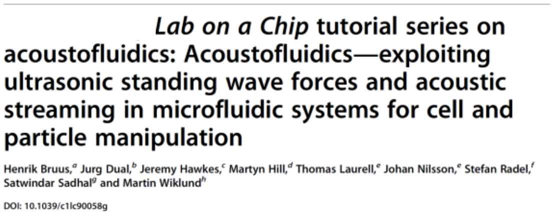
Microfl uidics



Acousti cs







Lab on a Chip tutorial series on acoustofluidics: Acoustofluidics—exploiting ultrasonic standing wave forces and acoustic streaming in microfluidic systems for cell and particle manipulation

Henrik Bruus,[a] Jurg Dual,[b] Jeremy Hawkes,[c] Martyn Hill,[d] Thomas Laurell,[e] Johan Nilsson,[e] Stefan Radel,[f] Satwindar Sadhal[g] and Martin Wiklund[h]

DOI: 10.1039/c1lc90058g

Acoustofluidics = ultrasound-based manipulations in microfluidic devices

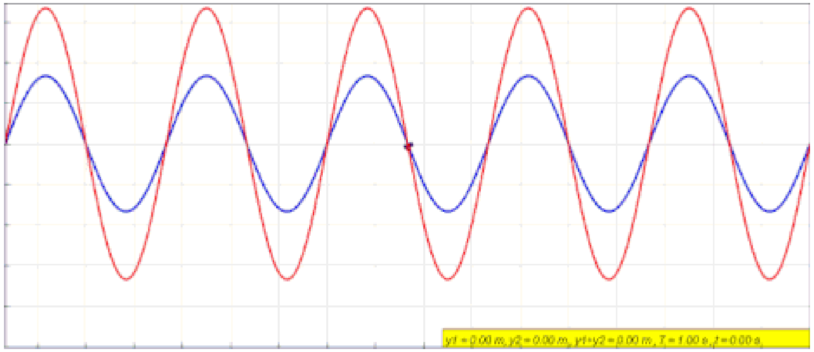
Acoustofluidics

- Operates in the MHz range → λ < 1 mm
- Maximum energy transfer at resonance frequency → generate a standing wave
- Criterion for a standing wave in micro-cavity:

$$Channel\ width = n * \frac{\lambda}{2}$$

$$wavelength\ \lambda = c/f$$

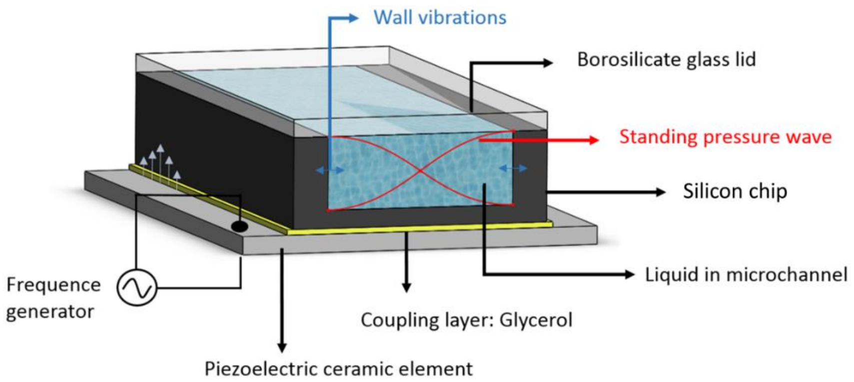
c: Speed of sound [m/s]
f: Frequency [Hz]
λ: Wavelength [m]



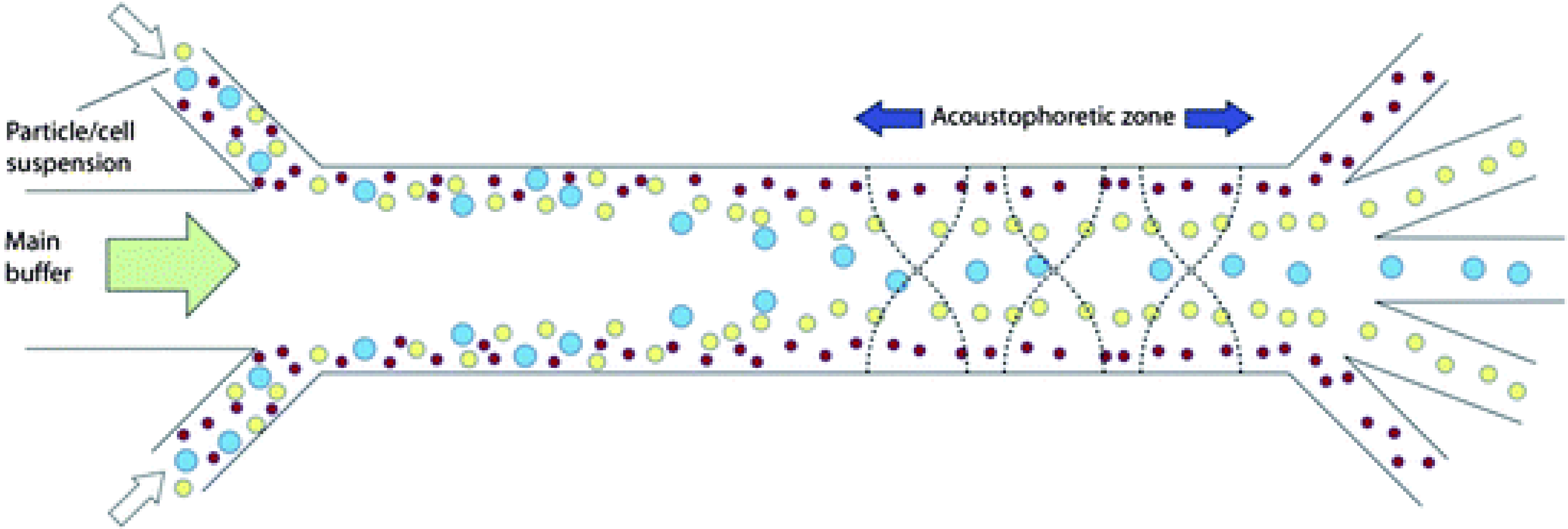
$$f(x,t) = A * e^{i(kx \pm \omega t)}$$

Acoustofluidics

- **Bulk acoustic waves (BAW)**
  - Whole device vibrates and standing wave in generated in “matched” direction
  - Generated by piezoceramic element (PZT)
  - Chip made of non-elastic material to ensure reflection of pressure wave (glass; silicon; metals; …)
  - Frequency: 1 - 10 MHz



Acoustophoresis of particles



A. Lenshof. Lab on a Chip, 2012

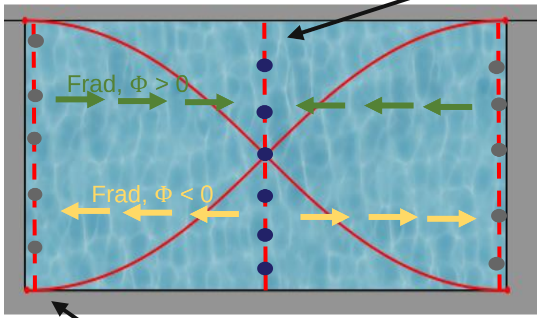
Acoustic manipulation of particles

Particles are affected by acoustic field:

- Radiation force: $F_{rad} = n4\pi\ \Phi \boxed{a^3} \frac{E_{ac}}{\omega} \sin(n2\pi \frac{y}{\omega} + n\pi)$
- Stokes drag force: $F_{drag} = 6\pi\eta \boxed{a} \left(v_{liq} - v_{particle}\right)$

Particle diameter

- Small particles (<2 µm)
  - Mostly influenced by F_{drag}
  - Follow liquid vortices
- Large particles (>2 µm):
  - Affected by F_{rad}
  - Focus in pressure node or antinode depending on Φ. (Hard/Soft particle)

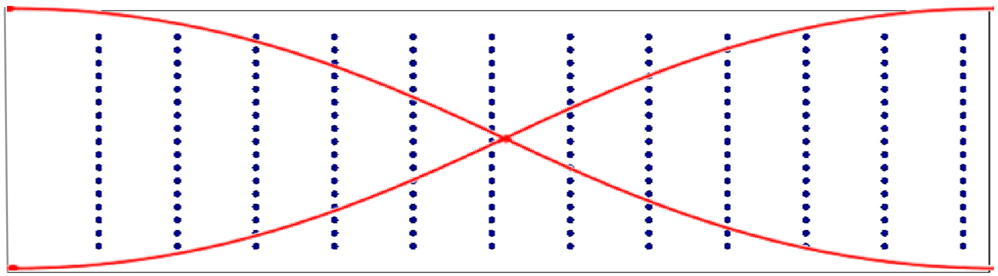


Hard particle on pressure node

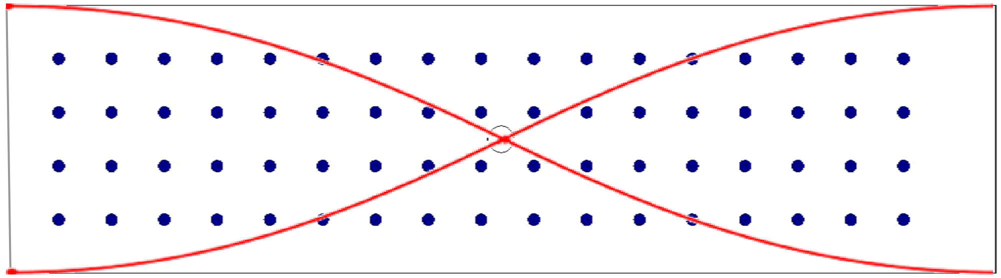
Soft particle on pressure antinode

Acoustic manipulation of particles

Polystyrene particles diameter= 0.5 µm

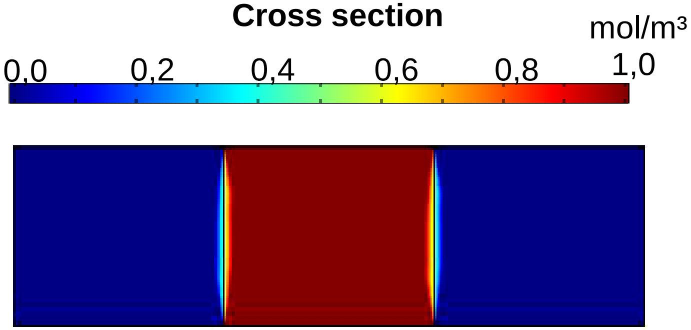


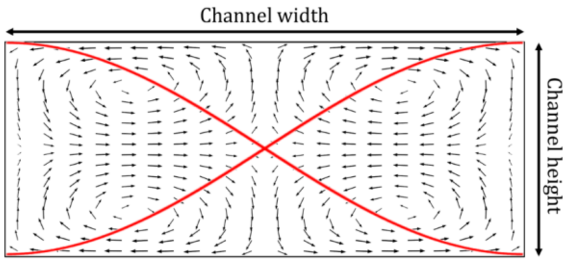
diameter= 5.0 µm



Comsol simulation, unpublished, µFlow group

Enhanced mixing with acoustics

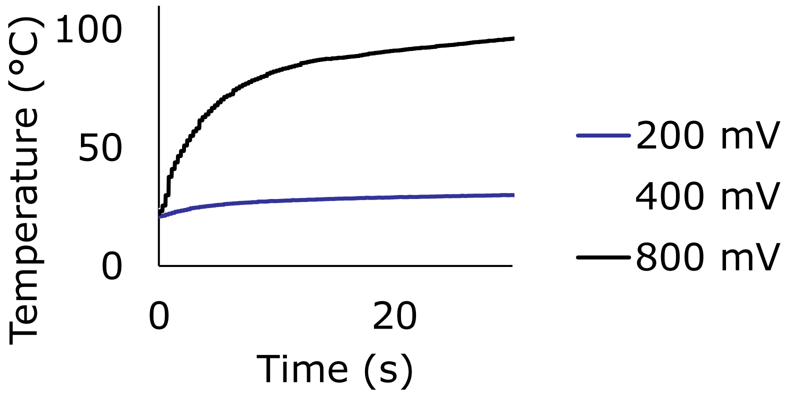


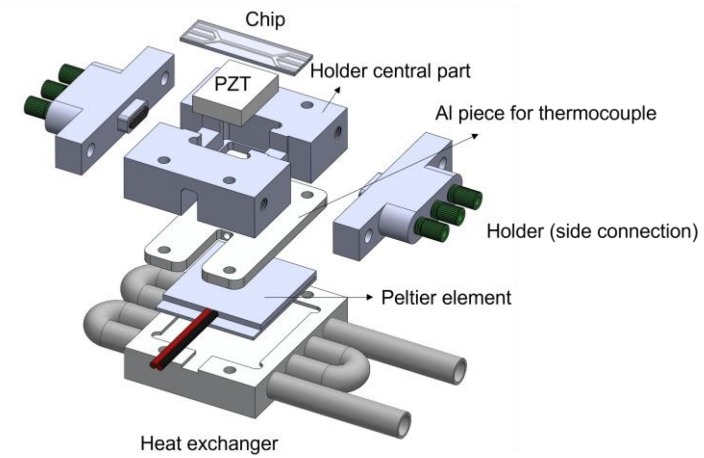


sub-s mixing
in a 375 µm channel

Gelin, P., Sukas, O.,Hellemans, K., Maes, D., De Malsche, W. (2019), Study on the mixing and migration behavior of micron-size particles in acoustofluidics, Chemical Engineering Journal, 369, 370-375

Acoustics - heating considerations



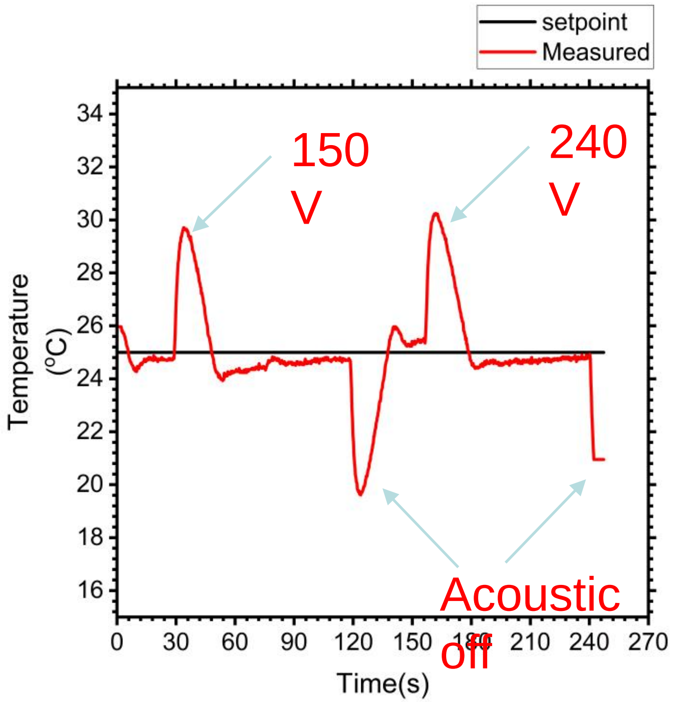


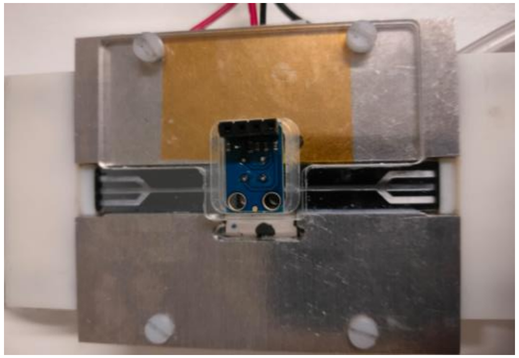
When actuated, the PZT generates heat depending on the voltage applied

-> interference with the primary source of waves.

Solution: Peltier-based PID feedback controller

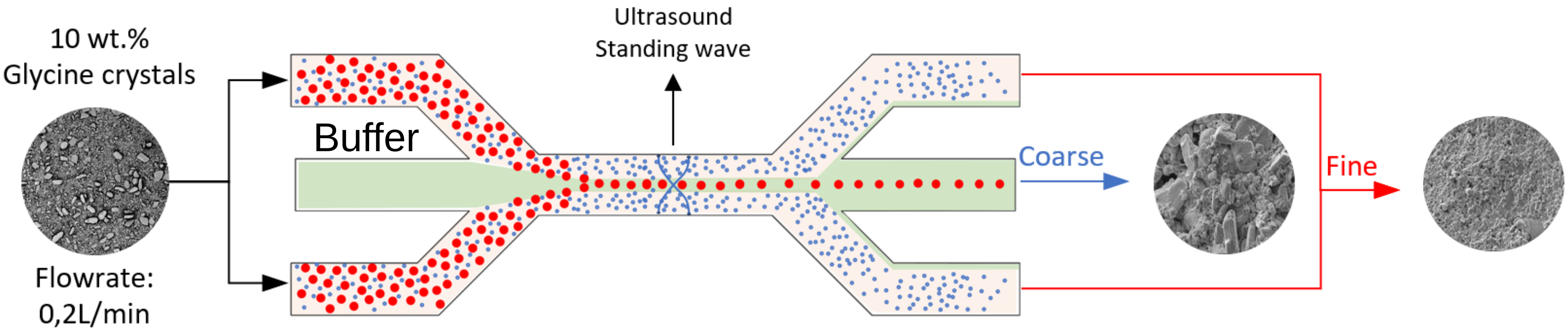
Acoustics - heating considerations





Infrared sensor

Acoustofluidic separation



Acoustic separation – high solid loads

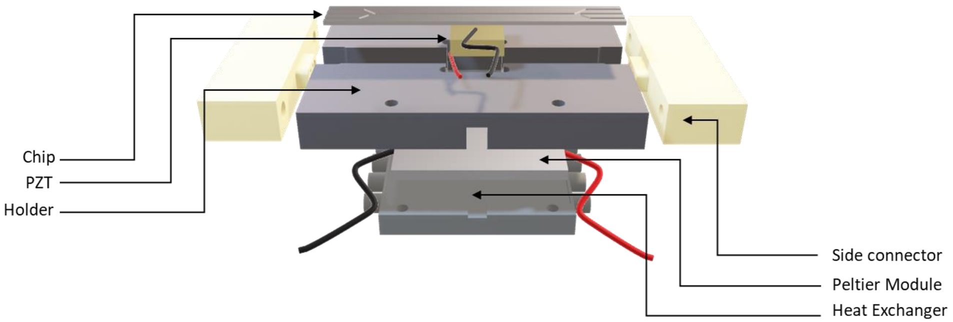
Process conditions:

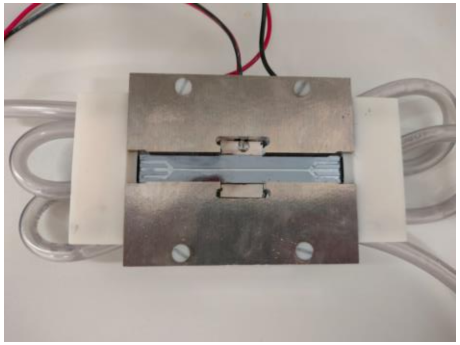
Flowrate: 3.6 mL/min

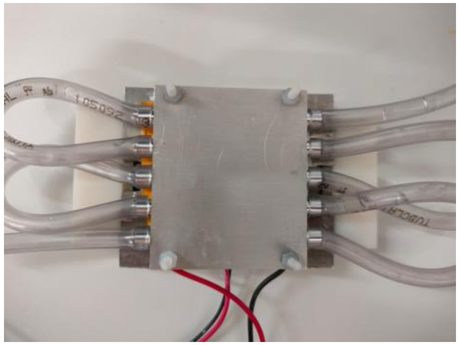
Concentration: 10,0%

Potential: 240 V

Temperature: 30°C







Stability of separation tested up to 24 mins

(vial empty)

Acoustic separation – high solid loads

Process conditions:

Flowrate: 3.6 mL/min

Concentration: 10,0%

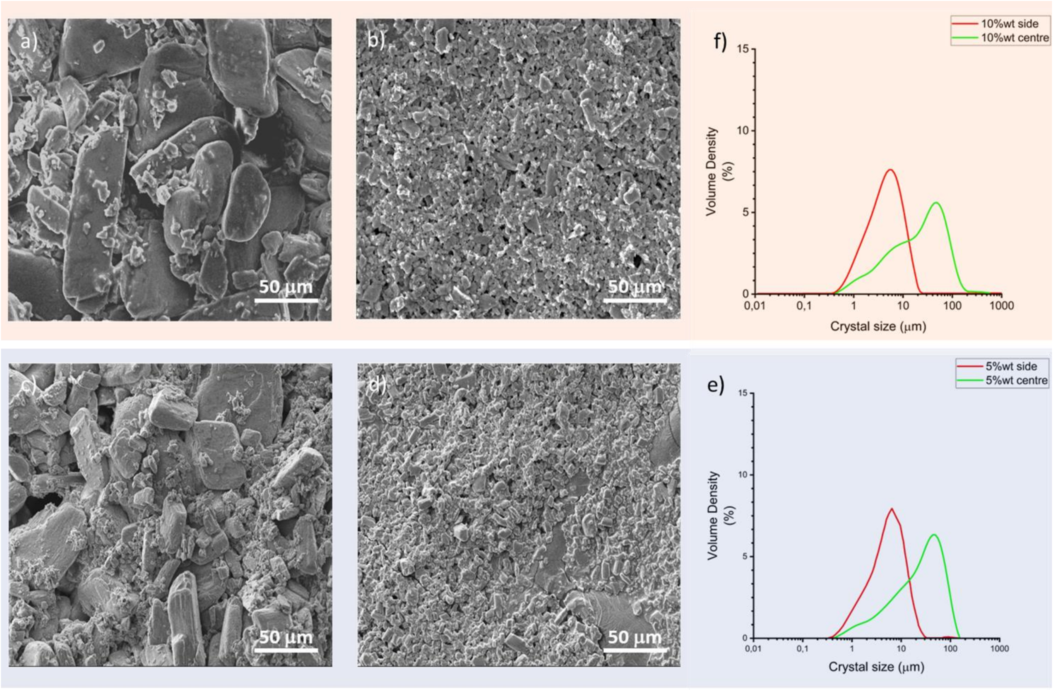
Potential: 240V

Temperature: 30°C

Separation confirmed by SEM & Particle sizing

5%
solid load

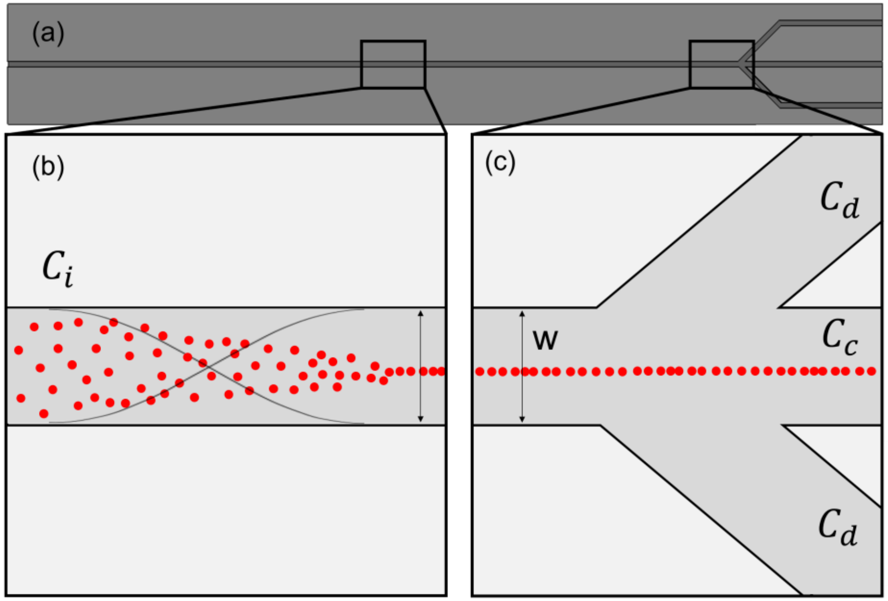
10%
solid load



center

side

Increase of cell suspension concentration



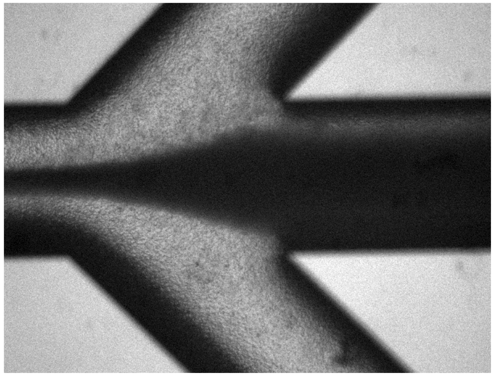
$$F_{rad} = 4\pi k\Phi a^3 E_{ac} sin(2yk + \pi)$$

$$Concentration\ factor\text{: } F_c = \frac{C_c}{C_i}$$

Saccharomyces cerevisiae (Yeast), 10^9 cells/ml

Increase of cell suspension concentration

Saccharomyces cerevisiae



Cells	Chip height (µm)	Potential (mV)	Cell volume content (%)	Cells/ml	Flow* (mg/min)	Fc
Yeast	250 µm	200	7,06	$2.65*10^{8}$	15	2,94
			14,11	$5.30*10^{8}$		2,22
			70,57	$2.65*10^{9}$		1,27
	435µm	400	14,11	$5.30*10^{8}$	50	1,99
					100	1,64
		800			50	2,73
					100	1,74

*1g considered as 1 ml

Parameters:

- Chip height
- Potential
- Solid content
- Cell initial concentration (solid content)
- Flow

Conclusions

- Laminar flows
  - Great, but not always…
  - Increasing channel sizes: diffusion limitations gain importance
  - Taylor-Aris dispersion reduces concentration, increases spreading and flow heterogeneity
  - Novel emerging lateral flow methodologies can address this
- Increasing throughput
  - Flow distribution critical
  - Enhancing (lateral) mass transport essential
  - Particles size determines whether particles focus
  - 2.5 D → 3D organization increases attainable throughput
- Many opportunities with (structured) μreactors
- Limited applications in industry, due to:
  - Low throughput
  - Fouling
  - Unknown technology