From microfluidics at TIPs to Secoya

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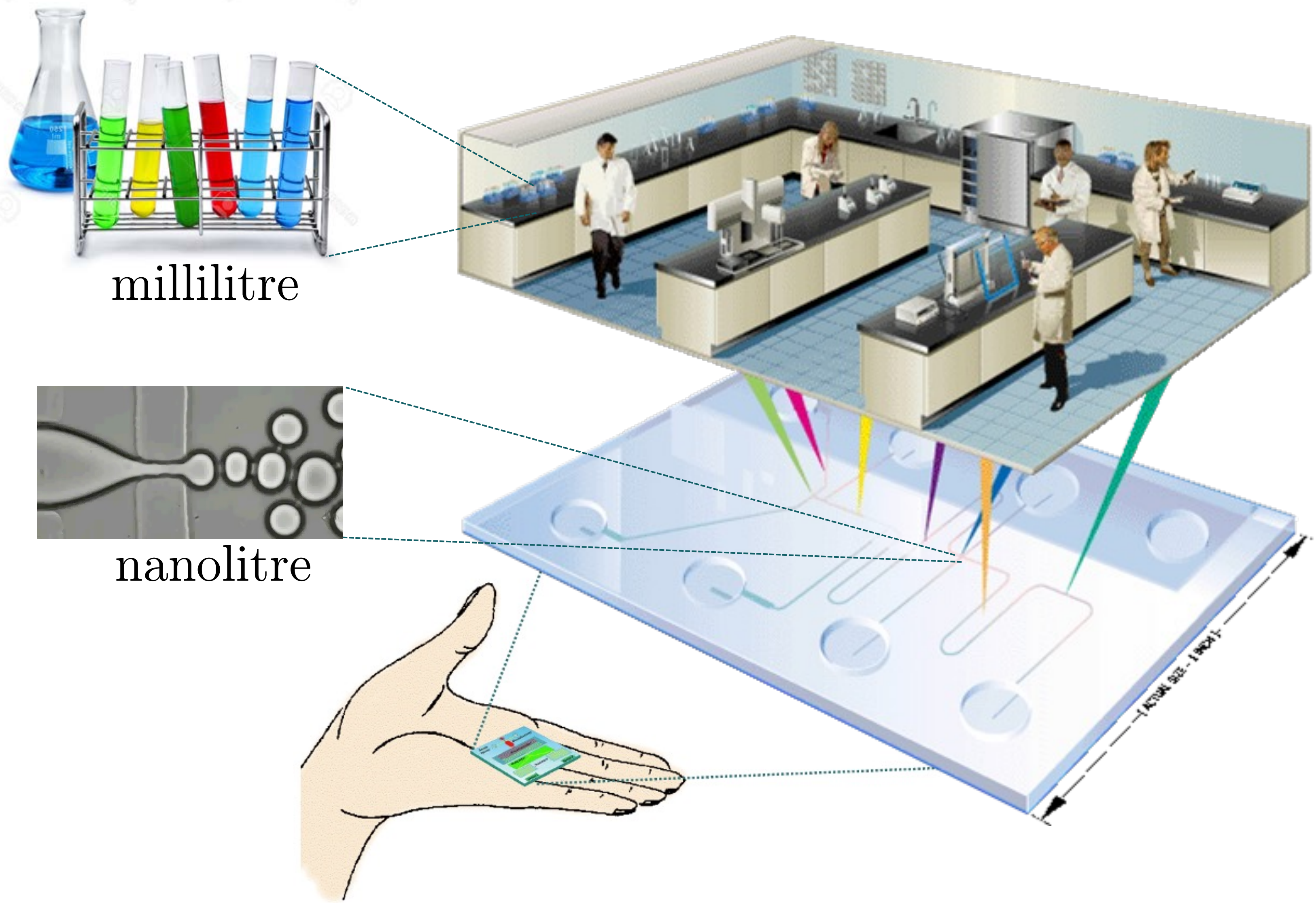
TIPs – Transfers, Interfaces & Processes
Université Libre de Bruxelles

CRISTA'DAYS - November 8th

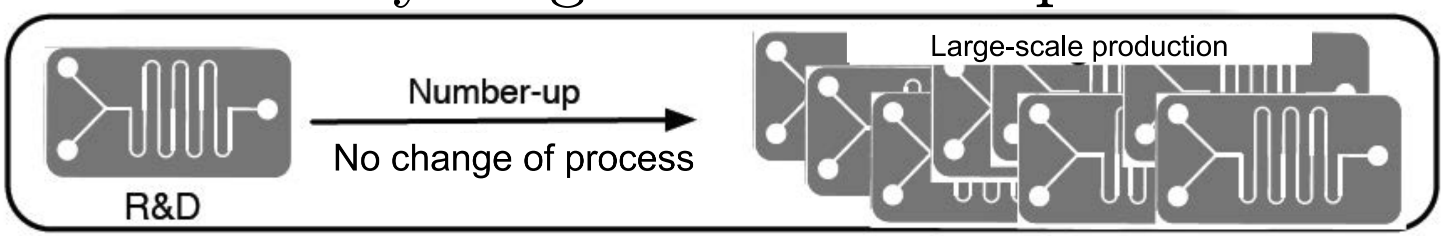
Microfluidics & Lab-on-a-chip



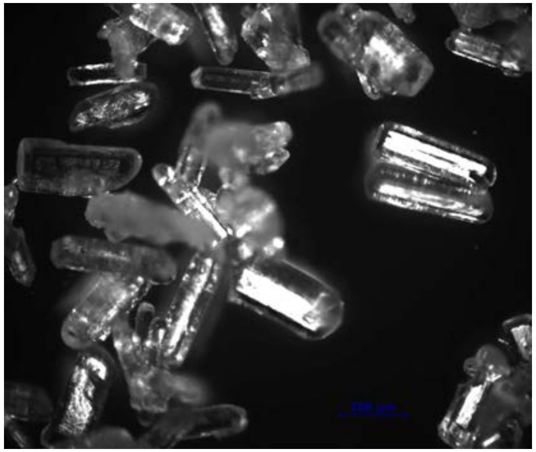
Microfluidics for production ?

- Better quality
- Lower footprint
- Lower consumption

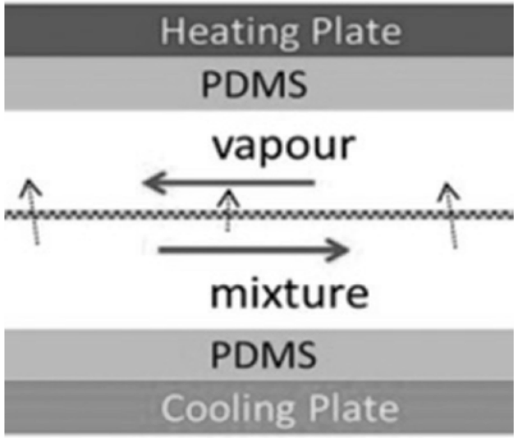
From early stage to full scale production



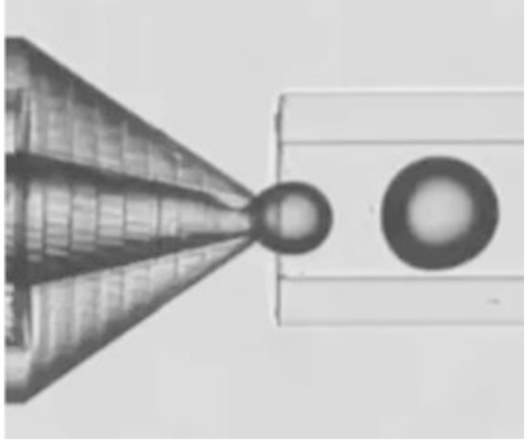
- Lower development cost
- Reduce time to market
- Flexibility in production



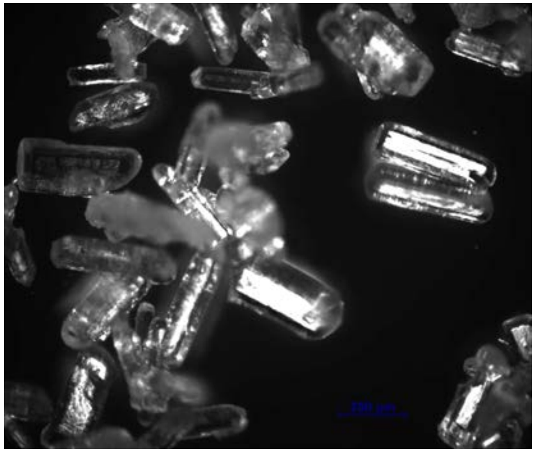
1) Flow crystallization



2) Solvent extraction by pervaporation



3) Micro-emulsification



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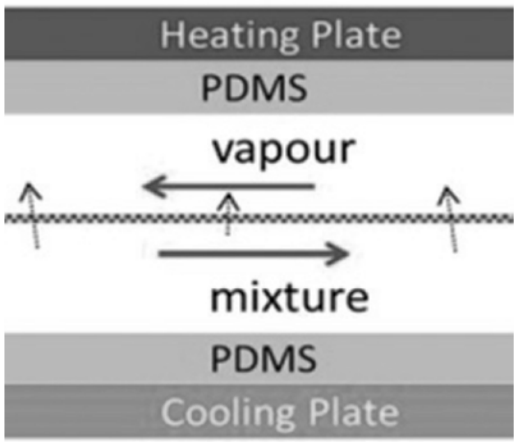

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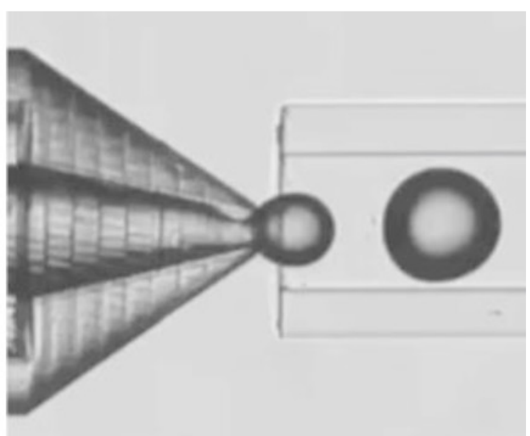
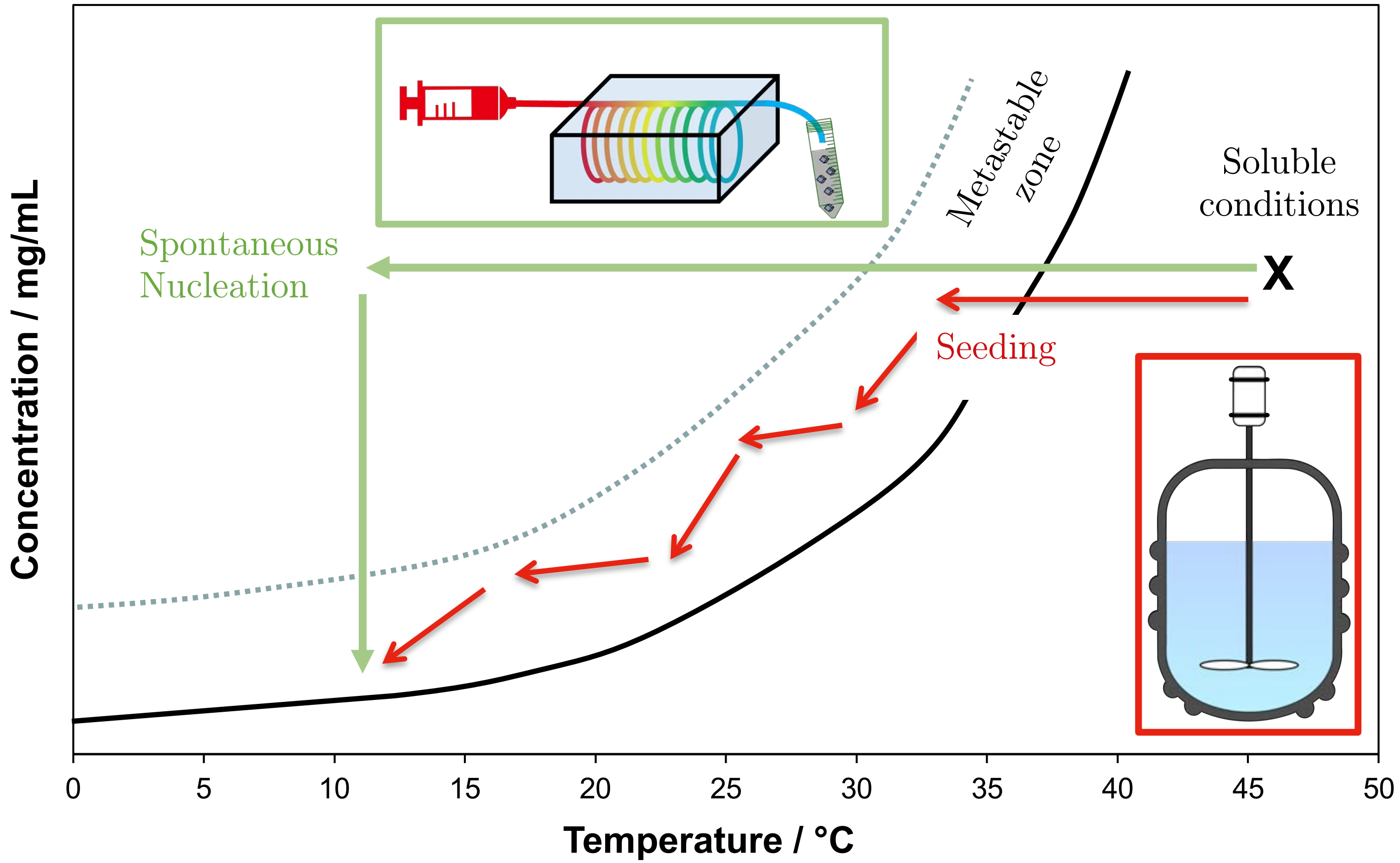
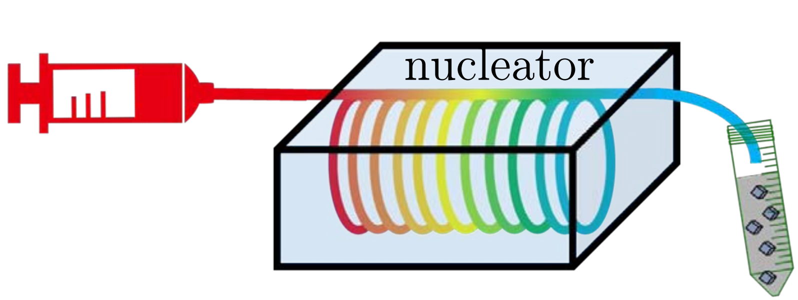


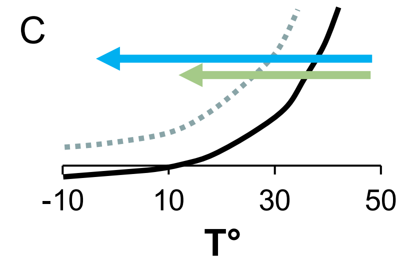
3) Micro-emulsification

Flow vs. batch crystallization of APIs



Fine control of the nucleation rate

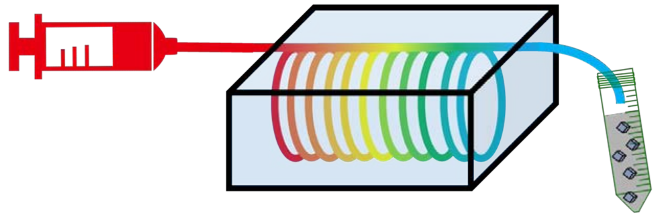


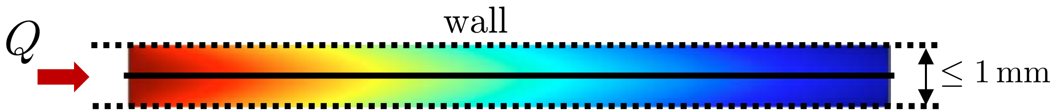


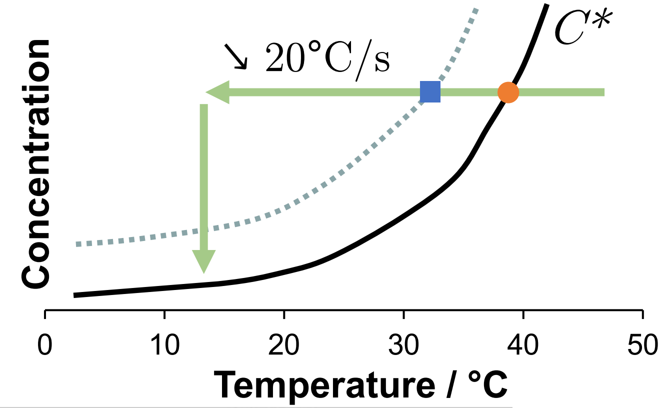
High nucleation rate

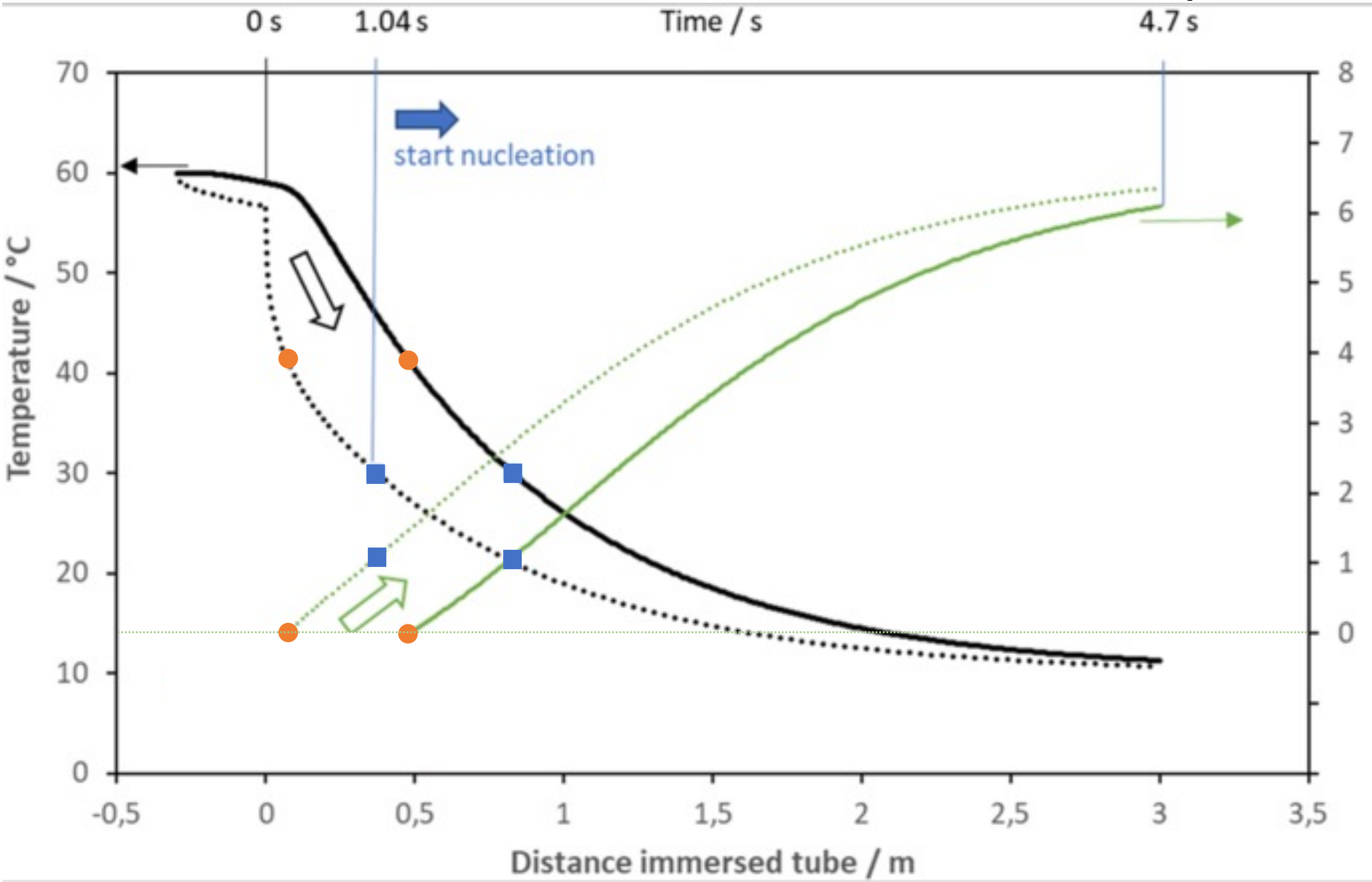
Low nucleation rate

Modeling







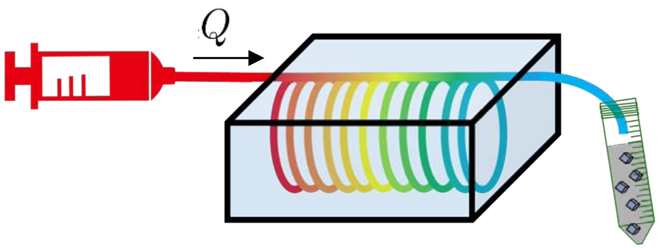


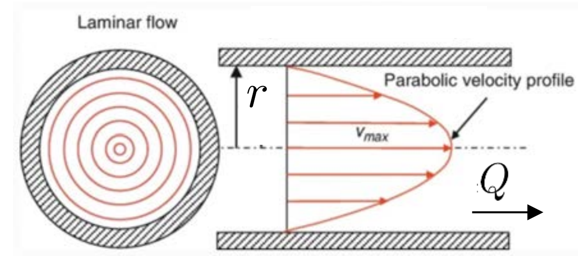
supersaturation

$$\sigma = \frac{C - C^*}{C^*}$$

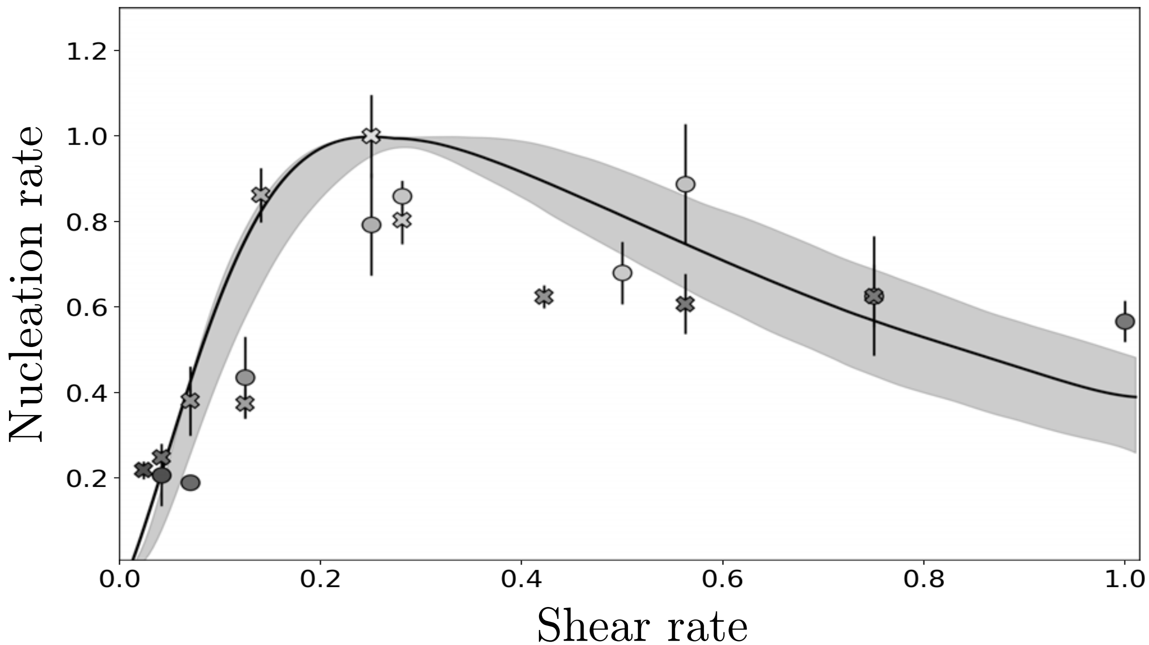
[Rimez, Septavaux, Debuysschère & Scheid, Journal of Flow Chemistry, 2019]

Influence of shear on the nucleation rate

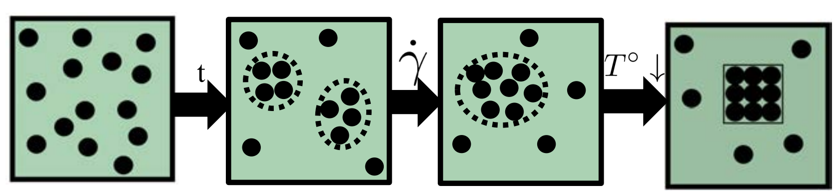




$$\dot{\gamma} = \frac{4Q}{\pi r^3}$$

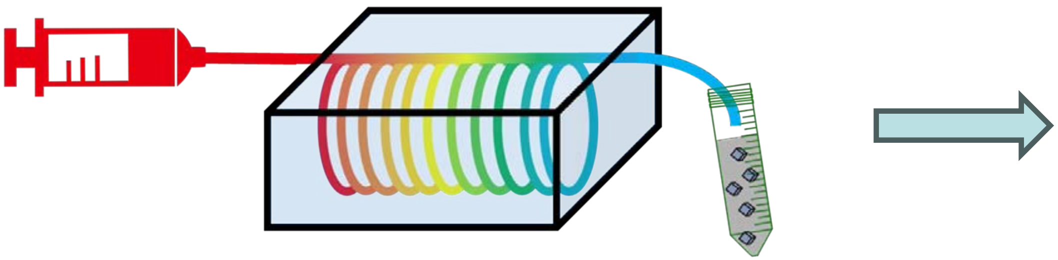


Non-classical nucleation theory:



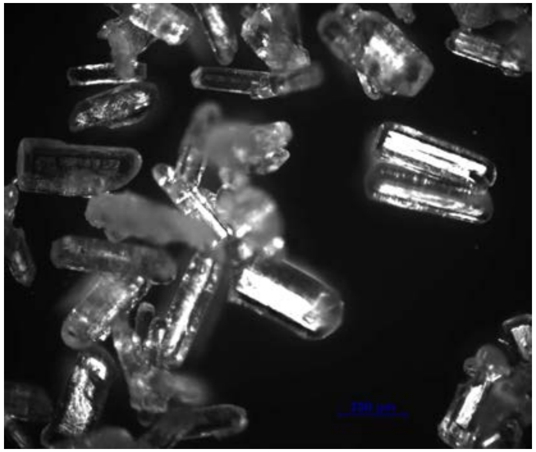
[Debuysschère, Rimez, Zaccone & Scheid, Crystal Growth and Design, 2023]

From TIPs to Secoya



Robin Debuysschère

Bart Rimez



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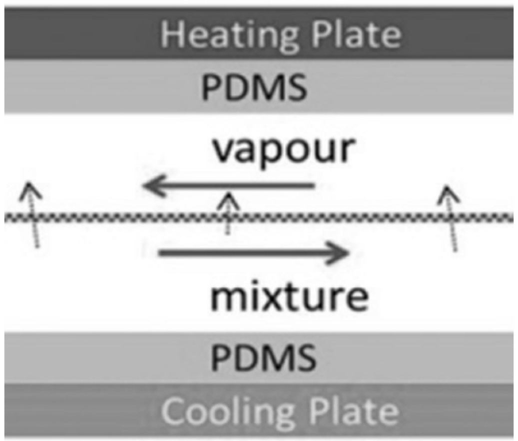
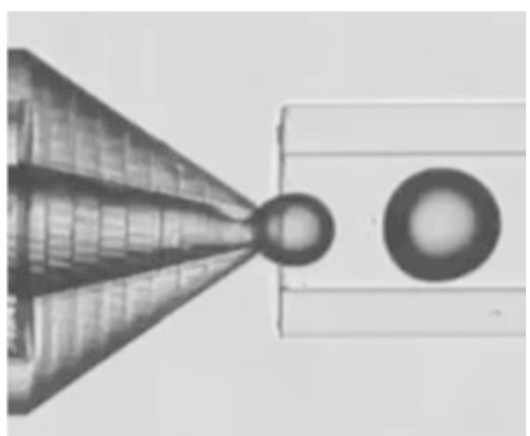
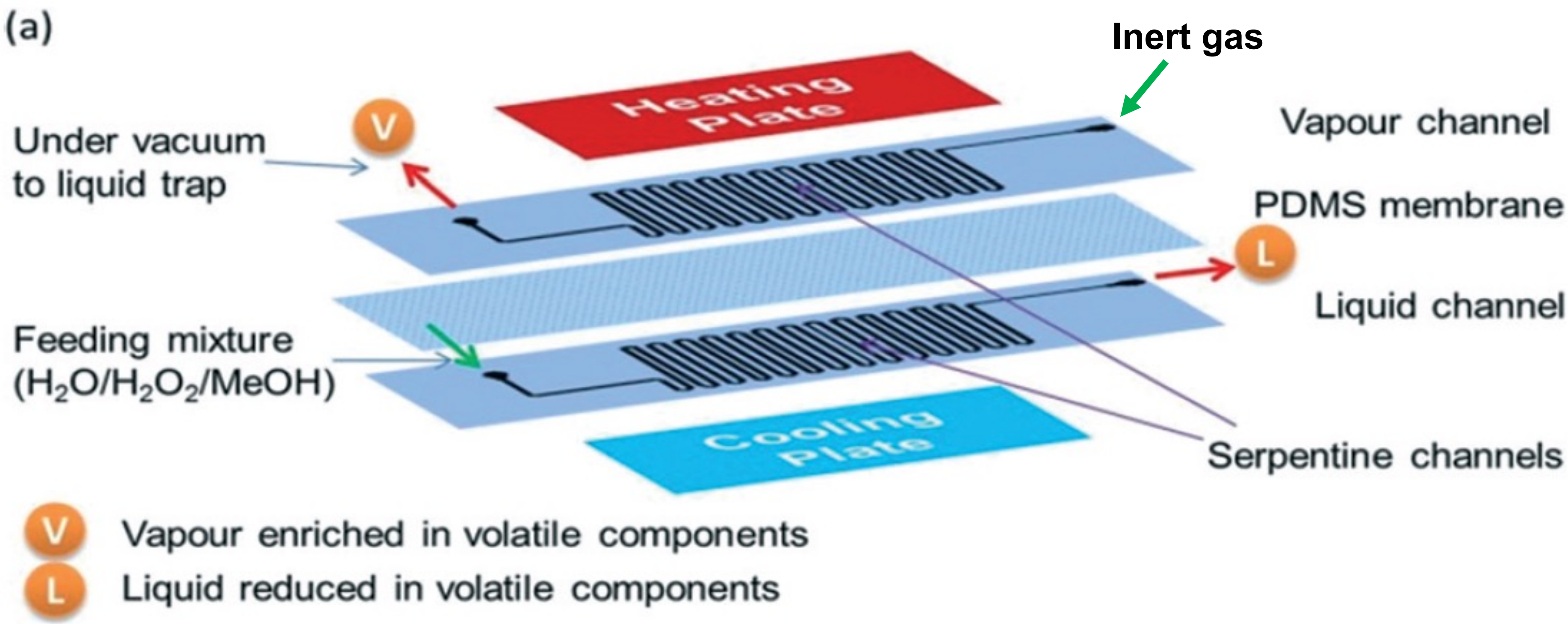


2) Solvent extraction by pervaporation



3) Micro-emulsification

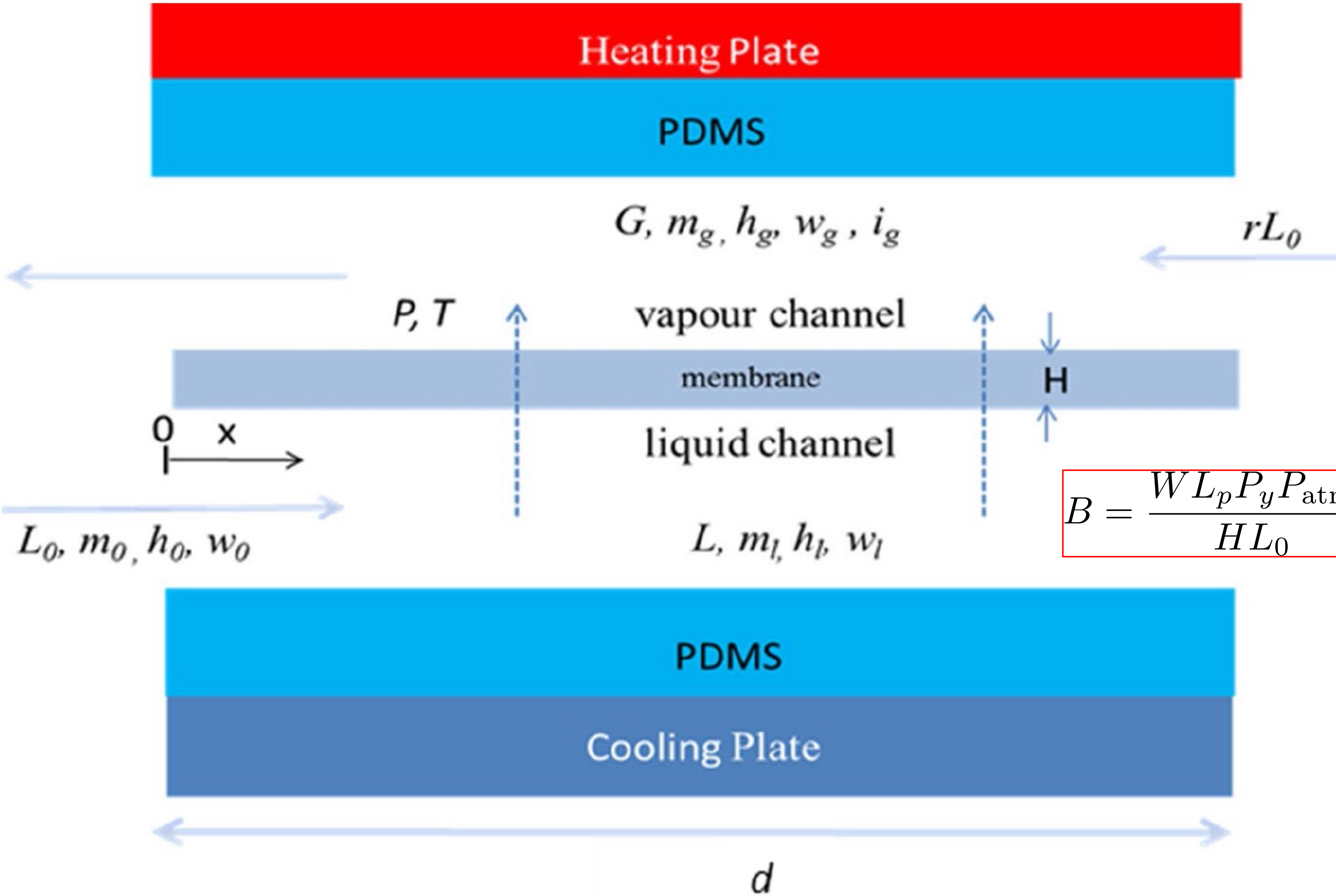
Separation by pervaporation



[Ziemecka, Haut & Scheid, Lab-on-a-chip, 2015]

Modeling

Purge-gas pervaporation



$$B = \frac{W L_p P_y P_{\text{atm}}}{H L_0}$$

Theoretical Efficiency

$$\eta_1 = 1 - \frac{L(L_p) m_l(L_p)}{L_0 m_0}$$

→ Quantifies the transfer of methanol from the liquid channel to the vapour channel

$$\eta_2 = \frac{L(L_p) h_l(L_p)}{L_0 h_0}$$

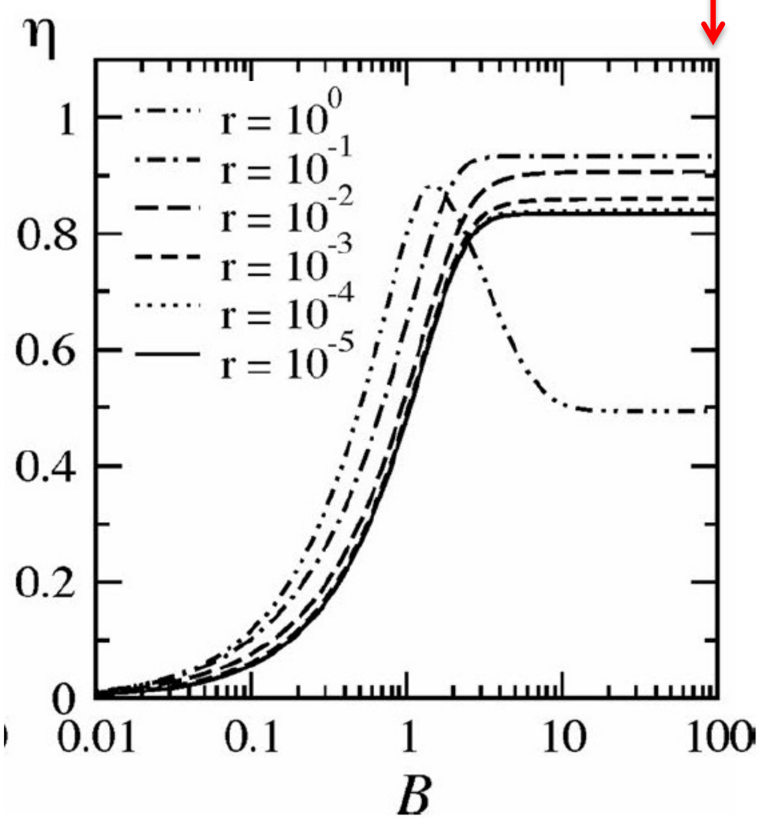
→ Quantifies the conservation of H_2O_2 in the liquid channel

$$\eta = \eta_1 \eta_2$$

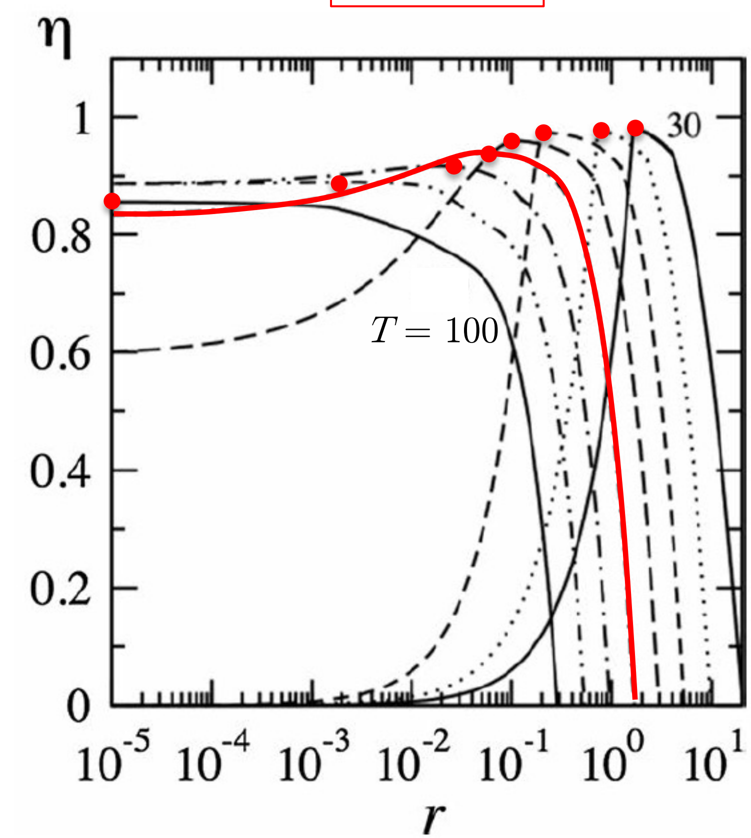
Overall efficiency of the chip

Theoretical Efficiency

$m_0 = 0.74,\ h_0 = 0.11,$
$T = 70°\text{C} - P = 0.5$ bar

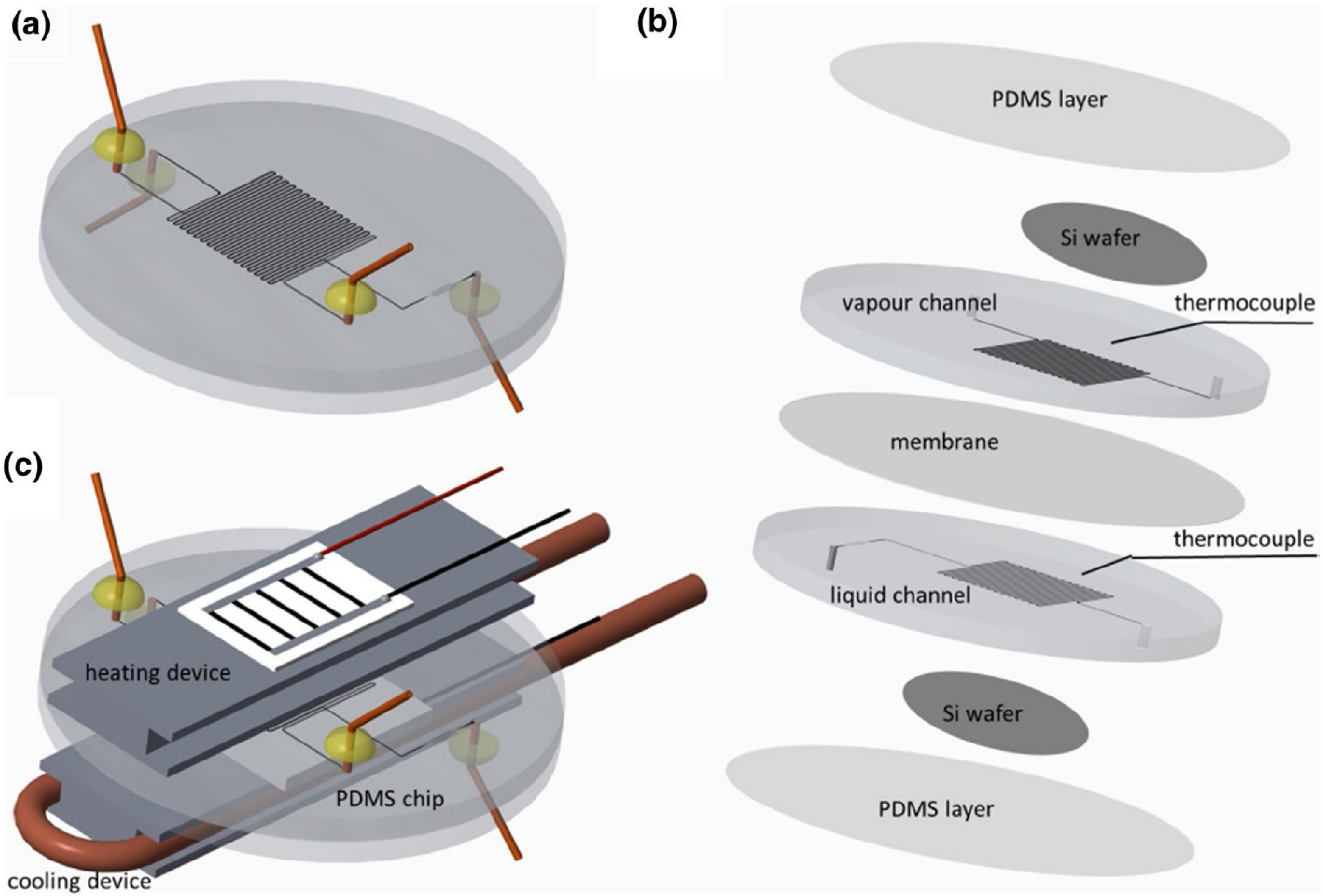


$B = 100$



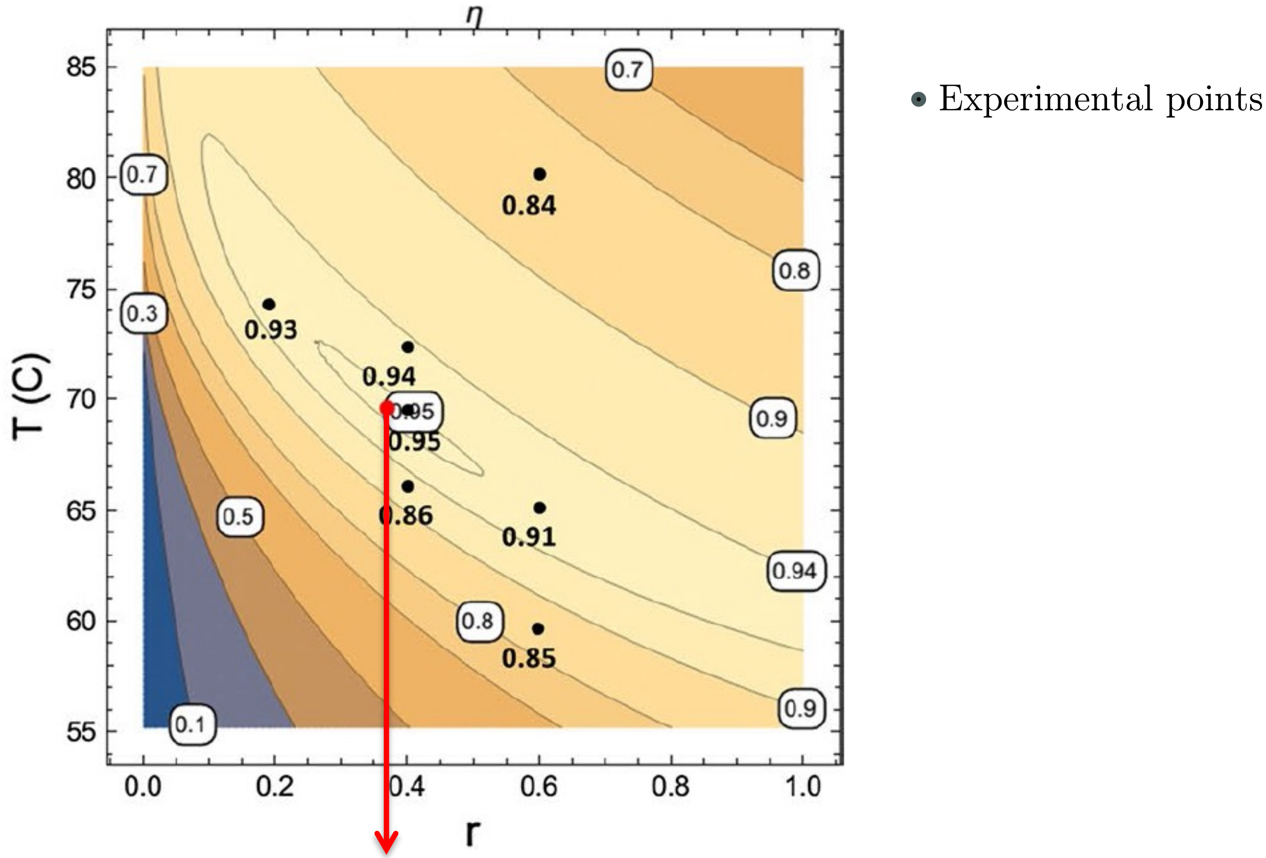
$$B = \frac{W L_p P_y P_{\text{atm}}}{H L_0}$$

Experimental proof-of-concept



Theory vs. experiment

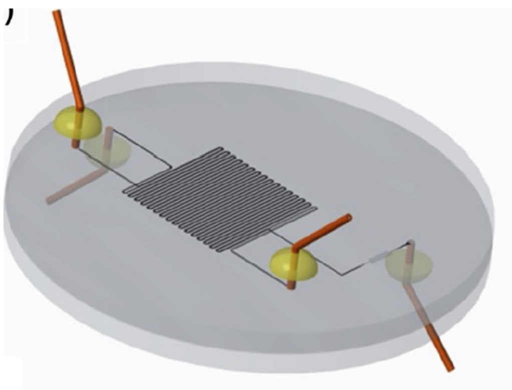
$B = 4.84$, $m_0 = 0.71$, $h_0 = 0.112$ and $P = 1$ bar.



Less than 1% methanol at the outlet
H2O2 concentration increase 3 times

[Ziemecka, Haut & Scheid, Microfluidics,& Nanofluidics, 2017]

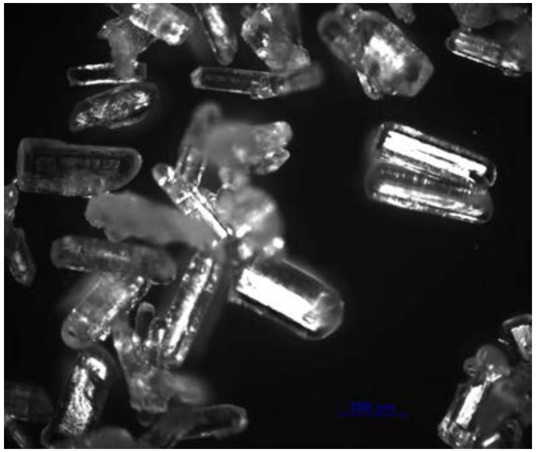
From TIPs to Secoya



Iwona Ziemecka

Benoit Haut

Jean Septavaux



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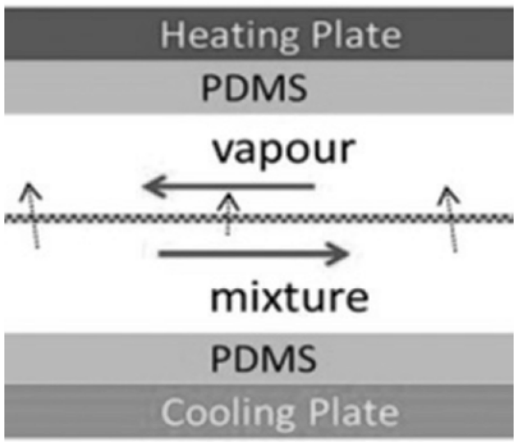

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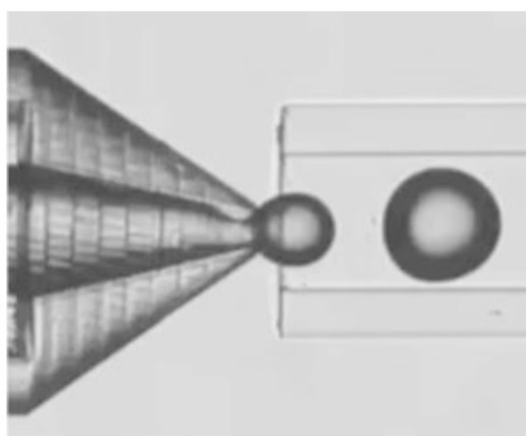
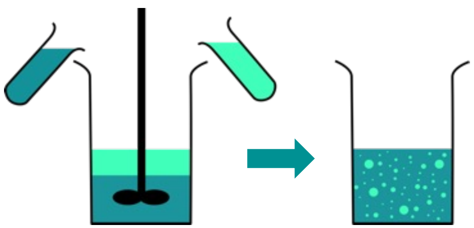


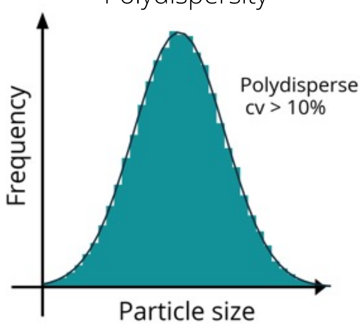
3) Micro-emulsification

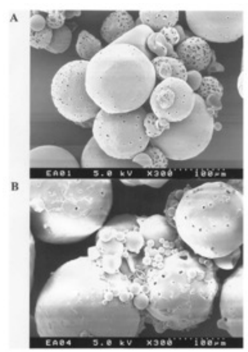
Micro-emulsification

Traditional emulsification in batch



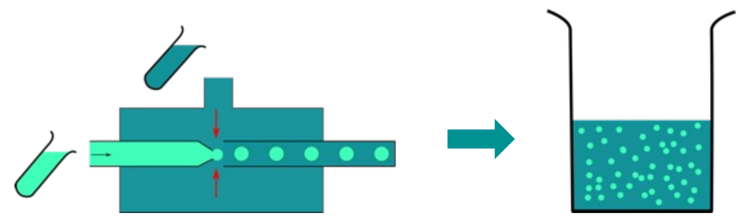
Polydispersity



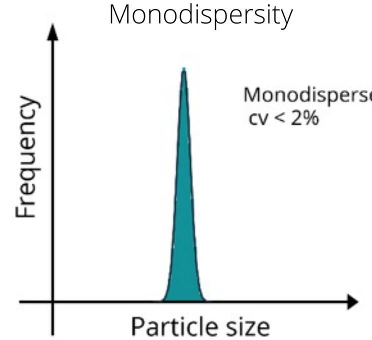


Poor sphericity

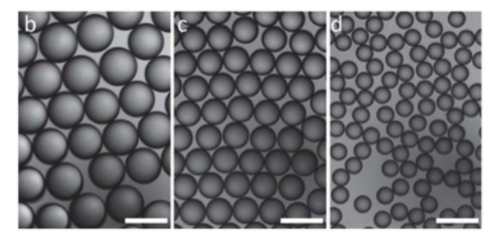
Microfluidic technology



Monodispersity

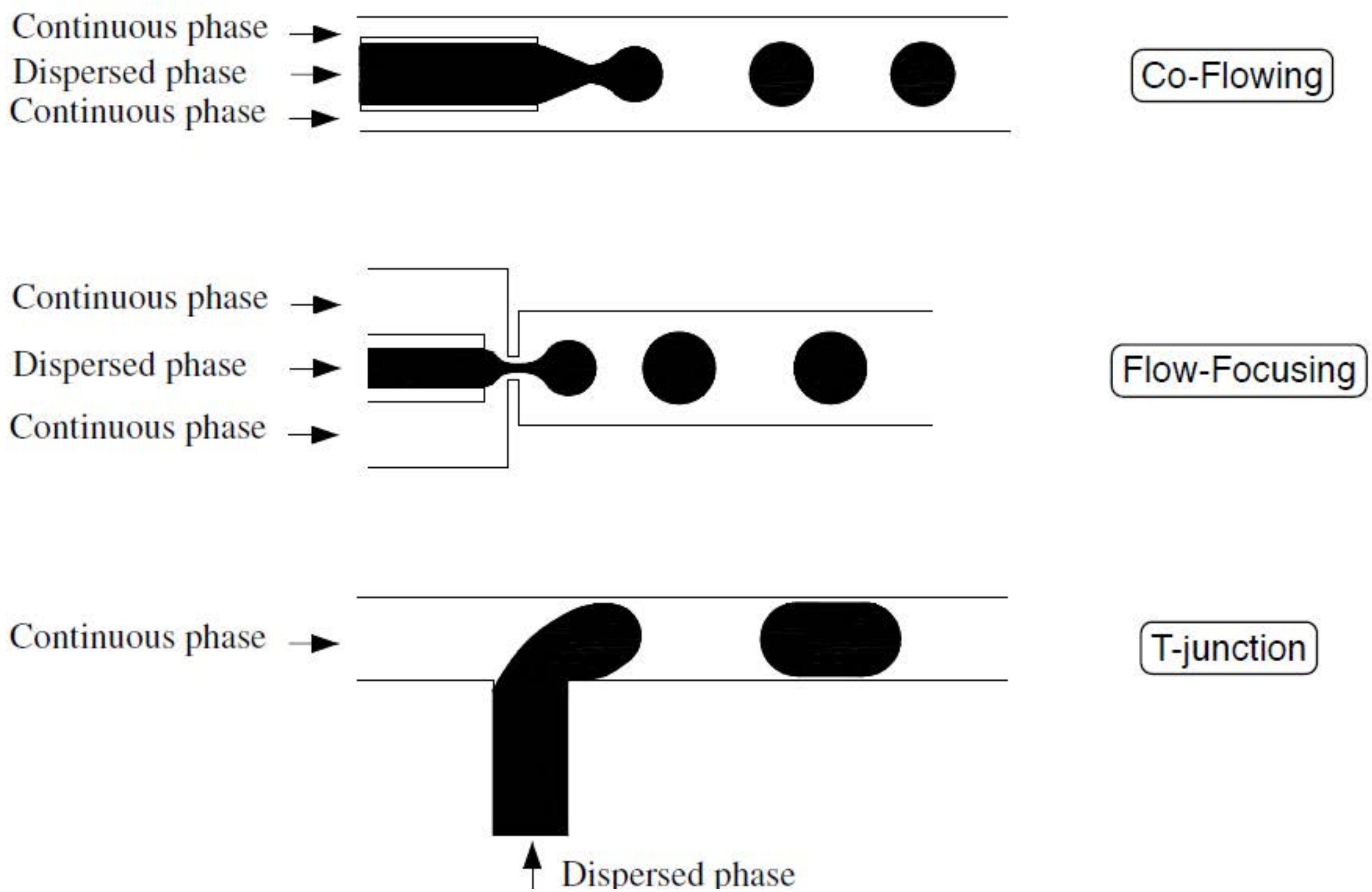


High sphericity

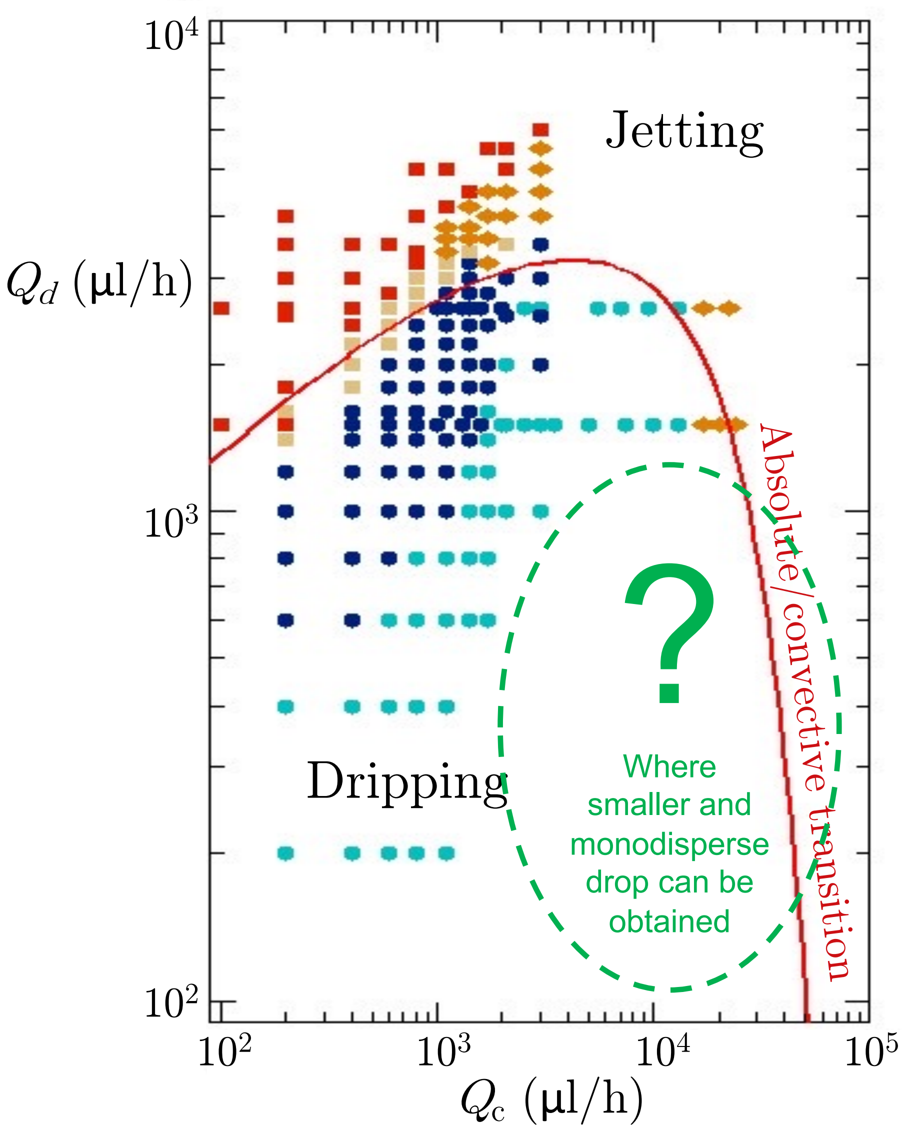


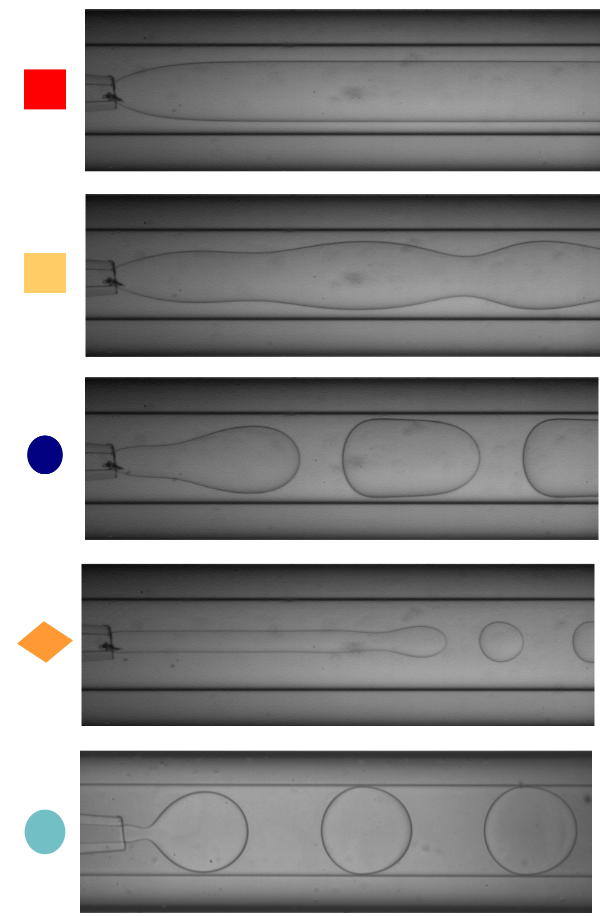
100 µm

Background
Different ways of making microdroplets



Co-flow



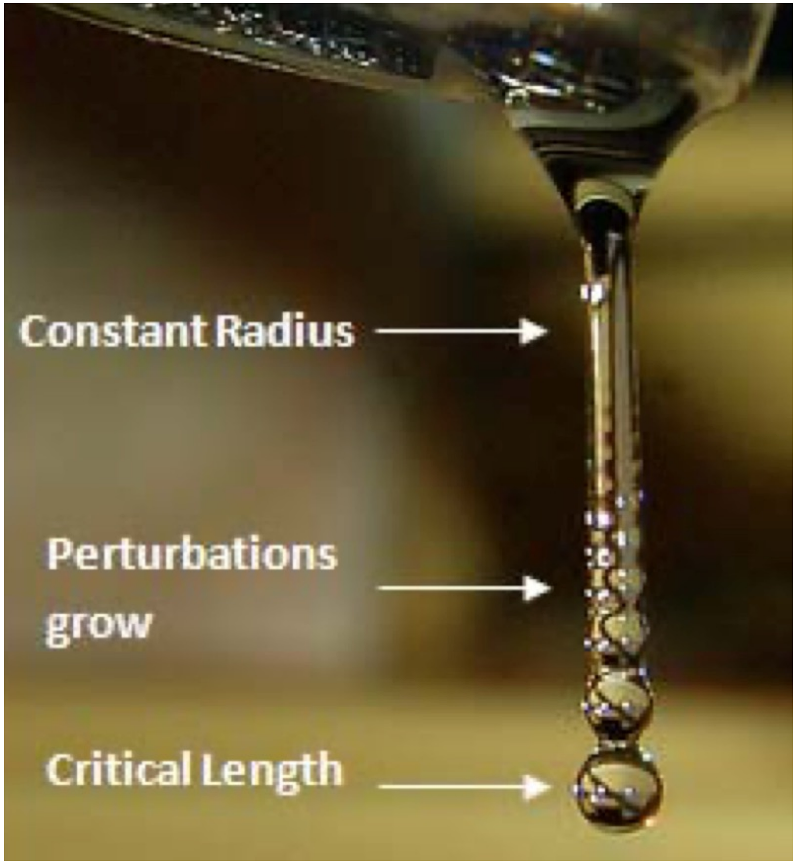


Guillot *et al.* Phys. Rev. Lett. 2007

Droplet generation: 2 mechanisms

1. Rayleigh-Plateau mechanism

(Dynamic instability)

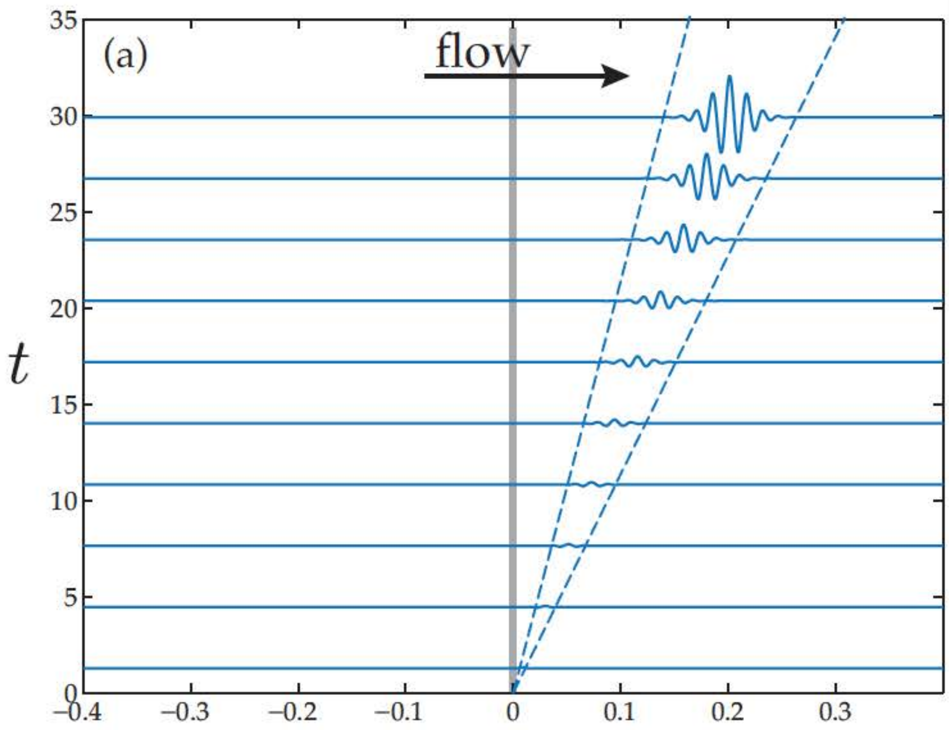


Dripping to jetting transition

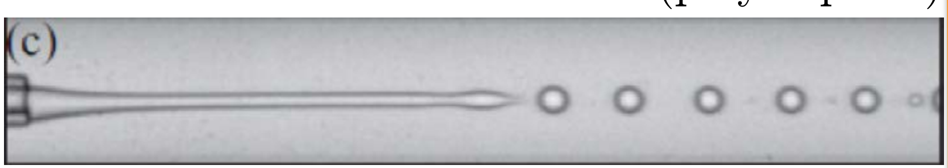
Rayleigh-Plateau mechanism

Convective instability → Jetting

breakup downstream from orifice

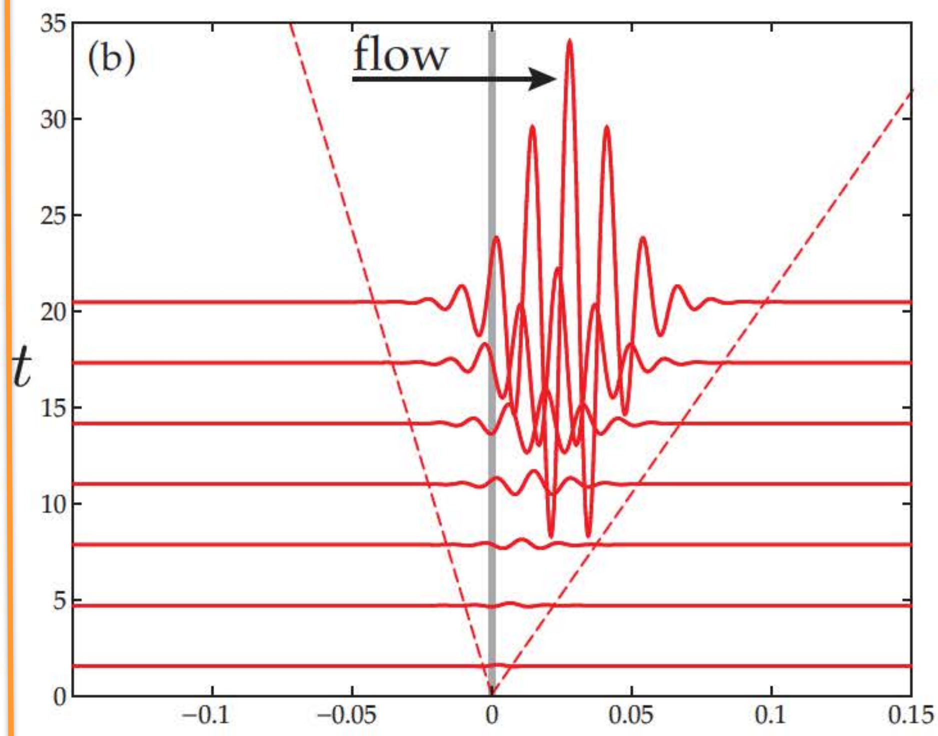


(polydisperse)



Absolute instability → Dripping

breakup at orifice



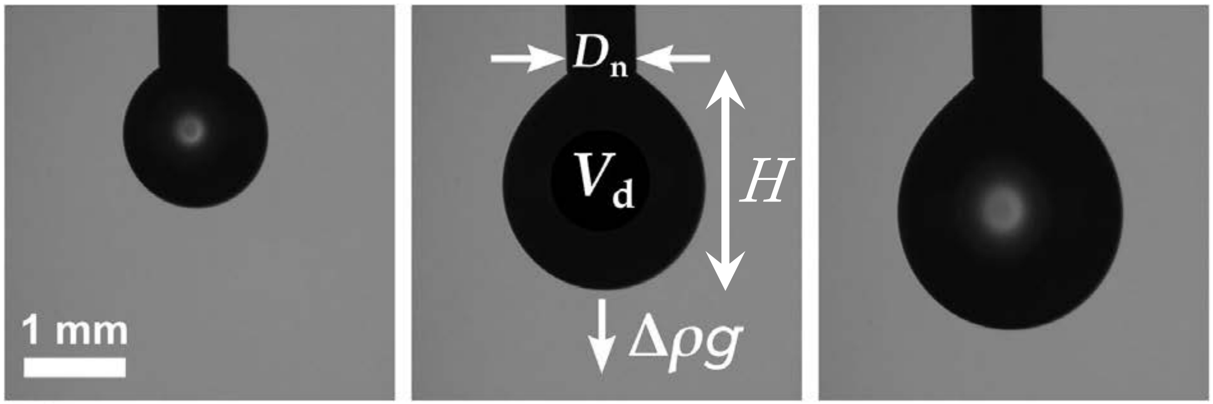
(monodisperse)

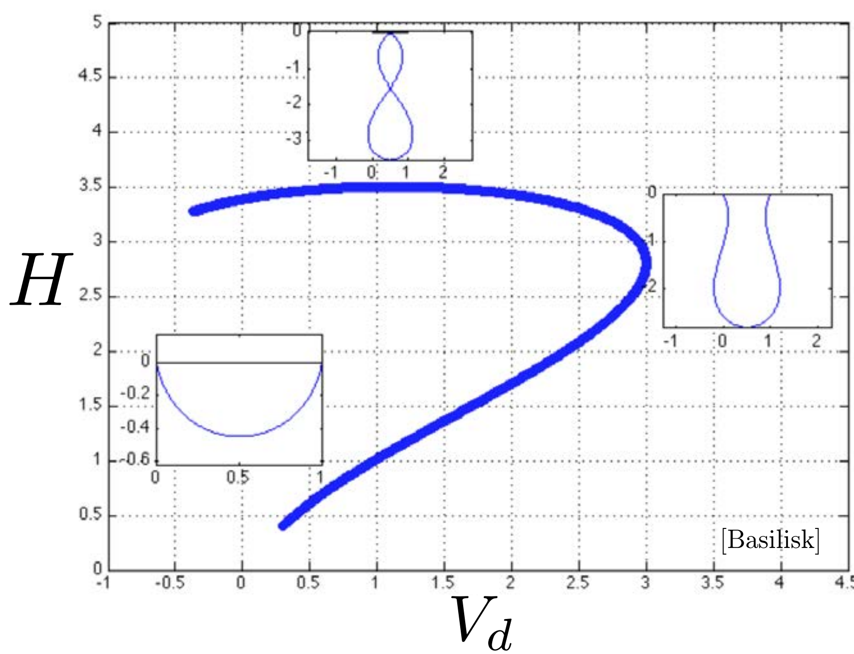
Utada et al. (2008)

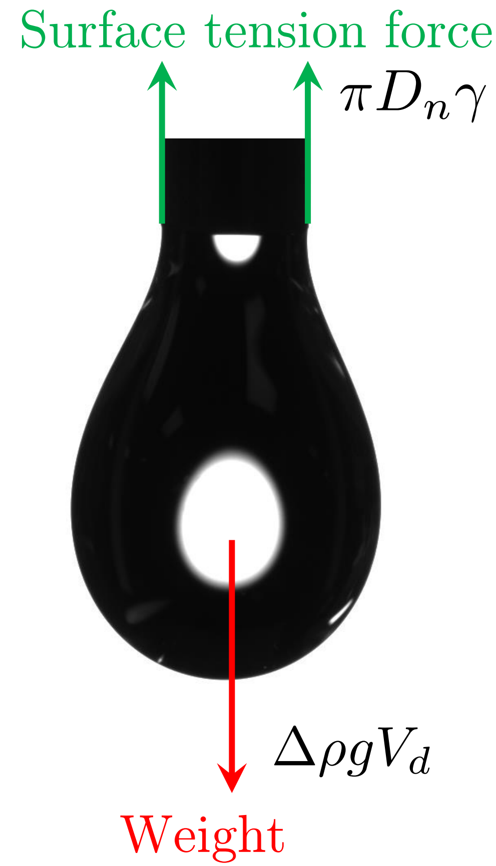
Droplet generation: 2 mechanisms

2. Pendent drop
(Static instability)

[Berry et al., JCIS, 2015]







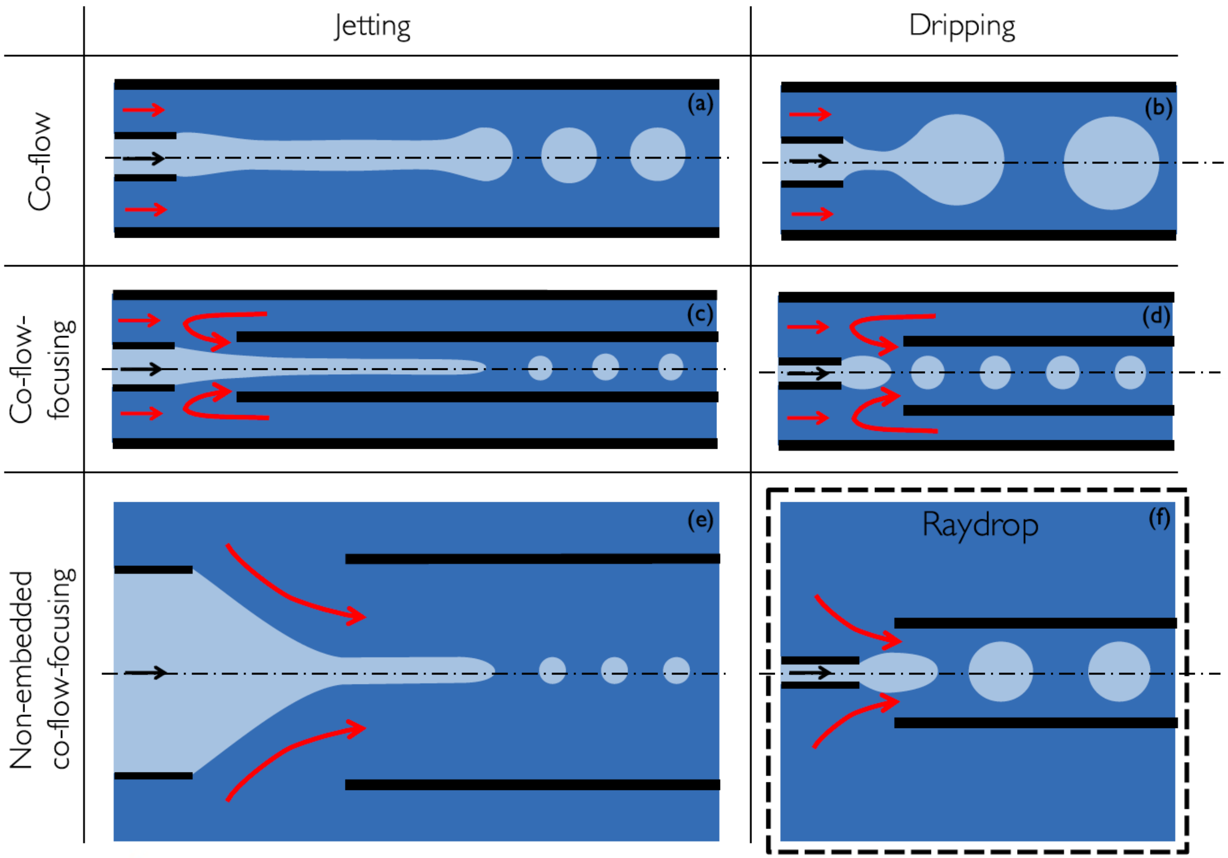
Worthington number:

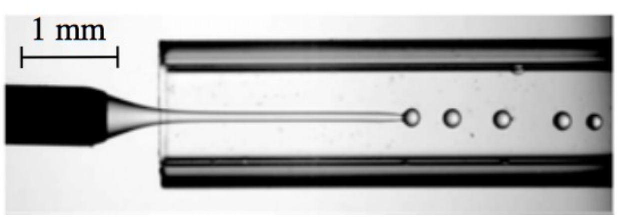
$$\mathrm{Wo} = \frac{\Delta\rho g V_{\mathrm{d}}}{\pi\gamma D_{\mathrm{n}}}$$

Micro-droplet generation

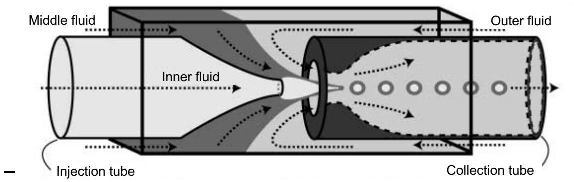
Rayleigh-Plateau mechanism
→ Dynamic instability

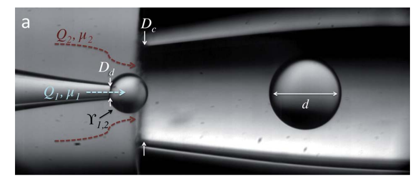
"Pendent droplet" mechanism
→ Static instability





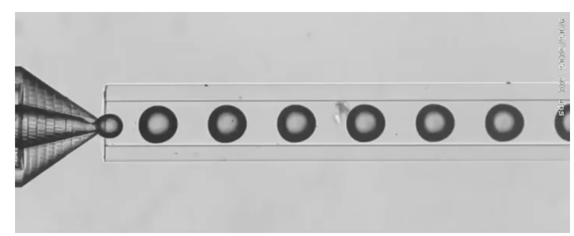
[Evangelio et al. 2016]





[Utada et al. 2005, Erb et al. 2011]

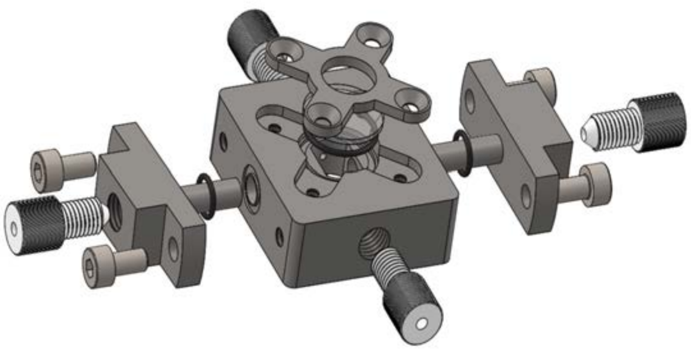
RAYDROP

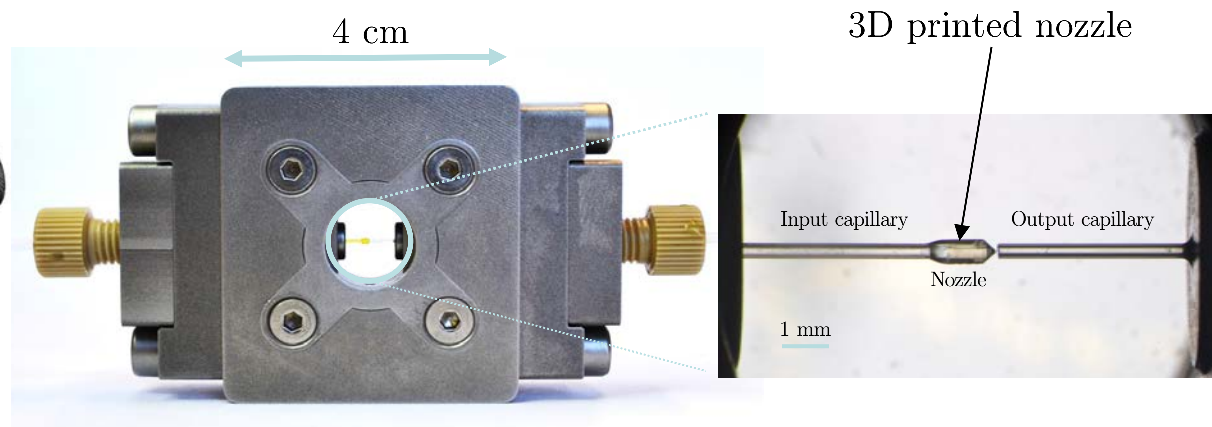


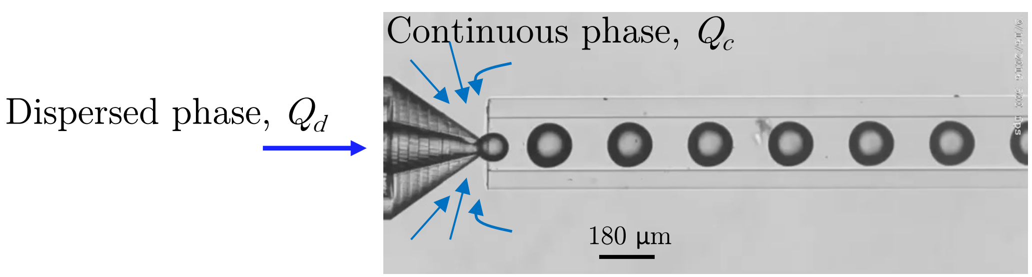
[Dewandre et al. 2020]

Raydrop

Non-embedded co-flow-focusing

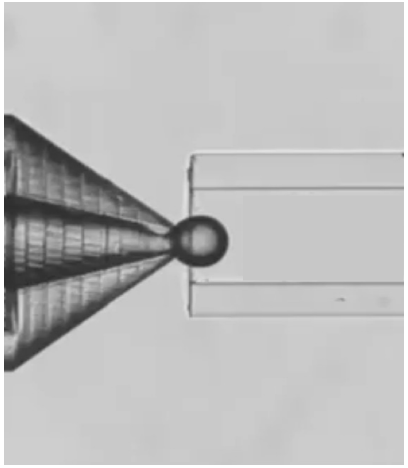






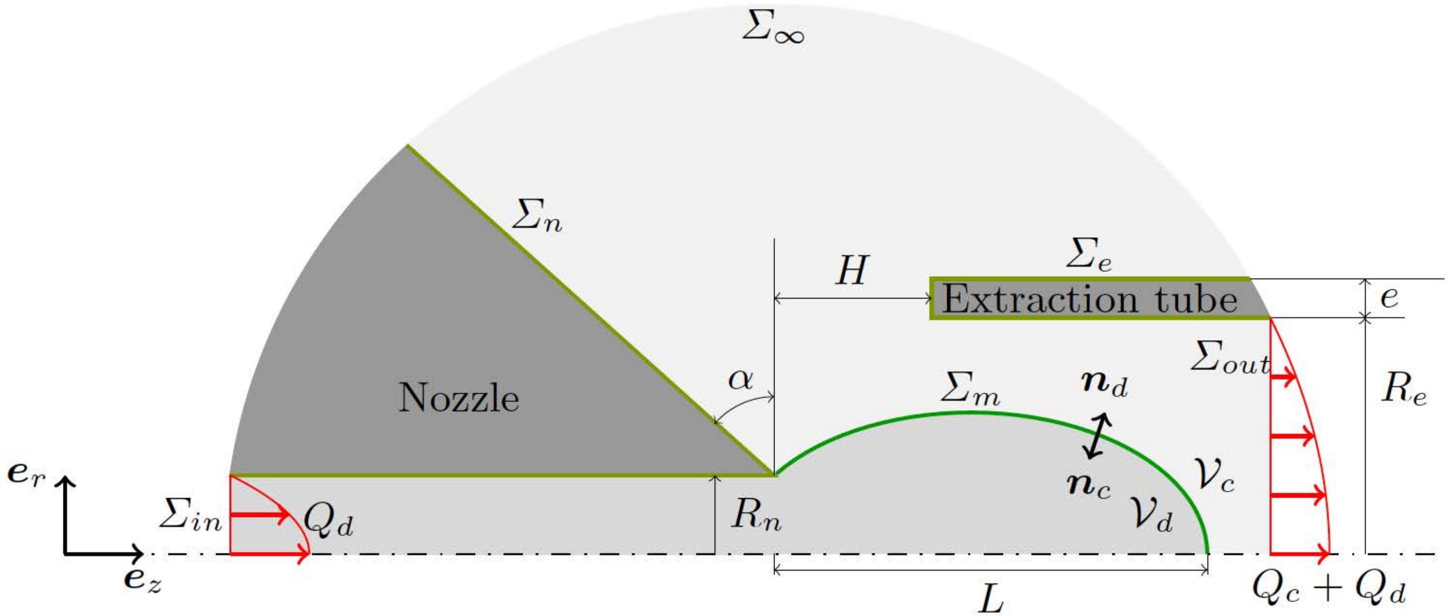
Water in mineral oil, 500 Hz

- No coating needed
- No surfactant needed
- W/O and O/W
- Miscible fluids
- 10 to 400 µm



Modelling

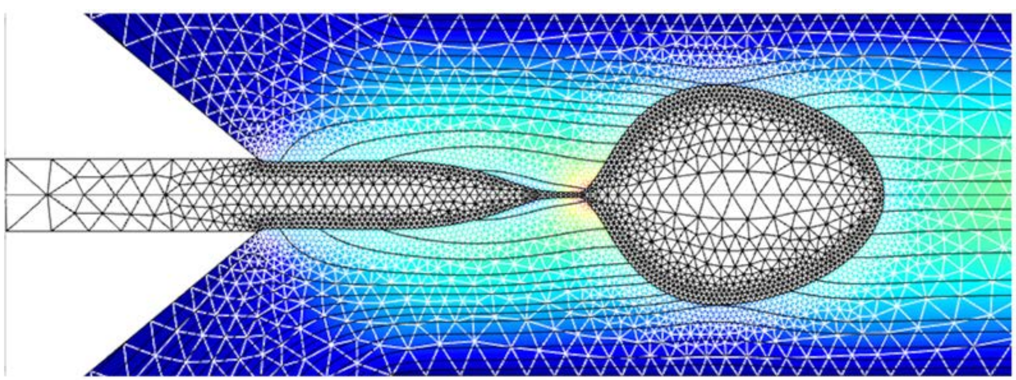
(Navier-)Stokes equations



$$Ca_c = \frac{\mu_c Q_c}{\gamma \pi R_e^2}$$

$$Ca_d = \frac{\mu_c Q_d}{\gamma \pi R_n^2}$$

$$\lambda = \frac{\mu_d}{\mu_c}$$



FEM + ALE + BALE
(Comsol Multiphysics)

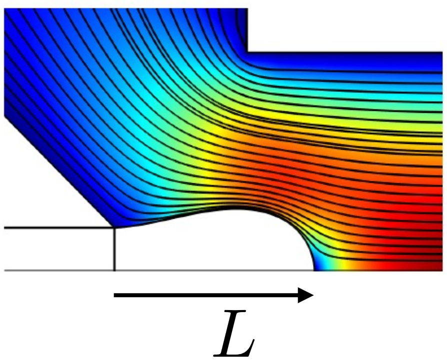
[Rivero-Rodriguez, Perez-Saborid & Scheid, JCP, 2021]

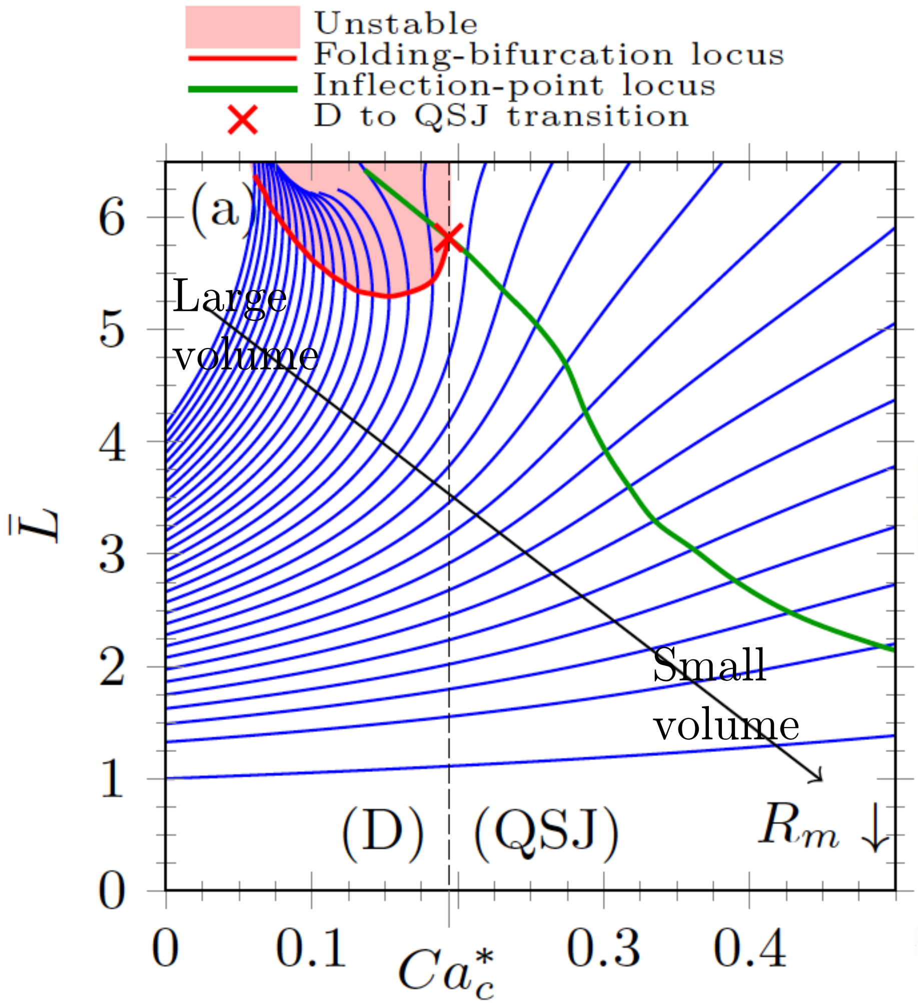
Dripping (D) to quasi-static jetting (QSJ) transition

$\lambda = 0$

Dripping

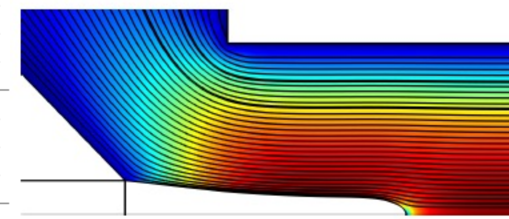
$Ca_c < Ca_c^*$

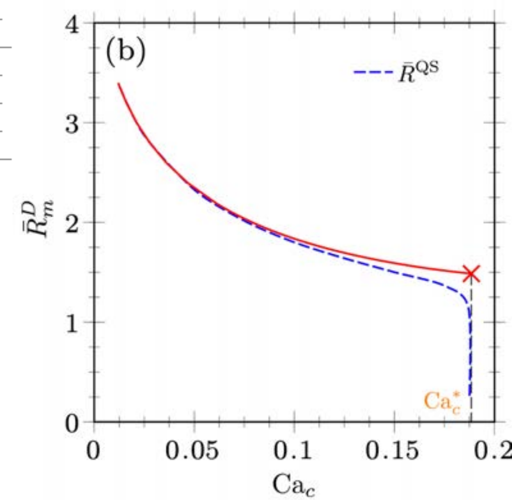




Jetting

$Ca_c > Ca_c^*$





$$Ca_c = \frac{\mu_c Q_c}{\gamma \pi R_e^2}$$

Dropsizer

How to mesure the size of a droplet?

Raydrop configuration: ◉ 30-150µm ○ 60-300µm ○ 90-450µm

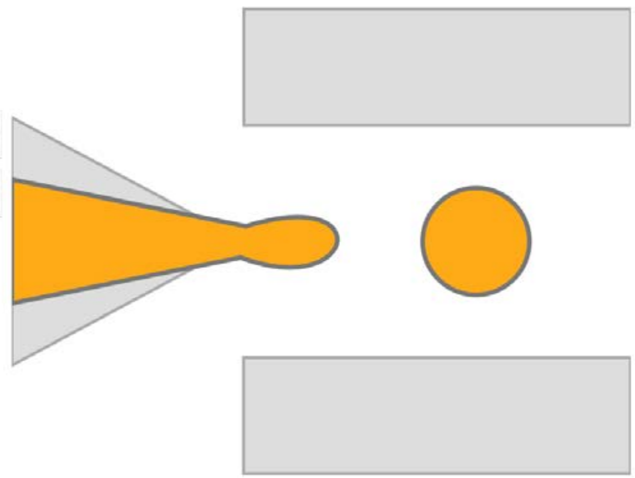
γ (mN/m) 50

μ_d (cP) 1

μ_c (cP) 23

Q_d (µl/min) 12

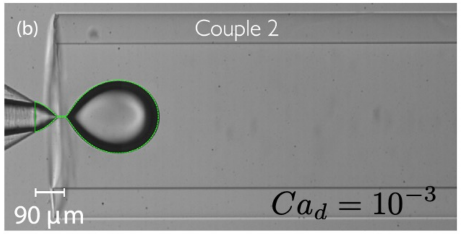
Q_c (µl/min) 113



69 µm, 1163 Hz

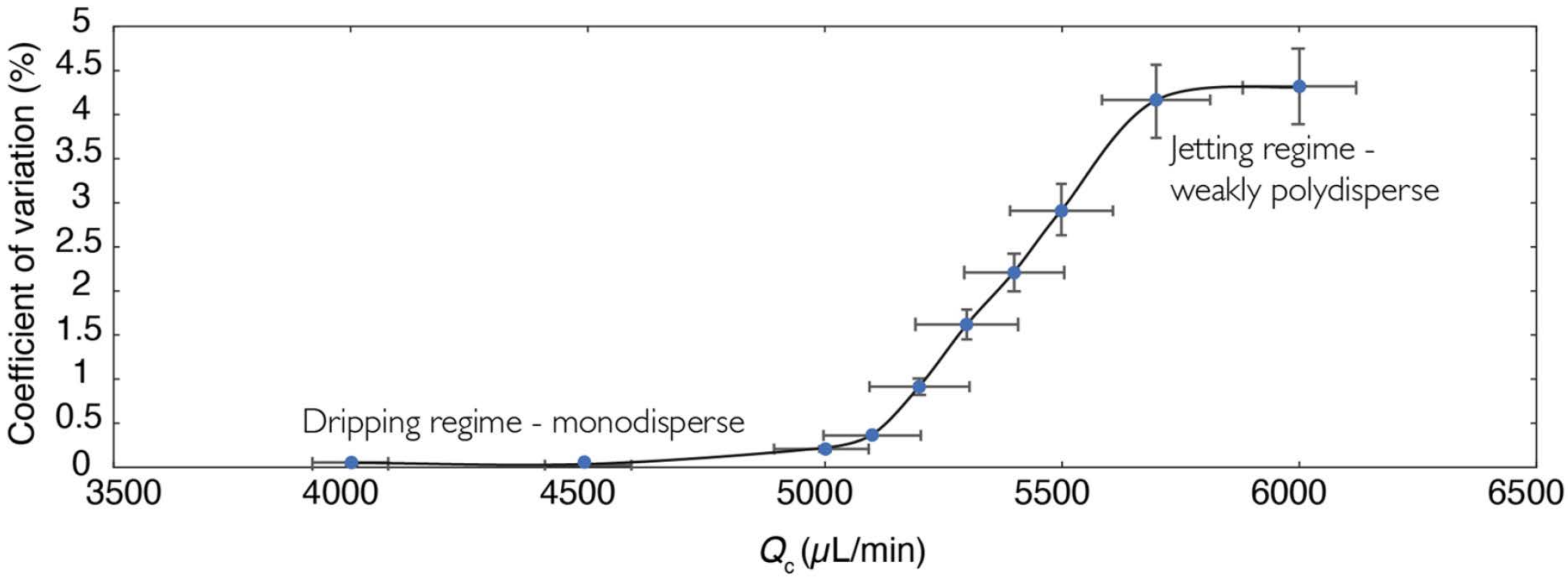
Qd/Qc > 1/10

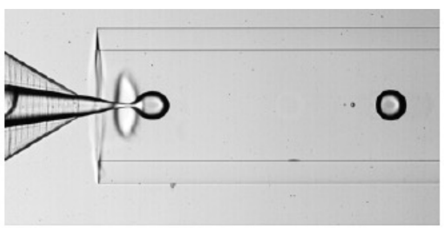
Screenshot



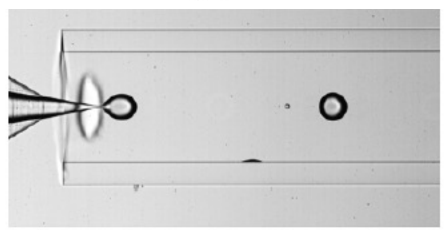
Dripping/jetting transition

Quasi-static limit $\quad Q_d \ll Q_c$

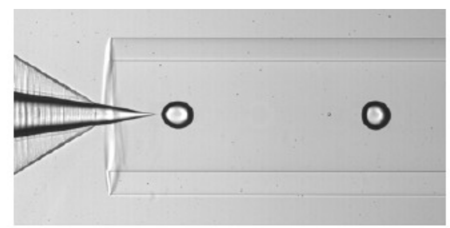




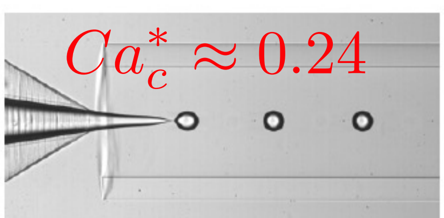
3500



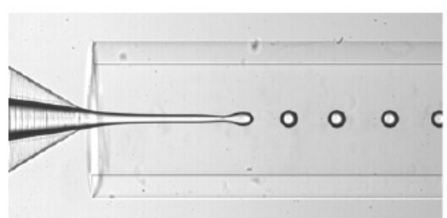
4000



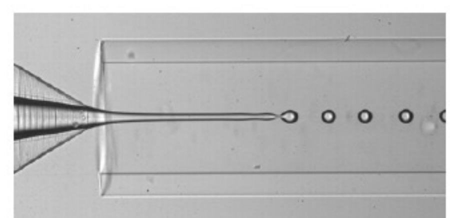
4450



5000

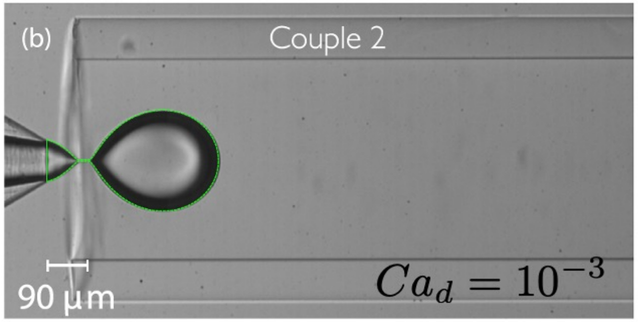


5700



6500

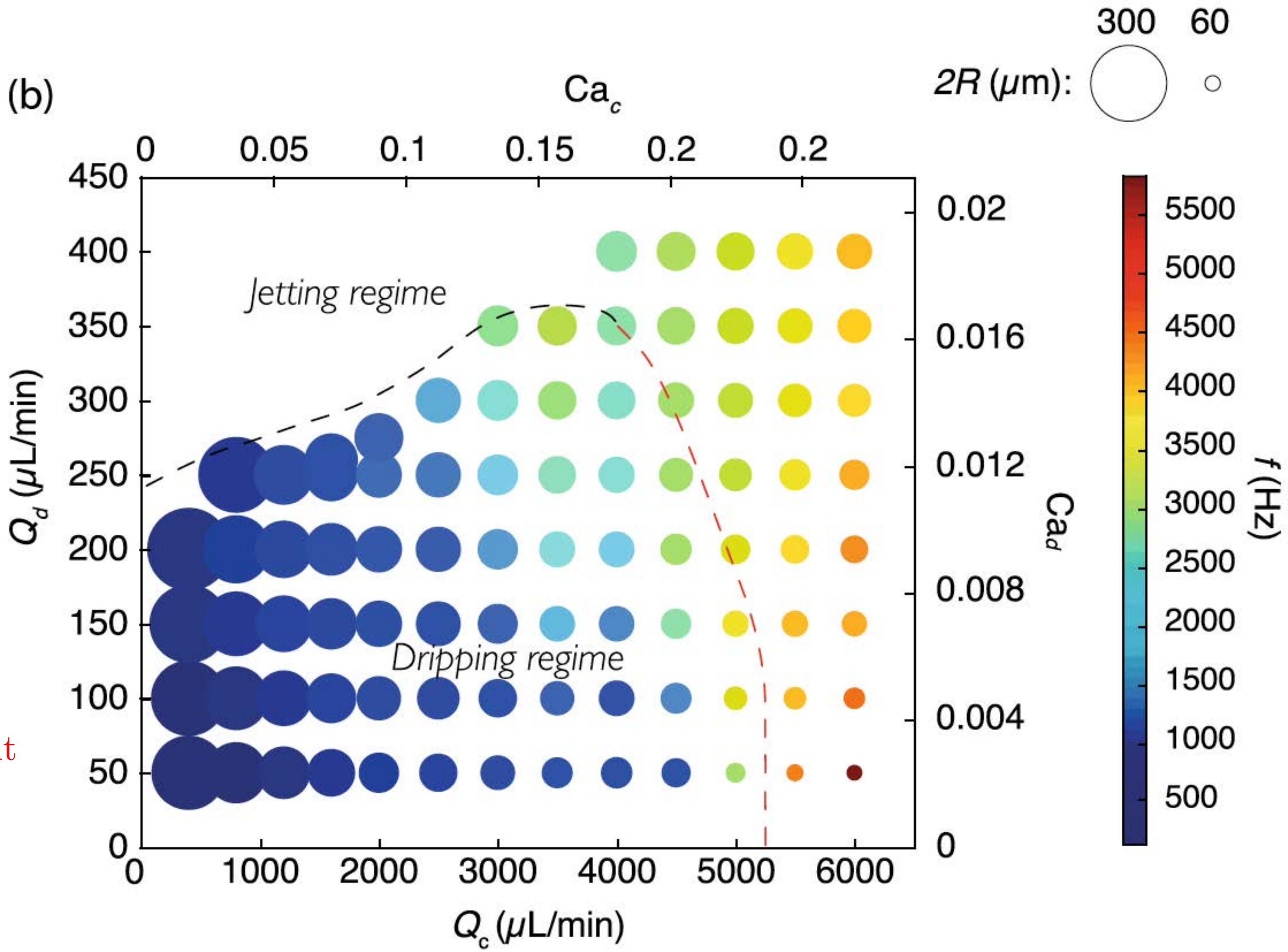
450μm



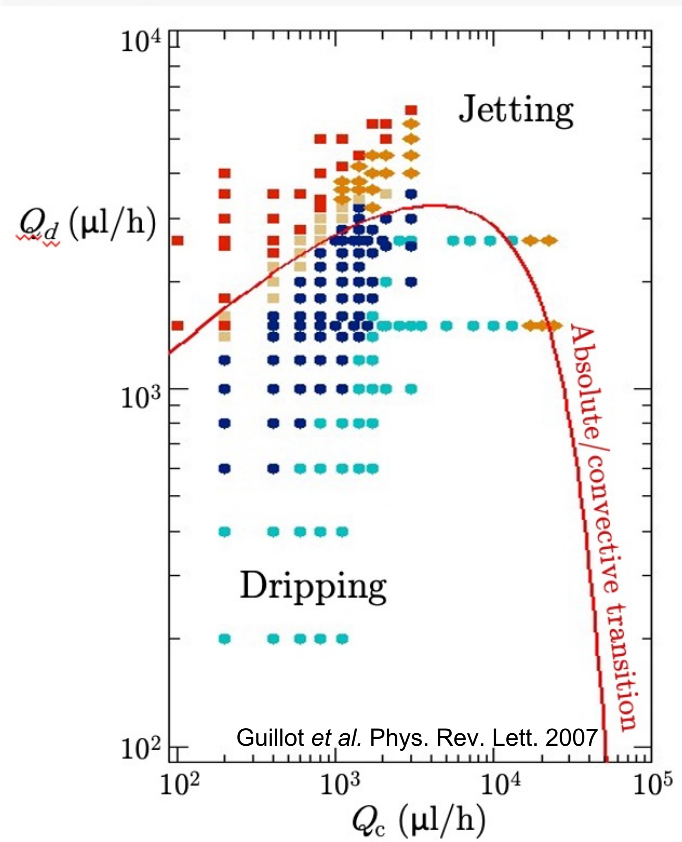
Phase diagram

$$\mu_c = 23\mu_d$$

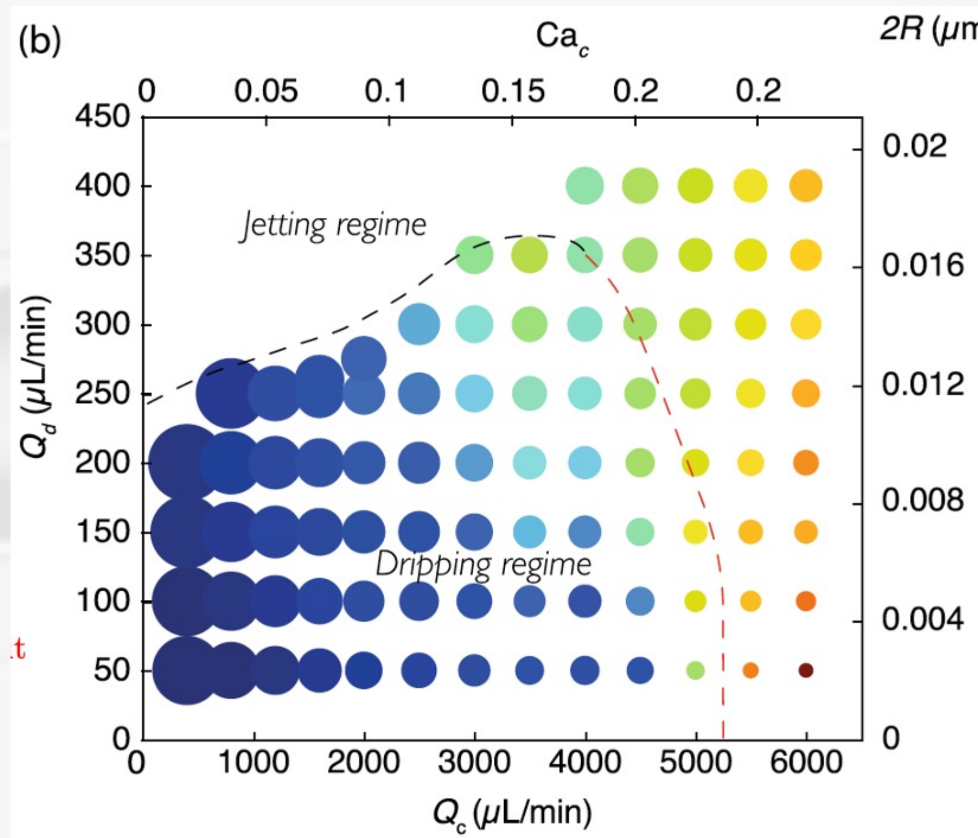
Quasi-static limit



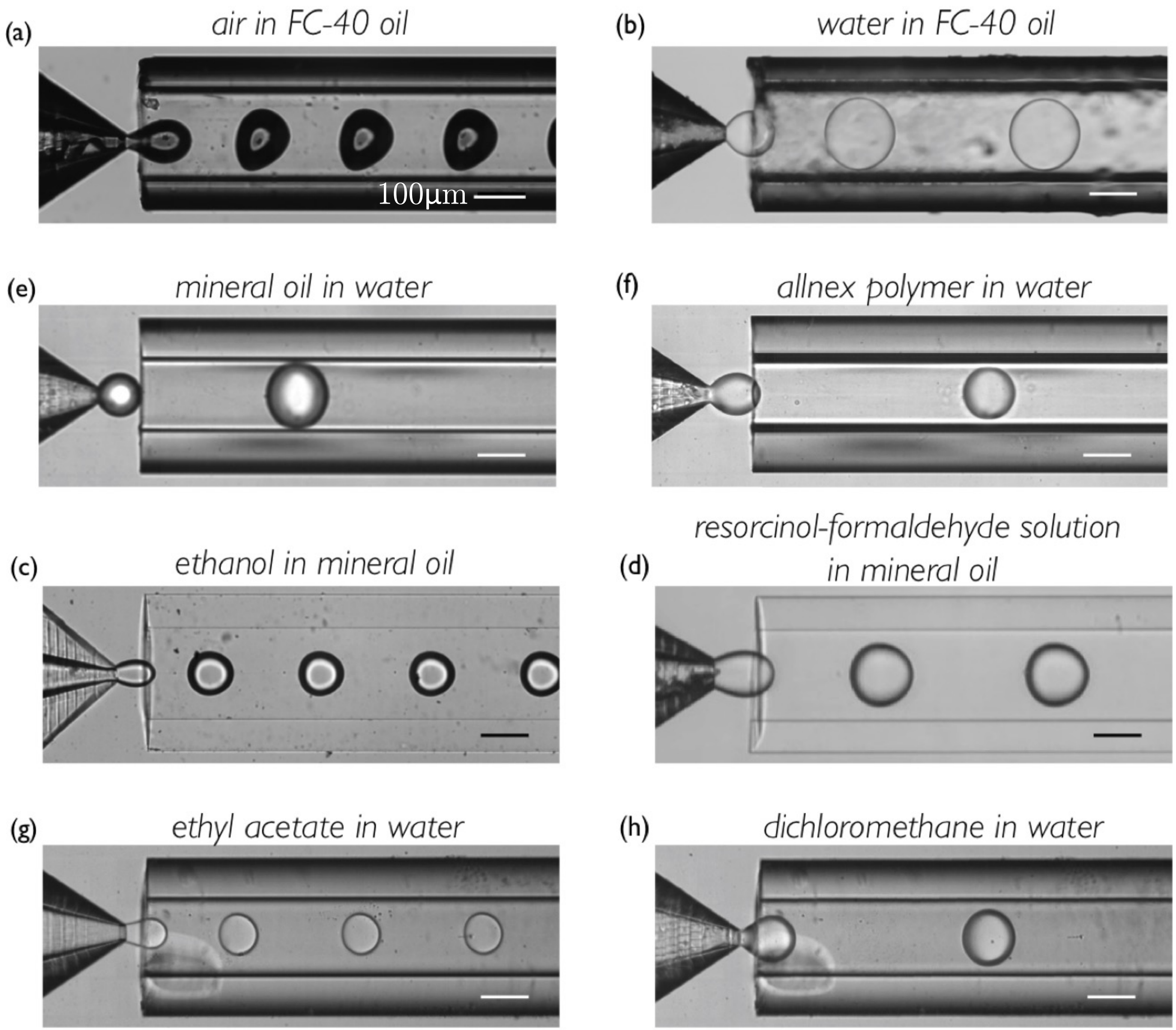
Universal µdroplet generator



From co-flow to Raydrop



Universality



From TIPs to Secoya

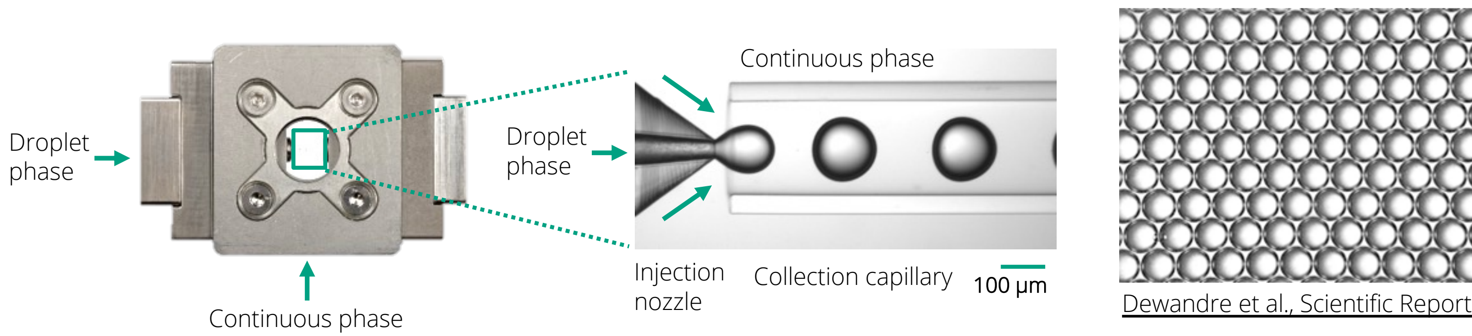
Javier Rivero Rodriguez

Youen Vitry

Adrien Dewandre

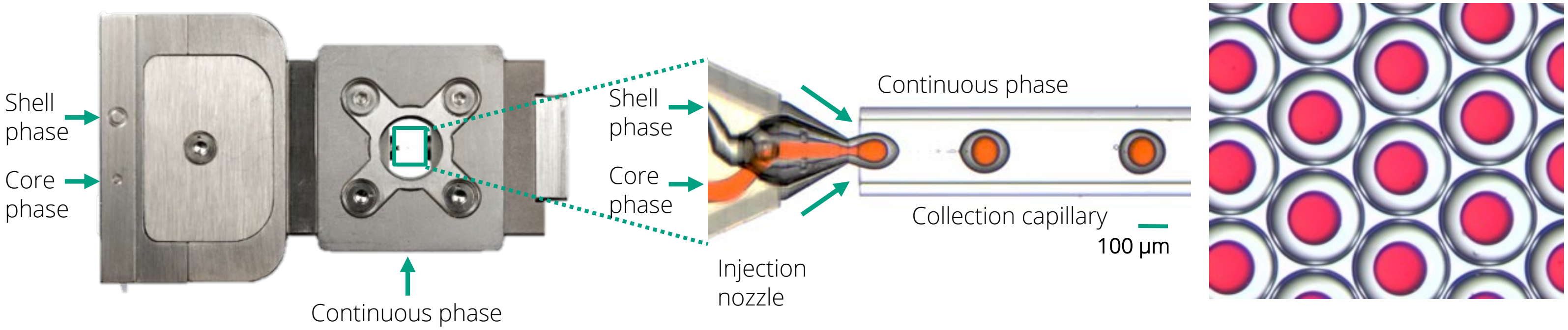
Single and double emulsions for encapsulation

Single Emulsion

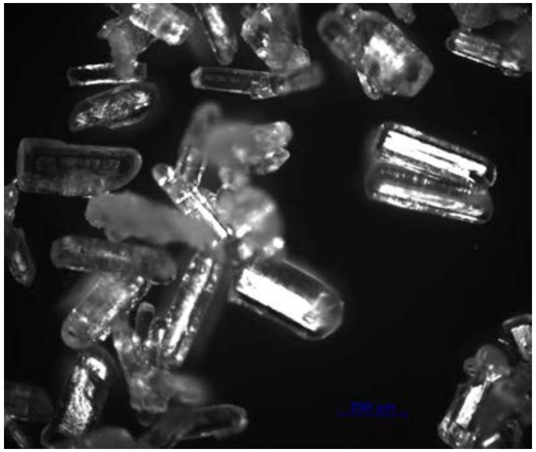


Dewandre et al., Scientific Reports 10, 2020

Double Emulsion

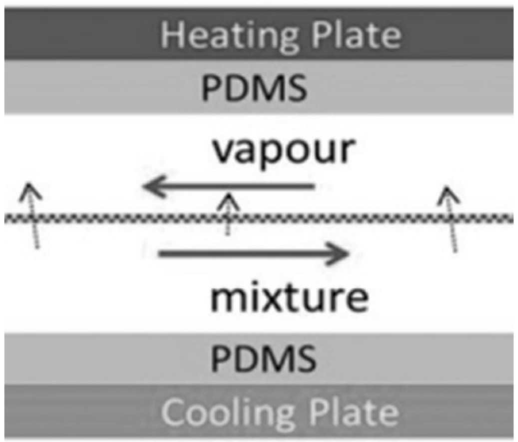


Secoya FLUIDIFY PHARMA



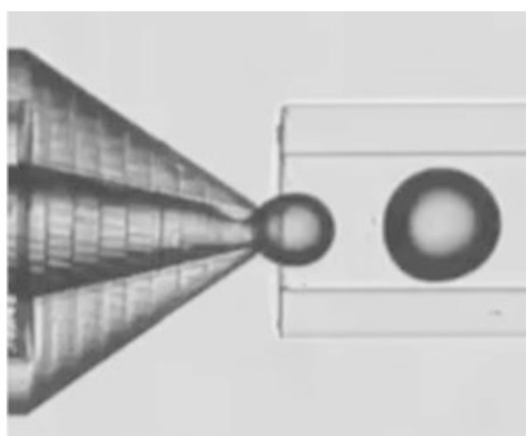
1) Flow crystallization

Secoya
FLUIDIFY PHARMA



2) Solvent extraction by pervaporation

Secoya
FLUIDIFY PHARMA



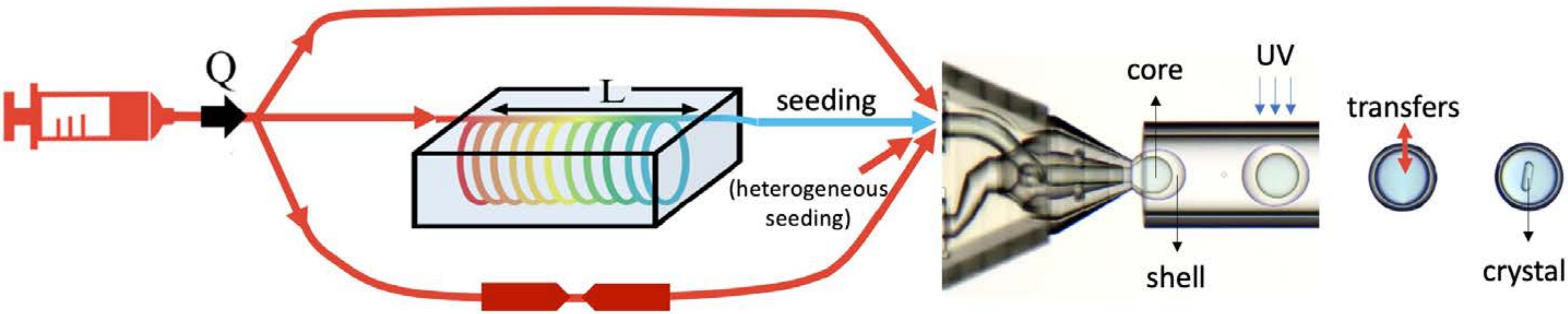
3) Micro-emulsification

Secoya
FLUIDIFY PHARMA

Making big volumes with small capillaries

Secoya
FLUIDIFY PHARMA

From Secoya to TIPs



Thanks for your attention