Micropore Technologies

“Precision emulsions and microparticles”

Membrane Emulsification versus Homogenisation

Benefits in Energy Usage and Process Efficiency

David Palmer – Micropore Technologies

Definition - emulsions

Emulsion – noun

"A fine dispersion of minute droplets of one liquid in another in which it is not soluble or miscible."

Example:

'oil beaten to an emulsion with a half tablespoonful of vinegar'

Definition - emulsions

Emulsions are usually specified as:

A dispersed phase (the droplet - DP) and a continuous phase (the supporting liquid - CP)

- Oil in water (o/w)
- Water in oil (w/o)
- Water in oil in water (w/o/w)
- Oil in water in oil (o/w/o)

When mixing stops, the phases start to separate.

Definition - emulsifiers

However, when an emulsifier is added to the system, the droplets remain dispersed, and a stable emulsion is obtained.

An emulsifier is a molecule in which one end likes to be in an oily environment and the other in a water environment.

The emulsifier positions itself at the oil/water or air/water interface and, by reducing the surface tension, has a stabilising effect on the emulsion.

The state of the art

In industrial settings, emulsions can be formed in a number of ways.

- Simple stirred tanks
- Shaking/Agitation/Ultrasonics
- Microfluidics
- Homogenisation
- Membrane emulsification

Each method has strengths and weaknesses.

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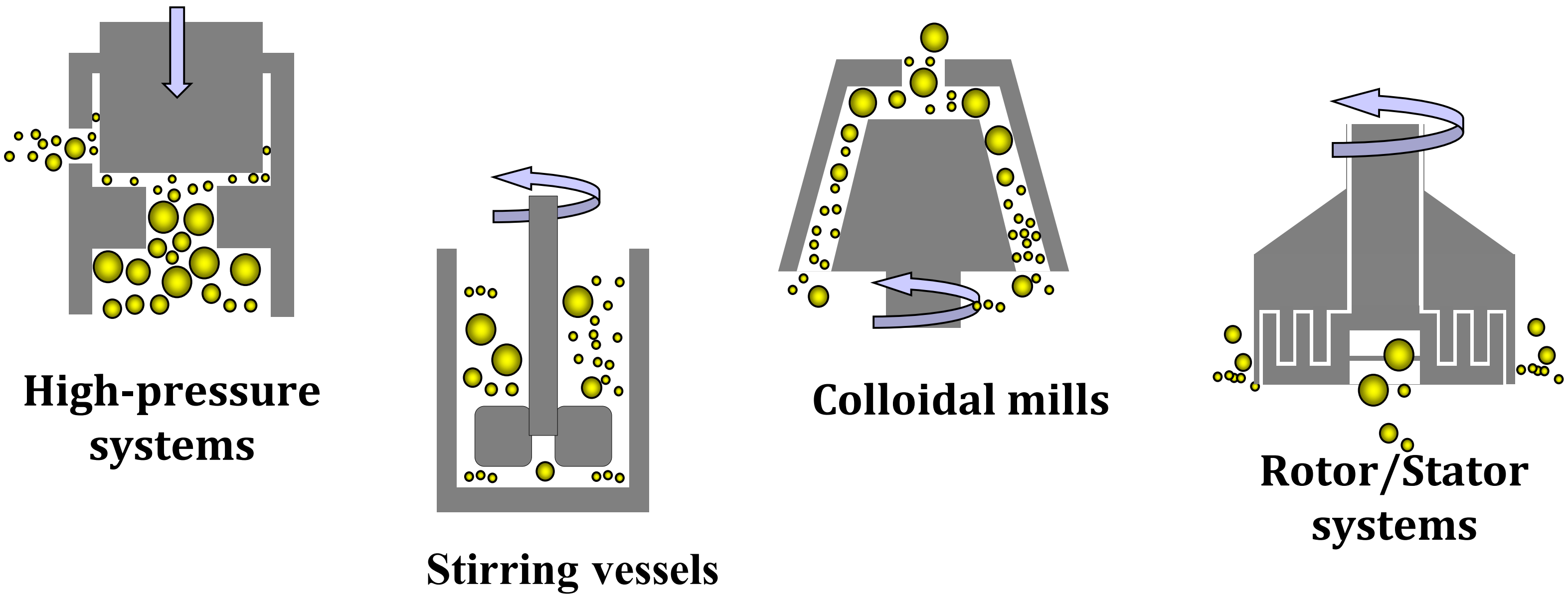
Homogenisation



Karbstein H. and Schubert H. 1995

Many different approaches

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Homogenisation

Most focus on a process of drawing in the DP through a screen or aperture using shear forces to break the DP droplets down further.

In-tank, in-line or recirculated, depending on the application.

Control can be gained by setting gaps, choosing screens, speed (rpm) or number of passes.

Homogenisation

Typically…

- High shear
- Powerful motors/energy intensive
- Noisy!
- Need to monitor DP droplet size via particle sizing/viscosity/opacity or turbidity/number of passes or time
- A chance that the emulsion could ‘invert’
  - Flip from w/o to o/w or o/w to w/o

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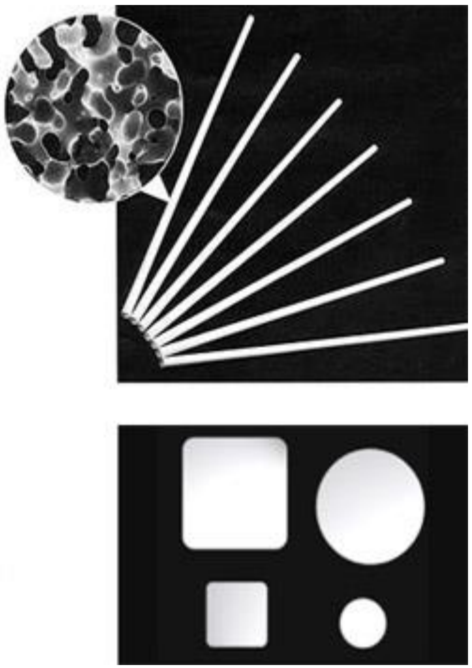
Membrane Emulsification

Membrane emulsification (ME) has been around since 1980’s but always limited to lab scale.

- Shirasu porous glass (SPG)
- Ceramics
- Silicone wafers
- More recently - Nickel/Stainless steel

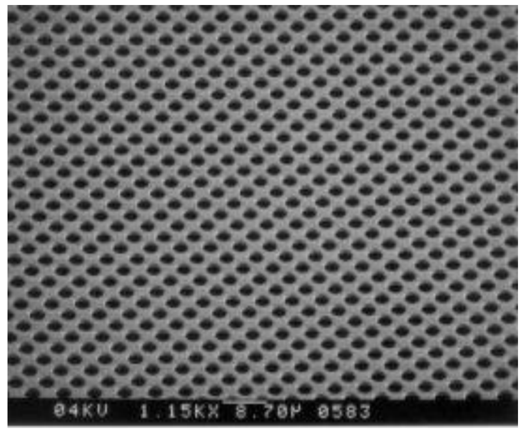
Different strengths and weaknesses

Membranes



SPG membranes
SPG Technology Co.,Ltd
Japan

Drop size
0.2 - 40 µm



Silicon Wafer Membranes
Nanomi Holland

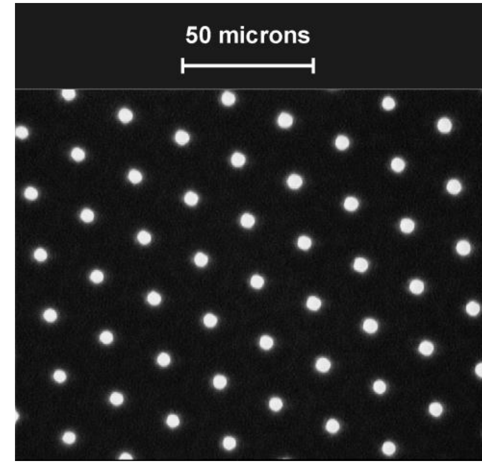
Drop size
0.5 - 250 µm

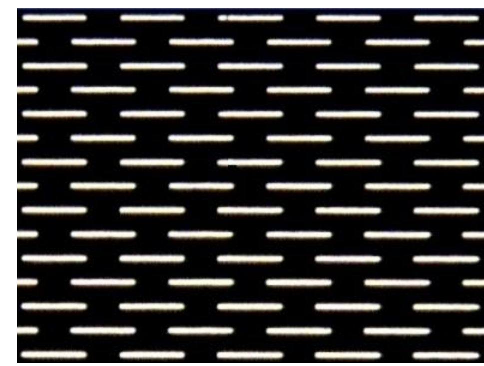
Ceramic membranes
TAMI industries (France)
Various other producers
Drop size
0.3 - 40 µm

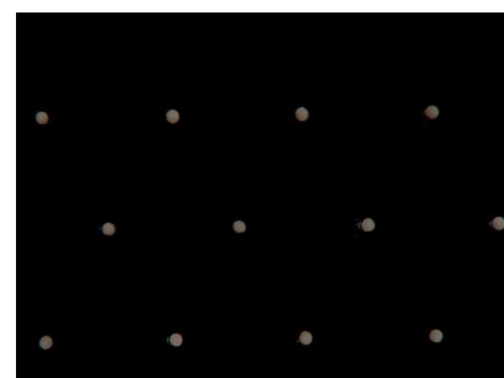
Metal Membranes

Precision engineered membranes are configured to suit the application.

- Patented membranes
- Robust material (316 SS)
- Laser drilled pores (3-350µm)
- Low shear/low pressure drop
- Zero fouling
- Specialised surface coatings
  - Hydrophilic/hydrophobic







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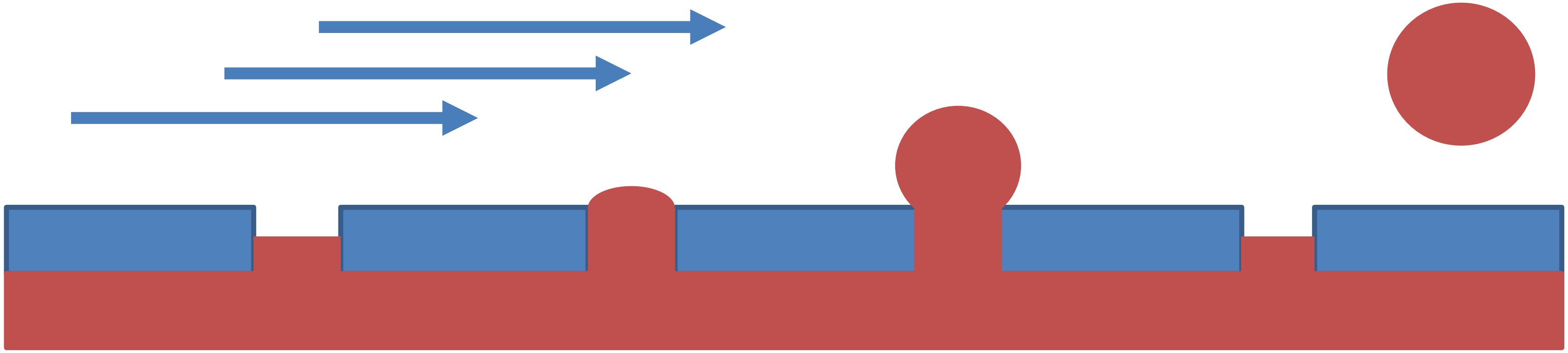
Membrane Emulsification

- This is the process of forming an emulsion by dispersing one phase into another through a porous membrane

- As the pores are all the same size, the emulsions produced are very narrowly-dispersed and of a high quality



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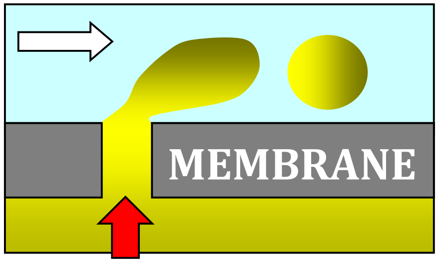
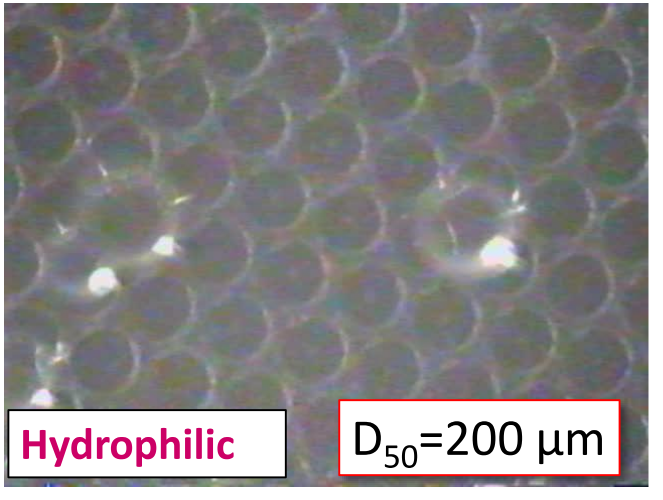
Making emulsions – drop by drop

Membrane emulsification



Injection of dispersed phase through membrane.

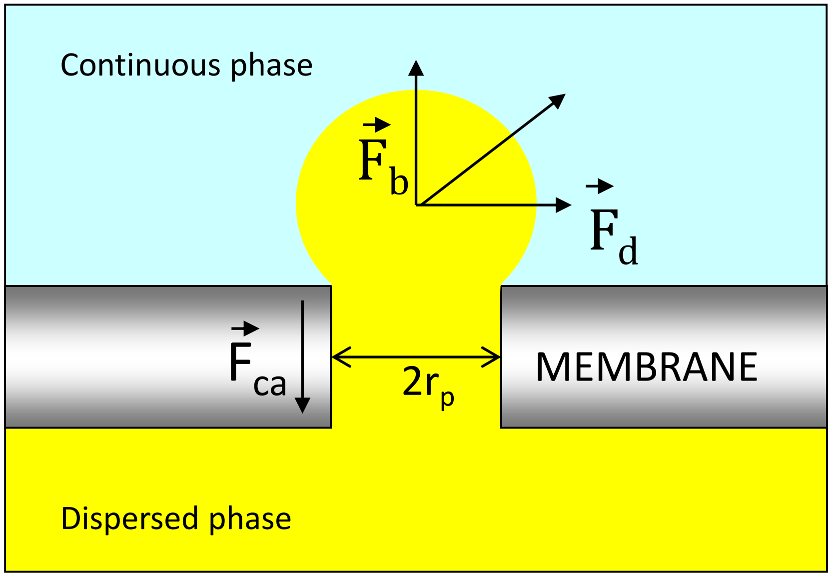


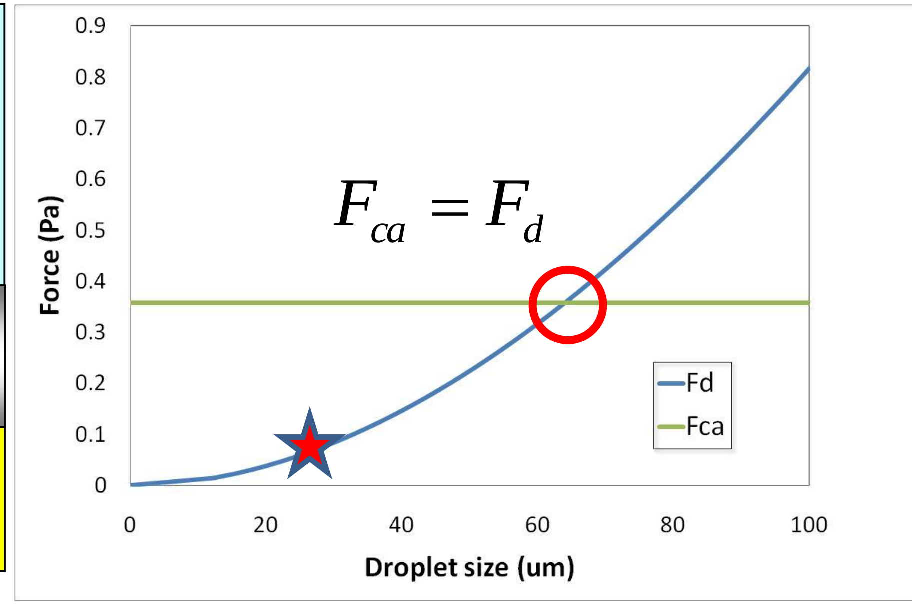
Apply shear
smaller droplets obtained

They use low energy per unit volume and give near-monosized distribution.

Loughborough University

FORCE BALANCE MODEL





F_{ca} - Capillary force

$$F_{ca} = f(\gamma, r_p)$$

F_d - Drag force

$$F_d = f(\tau_{\max}, r_p, d_d)$$

$$\tau_{\max} = 0.825 \eta \omega r_{trans} \frac{1}{\delta}$$

$$\pi d_p \gamma = 9\pi \tau_{\max} d_d \sqrt{\left(\frac{d_d}{2}\right)^2 - r_p^{\ 2}}$$

$$d_d = f(r_p,\ \tau_{max},\ \gamma)$$

Kosvintsev et al. 2008

Dragosavac et al. 2008

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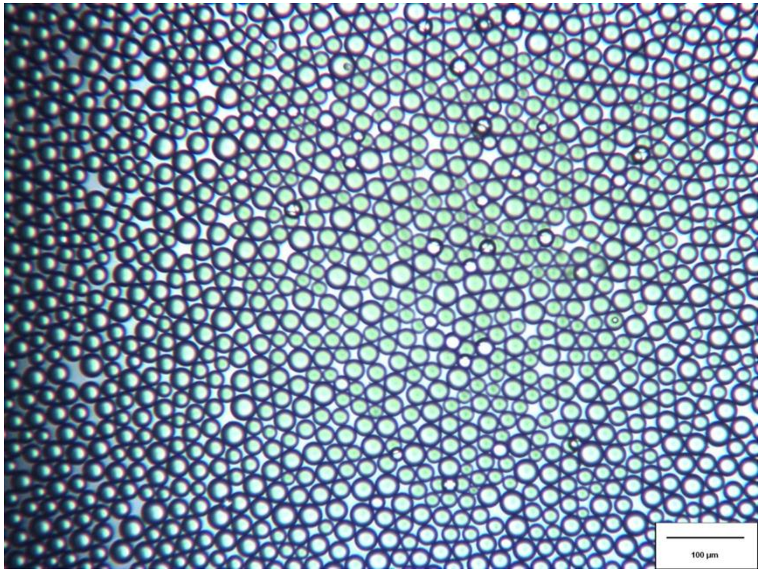
Membrane Emulsification Parameters

Drop size is a function of:

- Membrane geometry
- Shear stress
- Injection rate
- Liquid viscosities
- Interfacial tension



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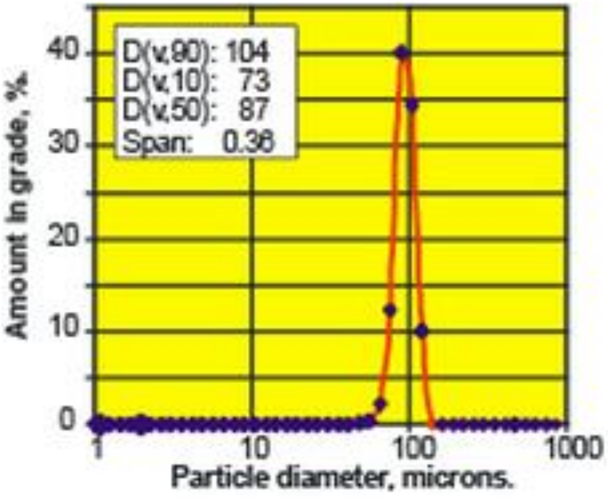
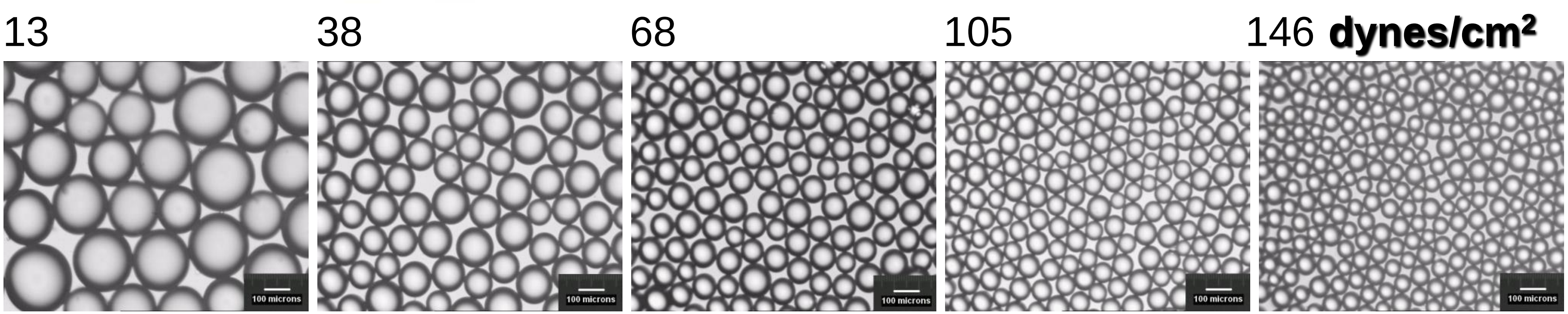
Membrane Emulsification





pressure drop is very low, due to the membrane design, so the shear is low and emulsification conditions are gentle

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Static membrane emulsification

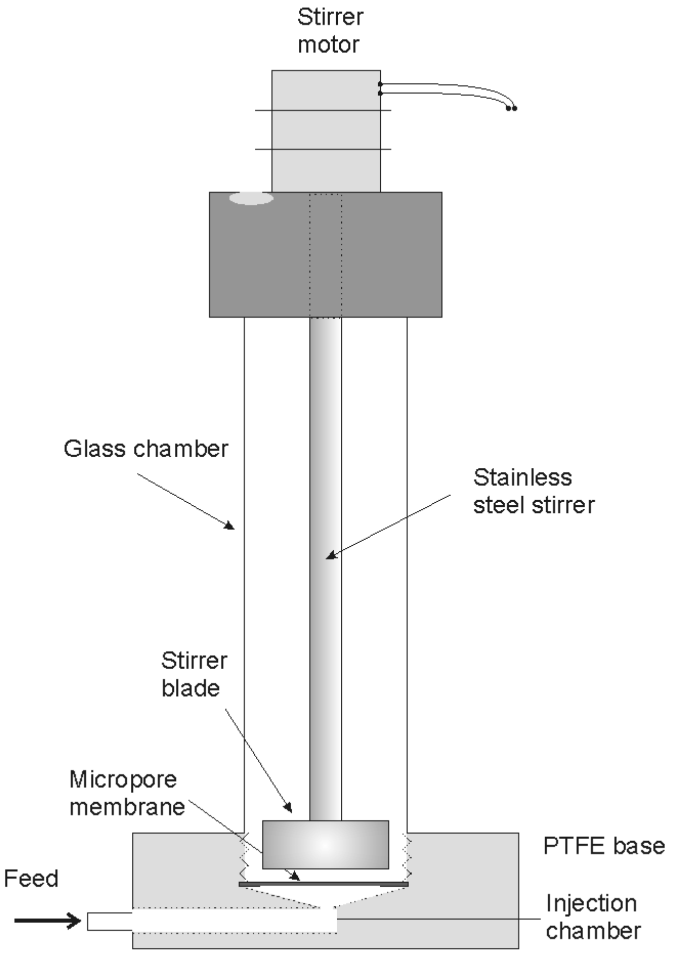
Scaling Up

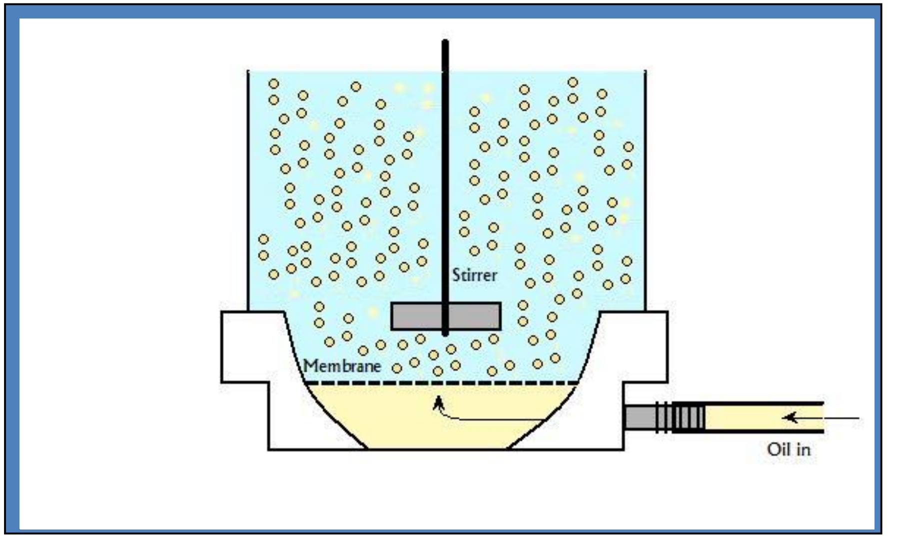
- Laboratory Dispersion Cell (Micropore LDC-1)
    - Small scale batch, laboratory equipment for formulation development

- Torsional Units (Micropore LTS-1)
    - Continuous process, with outstanding control of process parameters

- Crossflow Units (Micropore AXF/CXF)
    - CXF high volume continuous process
    - AXF aseptic high volume continuous process

Laboratory Dispersion Cell LDC-1





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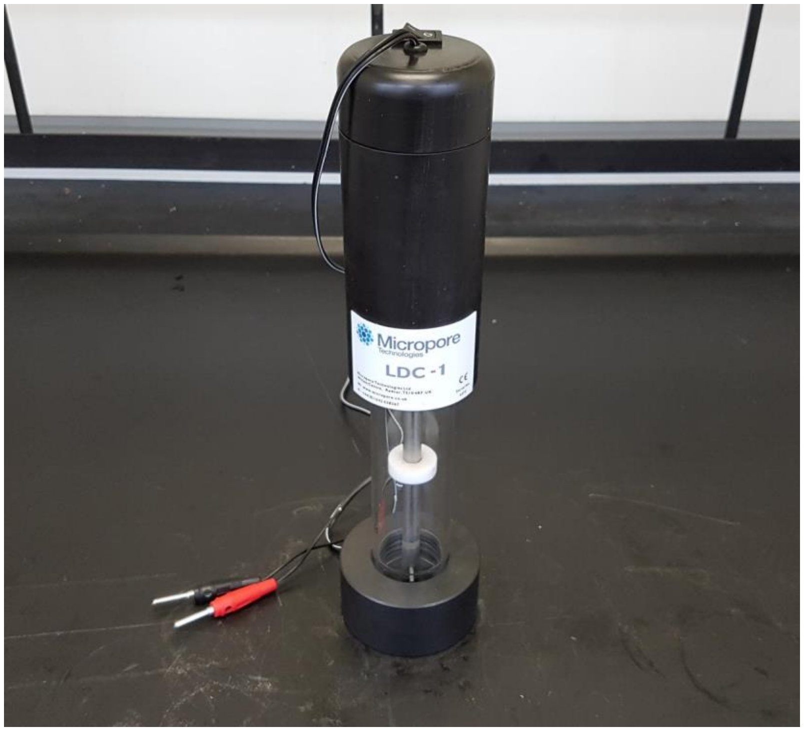
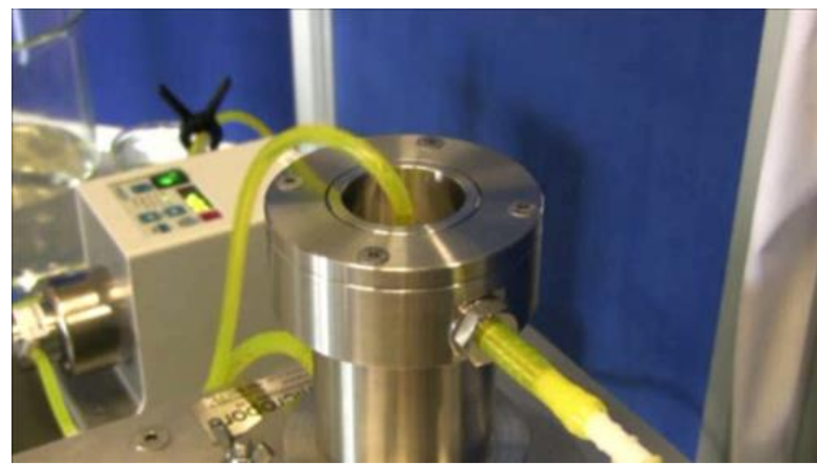
Static membrane emulsification

Laboratory Dispersion Cell LDC-1



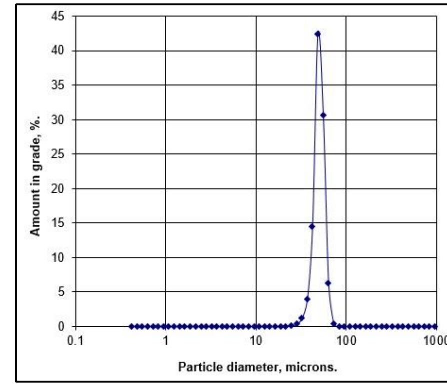
Torsional Unit LTS-1

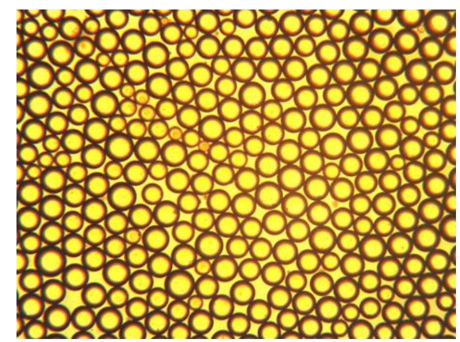
- Cylindrical membrane, welded onto central shaft
- Dispersed phase injected through central shaft
- Continuous phase flows through housing
- Continuous production of high quality emulsion



Torsional Unit LTS-1

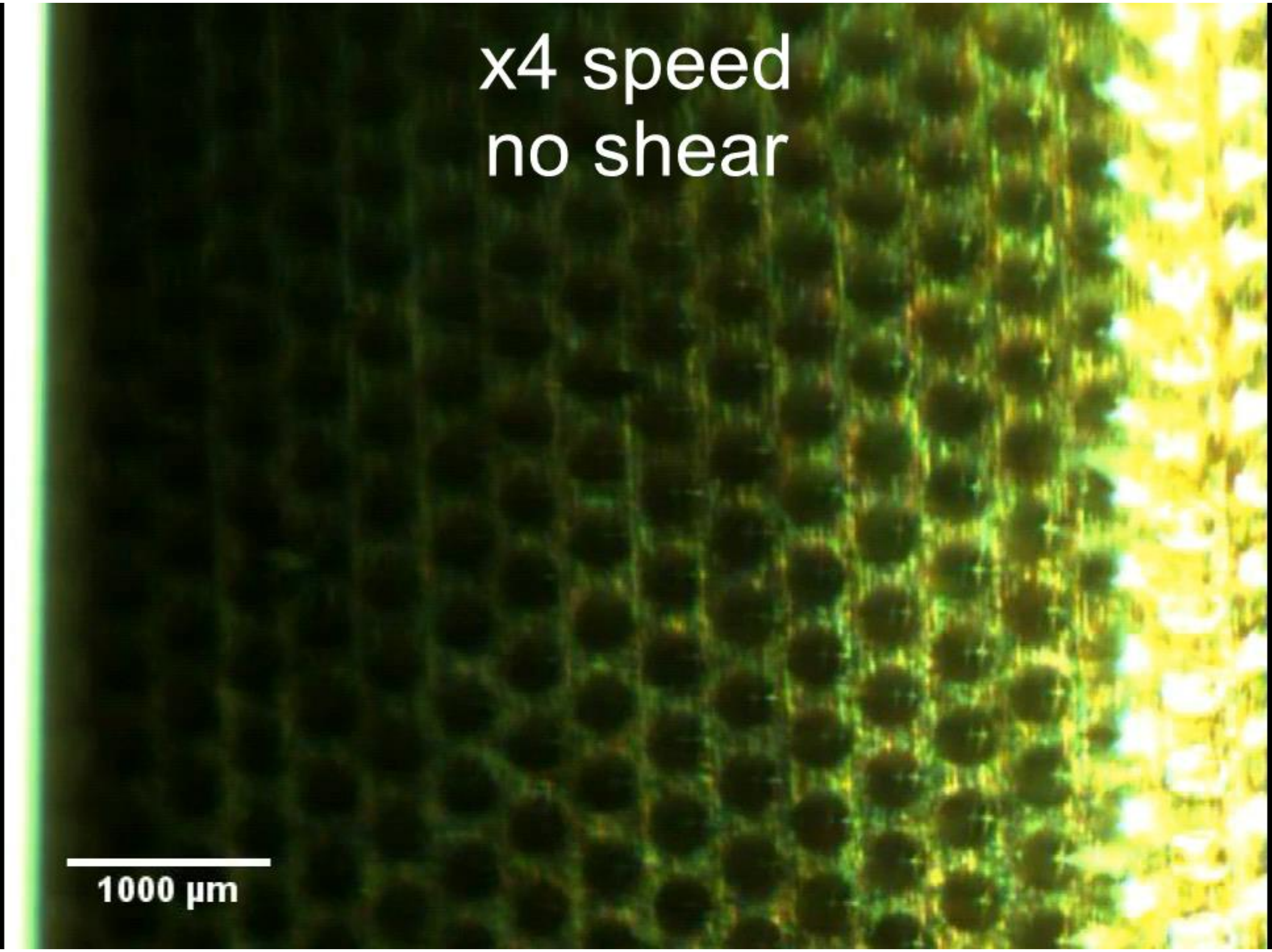
- Oscillating membrane - shear force detaches droplets at the point of maximum deceleration
- Droplet size controlled by injection rates, oscillation distance and frequency





Droplet generation, no shear

Membranes



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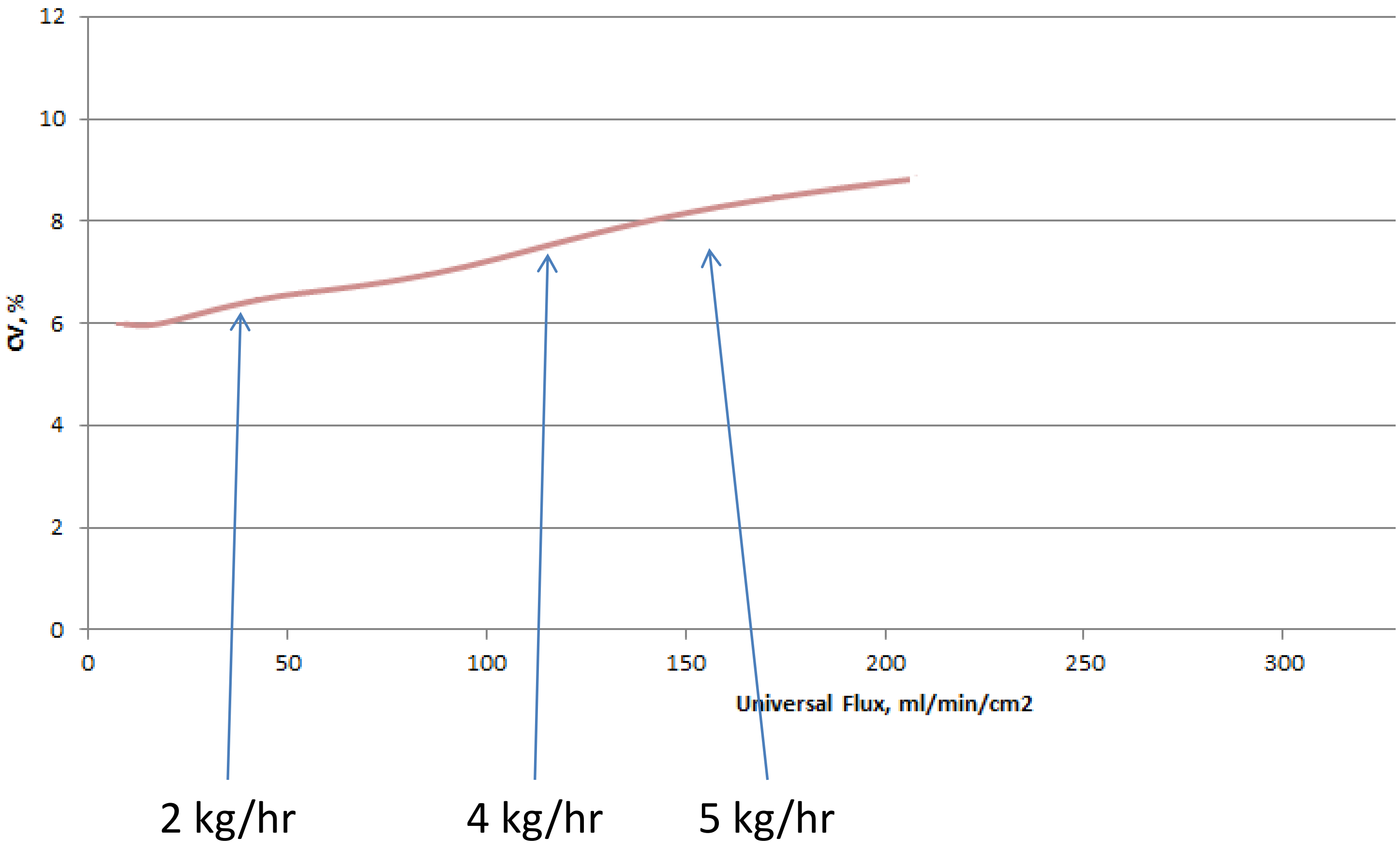
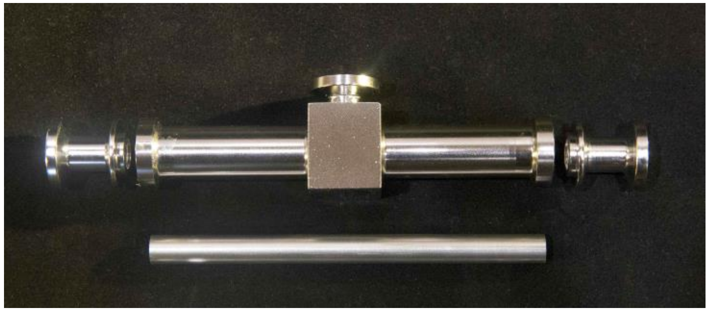
Torsional Unit – CV Data



Dispersed phase injection rate

Crossflow Units CXF/AXF

- Small ‘stand-alone’ device, no moving parts
- Maintains low % CV even at high throughputs (~10% at 18L/hr DP)
- AXF model designed for Aseptic applications, e.g. Food & Pharma
- CXF ‘Continuous Crossflow’ is the non-aseptic version for general industry



Aseptic Crossflow Unit AXF

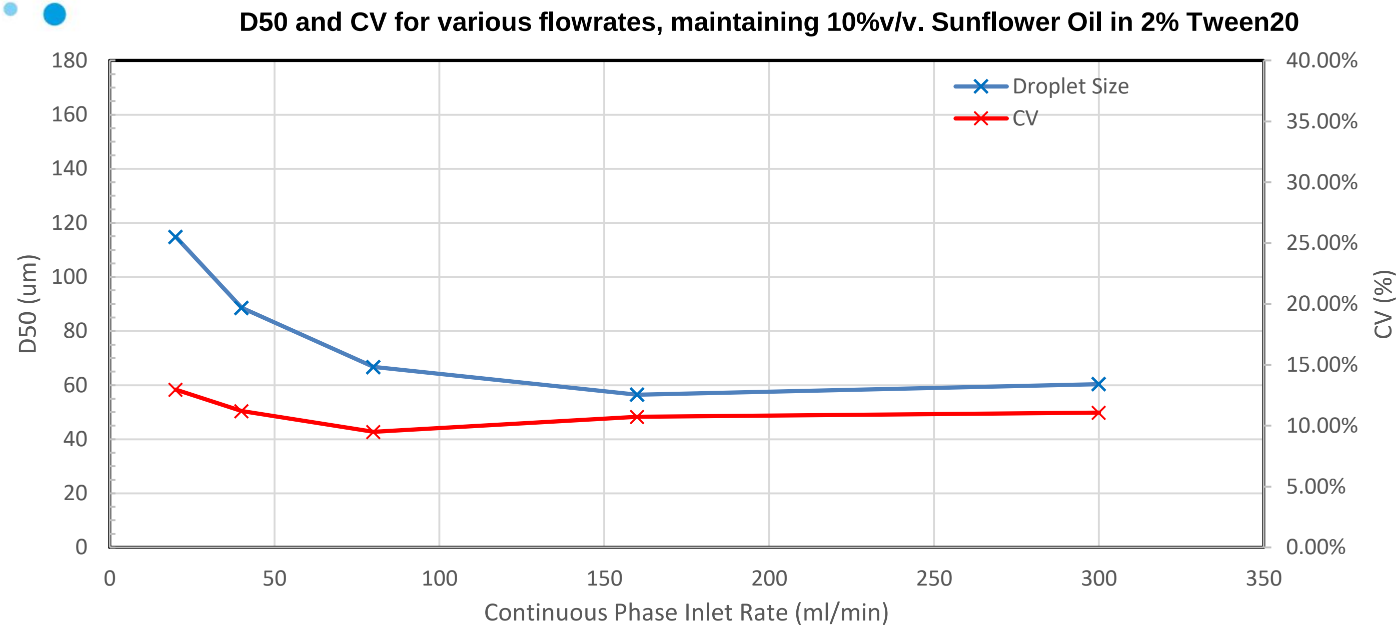


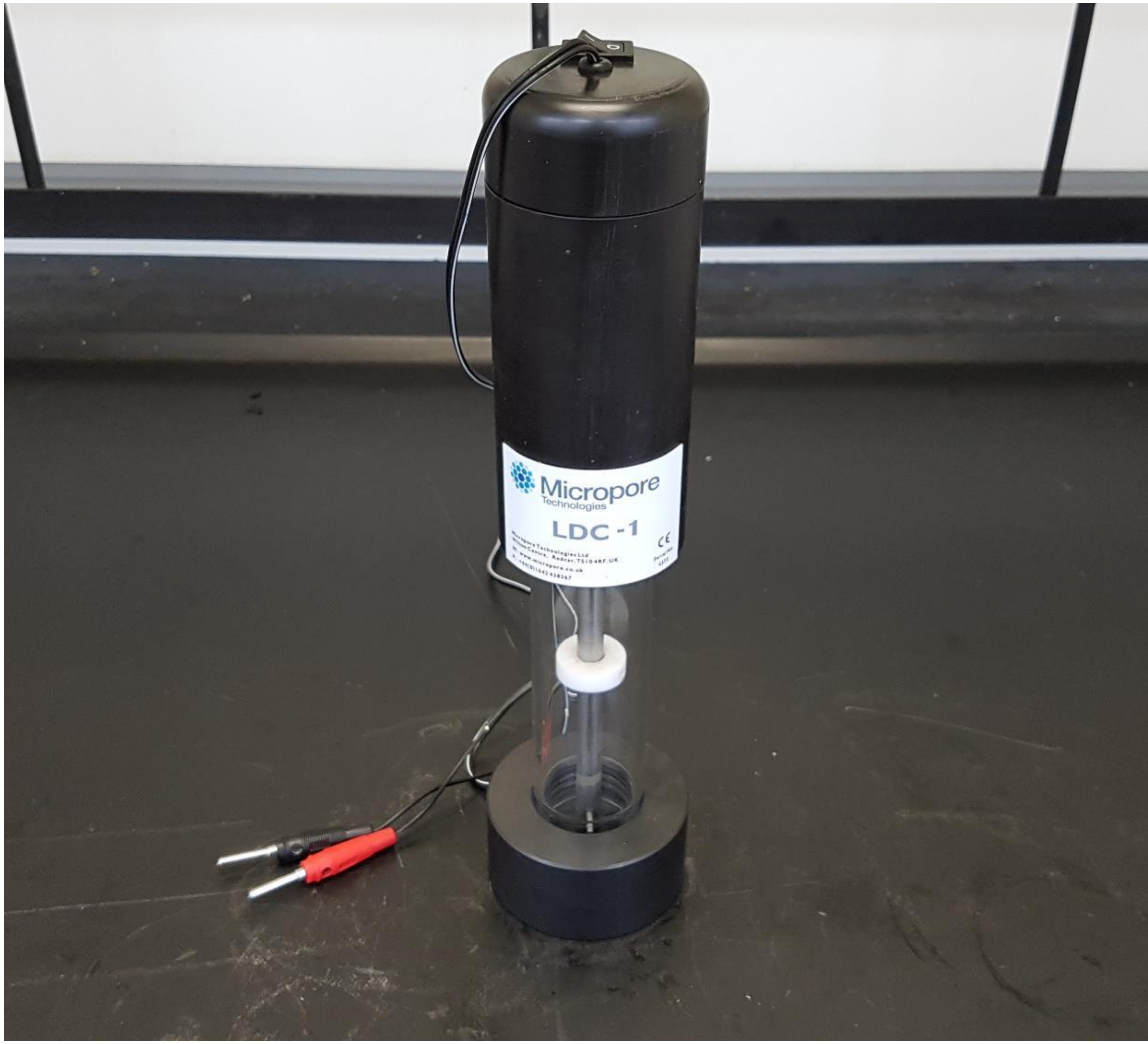
Figure 1 - D50 and CV versus Dispersed Phase Injection Rate. All data at 10%v/v. Sunflower Oil in 2% Tween20

Dispersed Phase Injection Rate	Continuous Phase Injection Rate	D50	CV
(ml/min)	(ml/min)	(µm)	(%)
20	180	114.8	12.96%
40	360	88.56	11.20%
80	720	66.74	9.49%
160	1440	56.49	10.73%
300	2700	60.37	11.07%

Static membrane emulsification

Micropore LDC-1

- Batch Process
- Disc membrane with stirrer
- Simple operation
- Droplet Size control:
  - Membrane pore size
  - Stirrer speed - Shear
  - Injection rate
- Syringe Pump for Injection
- Injection Rates 0.1 – 5ml/min
- 100 – 200ml total product
- Concentrations up to 20%



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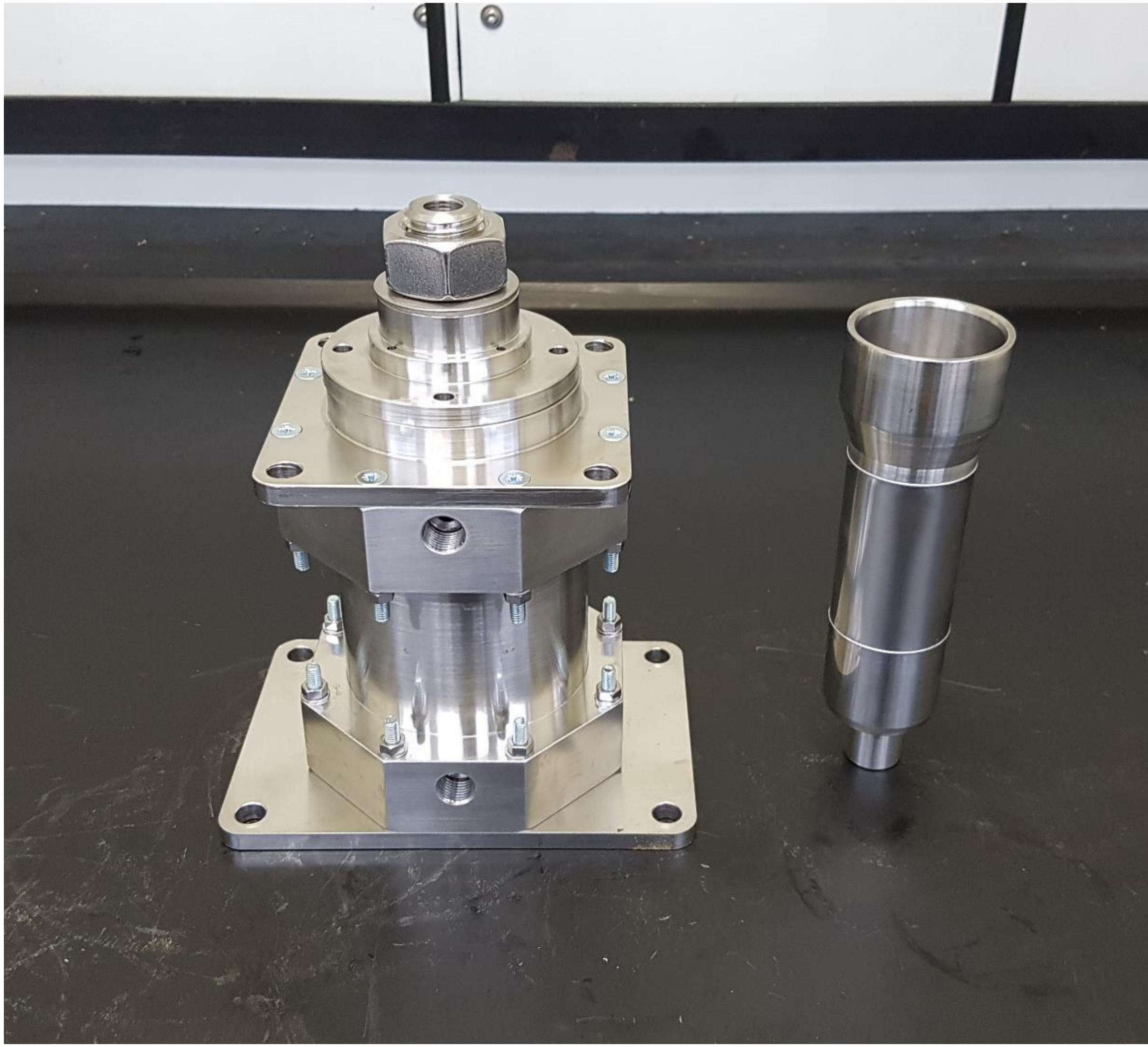
Technologies

Micropore LTS-1

- Continuous Process
- Cylindrical membrane with oscillation
- Droplet Size control:
  - Membrane pore size
  - Oscillation profile- Shear
  - Injection rate
- Pumps for continuous and dispersed phase flow
- 1 – 10kg/hr total product
- Concentrations up to 40%



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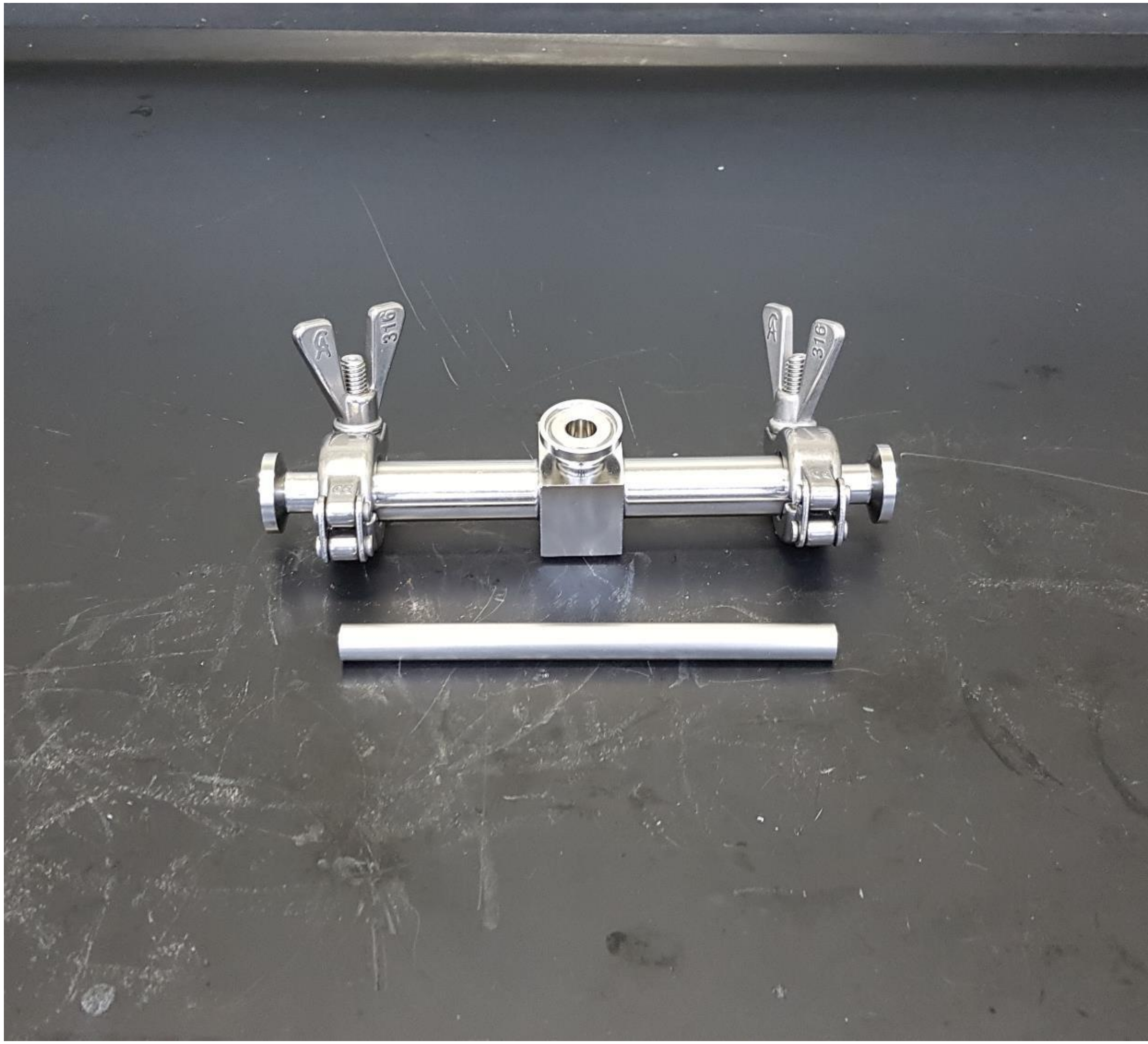
Micropore AXF-1

- Continuous Process
- Cylindrical membrane with crossflow
- Droplet Size control:
  - Membrane pore size
  - Crossflow velocity- Shear
  - Injection rate
- Pumps for continuous and dispersed phase flow
- 10 – 200kg/hr total product
- Concentrations up to 40%



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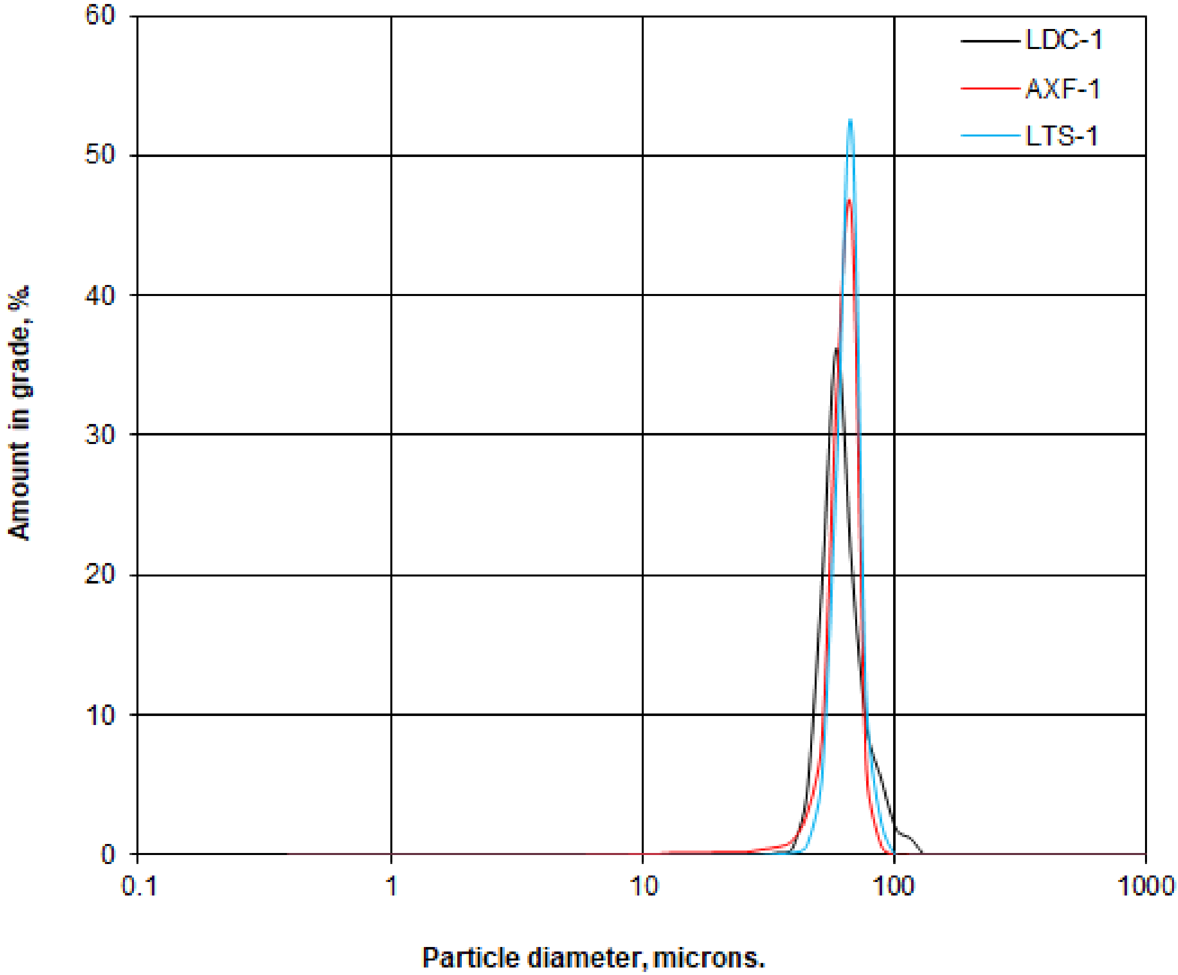
Comparative Performance



	CV (%)
LDC-1	21
LTS-1	11
AXF-1	16

Maintains & improves narrow psd/CV

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Membrane emulsification - Benefits

- **High quality, reproducible emulsions**
  - Narrow particle size distribution (psd) / Low coefficient of variation (CV)
  - Reproducible droplet size control
  - Low shear, gentle processing

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Membrane emulsification - Benefits

- Scalable
  - Dispersion cell → Torsional Unit(s) → Crossflow Unit(s)
  - Maintains narrow psd/CV
  - Industrial quantities (currently up to 200L/hr)

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Membrane emulsification - Benefits

- Compared to traditional homogenisers
  - Energy savings (2 kW vs 40 kW)
  - Small equipment footprint
  - Low noise
  - Reduced waste, fewer inversions

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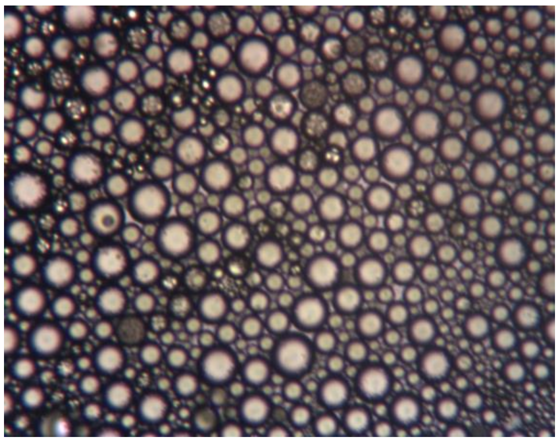
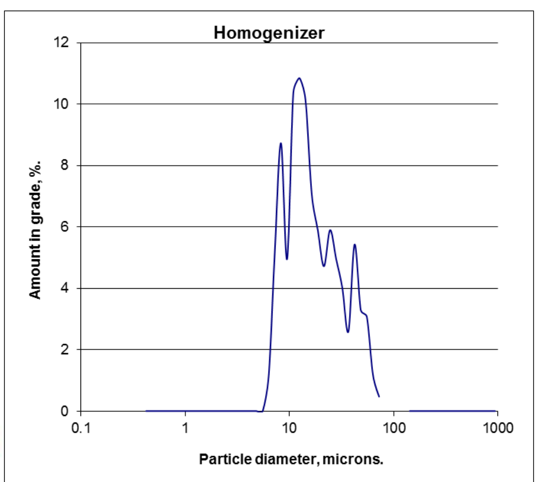
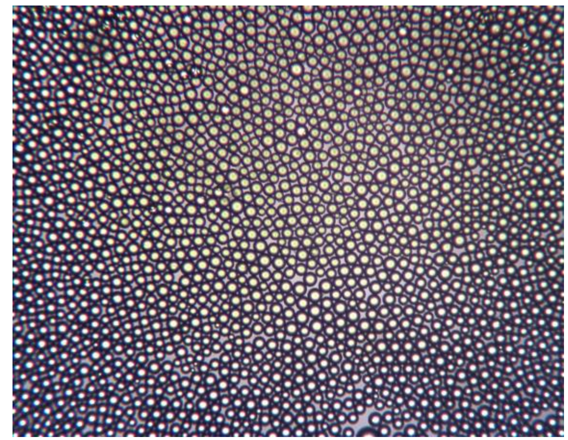
Comparison – sunflower oil in 2% tween 20 solution

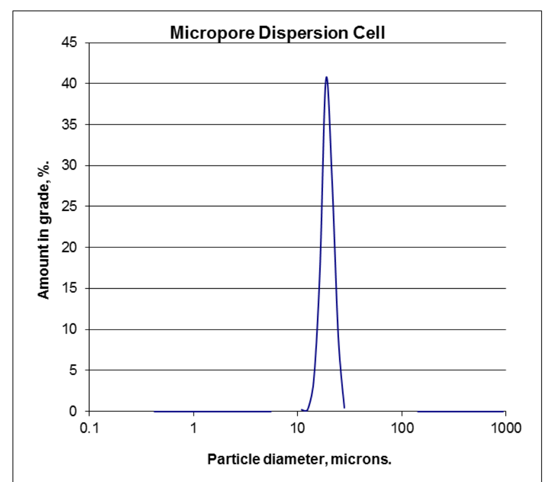
Homogenisation



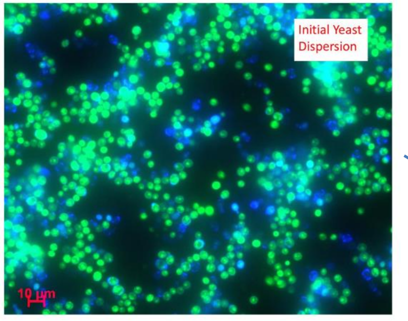


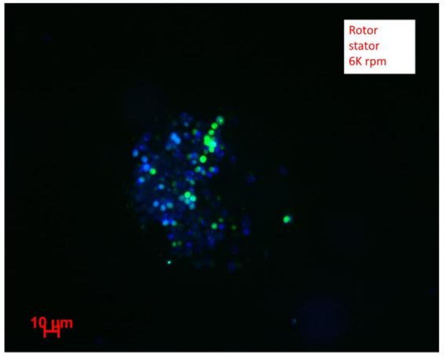
Membrane emulsification

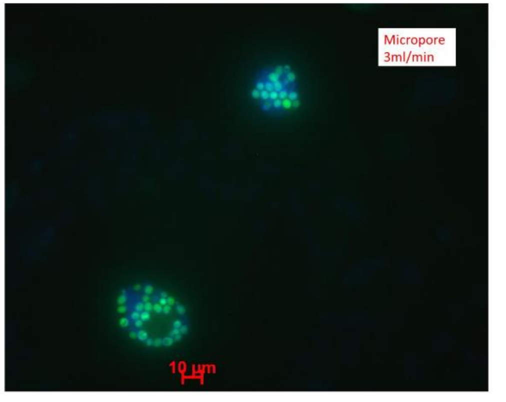




Yeast Viability – homogeniser vs Membrane emulsification







European Union
European Regional
Development Fund

CATAPULT
High Value Manufacturing

cpi

Homogenisation vs. Membrane emulsification

System	ml/min	Agitator (rpm)	Time (min)	Flux (L/h/m2)	% Viability	Yield
Initial	-	-	-	-	80	-
Membrane Emulsifier (Micropore LDC-1)	1	200	10	45	76	95
	3	700	3	136	79	99
	5	1500	2	227	74	93
Rotor Stator	-	1500	2	-	31	39
	-	3000	2	-	50	63
	-	6000	2	-	53	67

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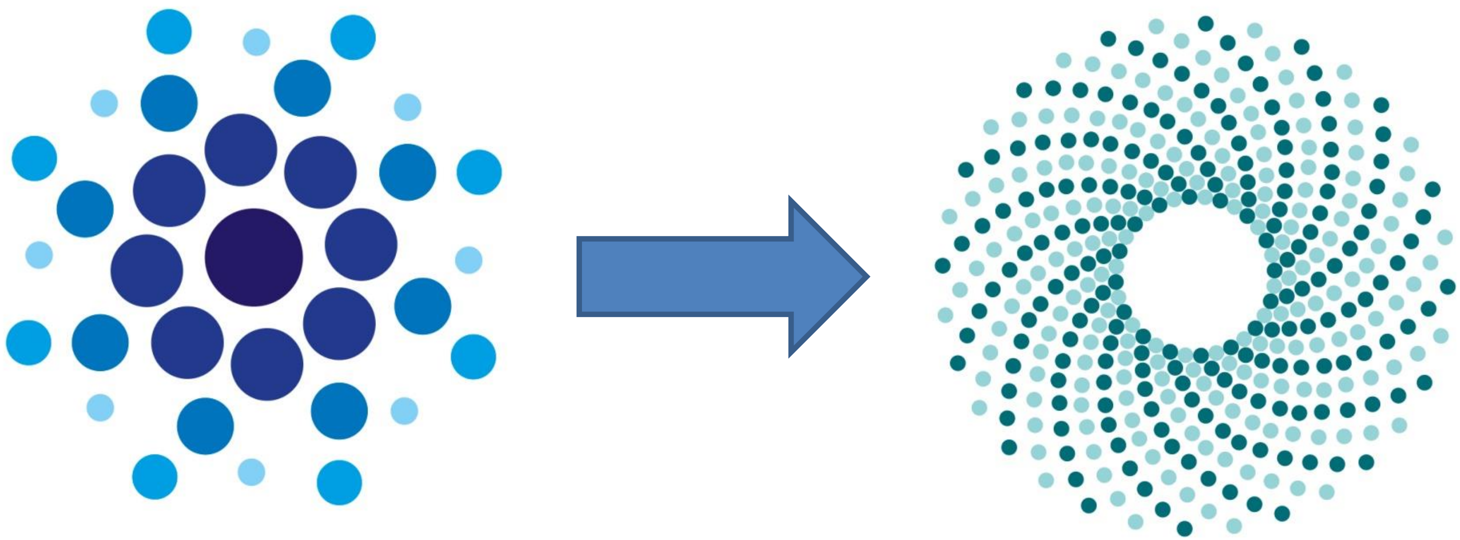
Focus areas



Emulsification

Particle Production

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Encapsulation

What is microencapsulation?

Dictionary definition : microcapsule (micro|cap¦sule) - noun

“a minute capsule used to contain drugs, dyes, or other substances and render them temporarily inactive.”

Essentially a technique to isolate/entrap or stabilise materials.

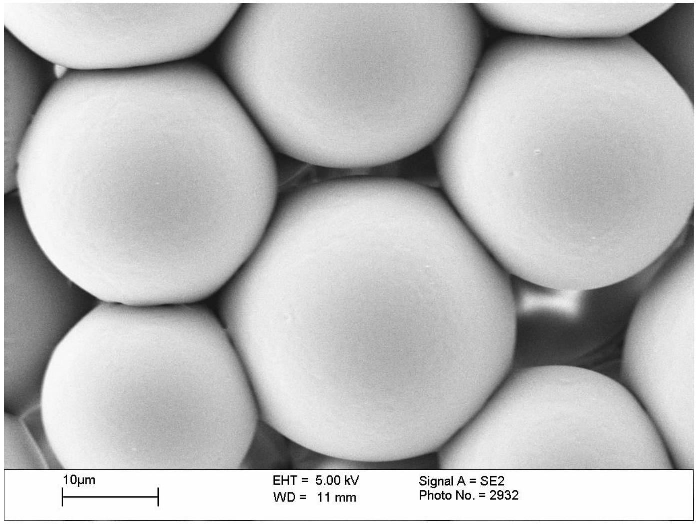
And to control the release of the encapsulated material.

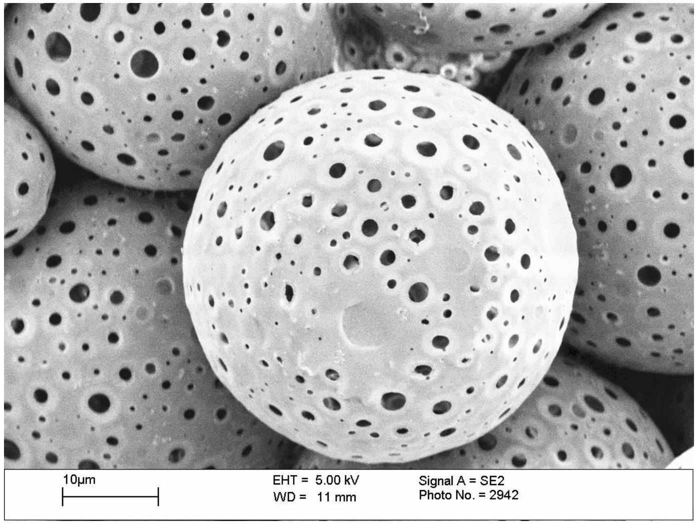
* http://oxforddictionaries.com

Encapsulation

From emulsions to delivery systems…

We also develop microcapsules/microbeads containing active ingredients





PLGA particles made using a LDC-1 Dispersion Cell

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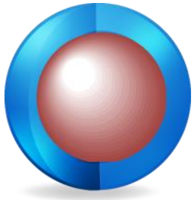
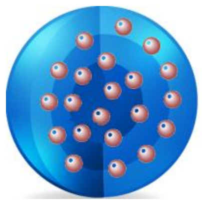
Pictures courtesy of Dr. Gilda Gasparini

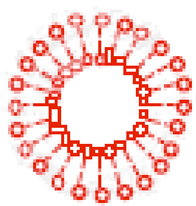
Particle Morphology



Core/shell

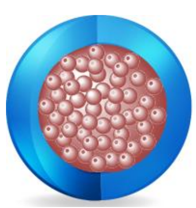


Matrix



Liposomes

Multiple emulsions

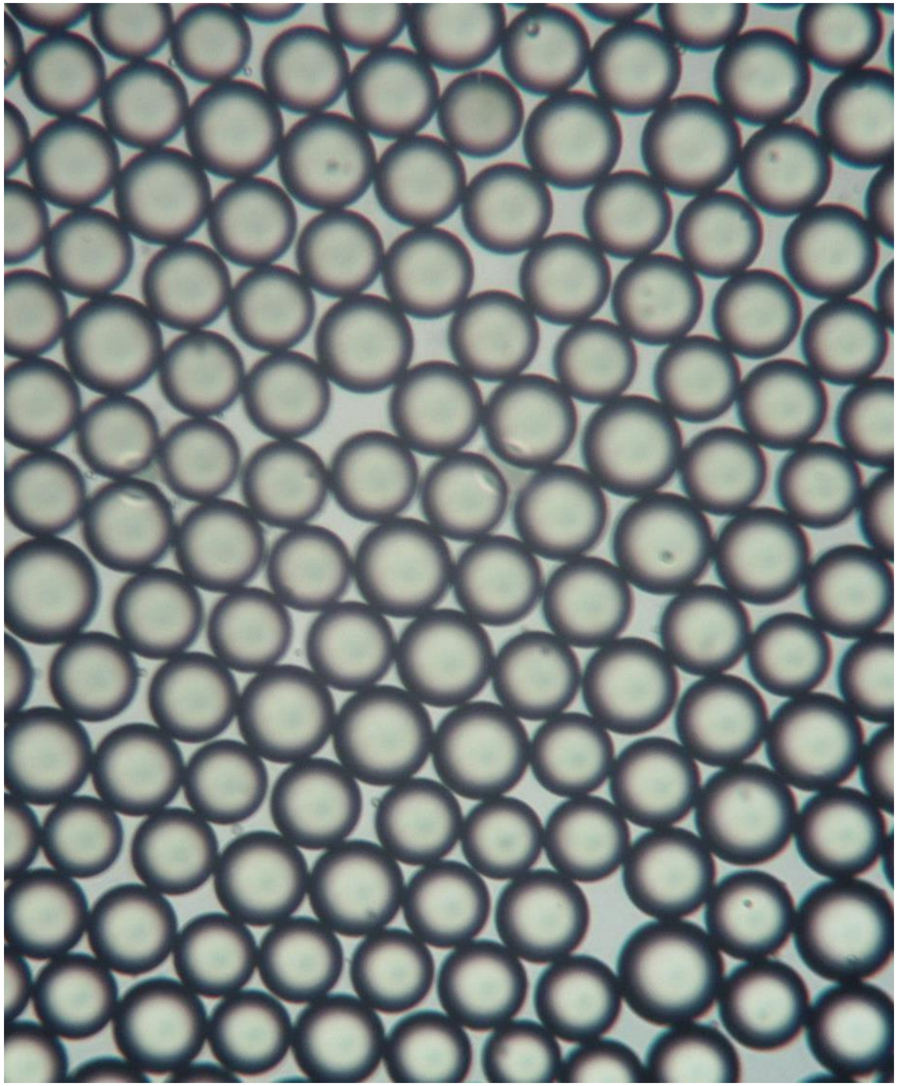


w/o/w

o/w/o

Oil in Water

No Membrane Coating Required



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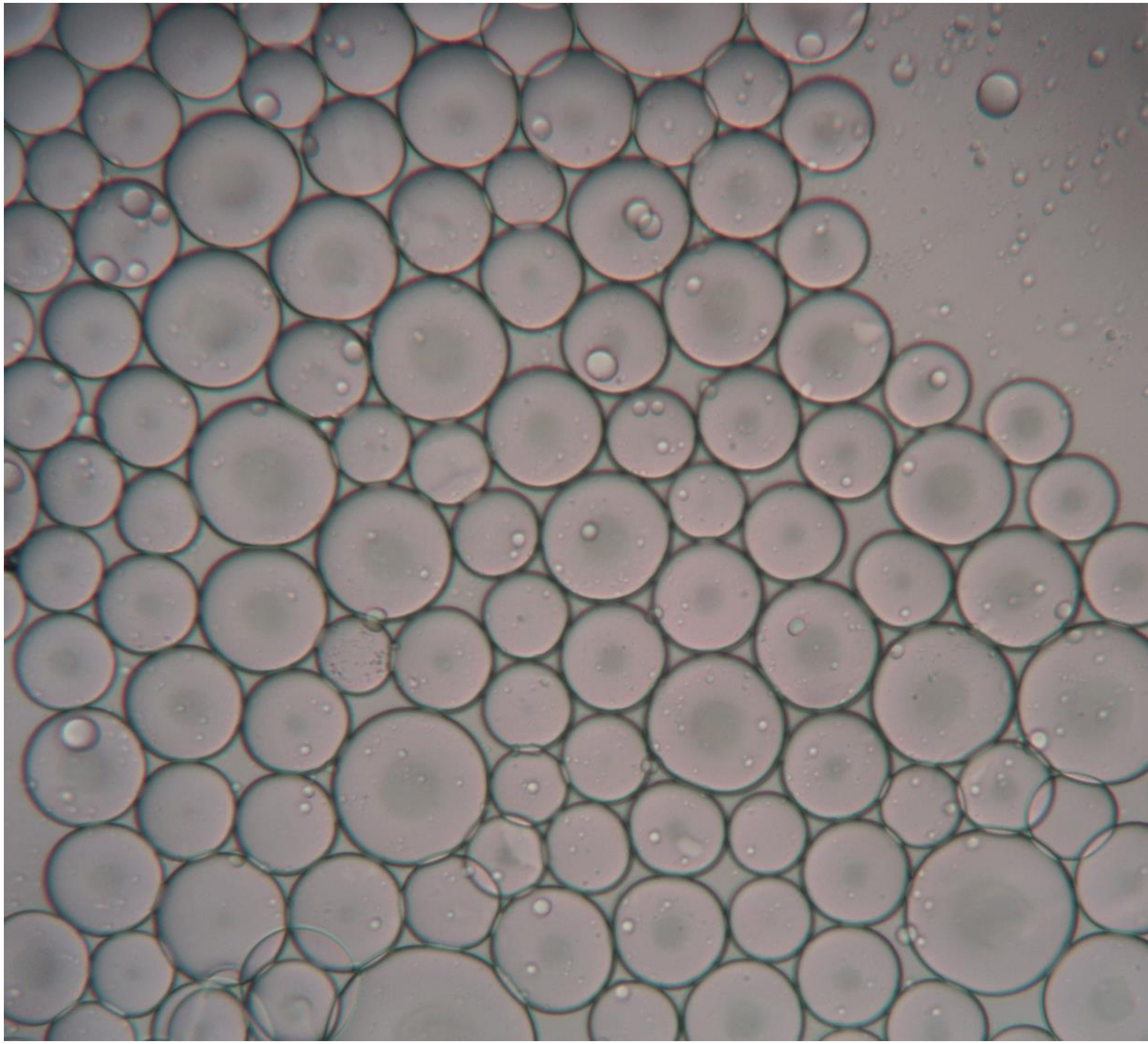
Water in Oil

- **Hydrophobic coating applied to membranes**



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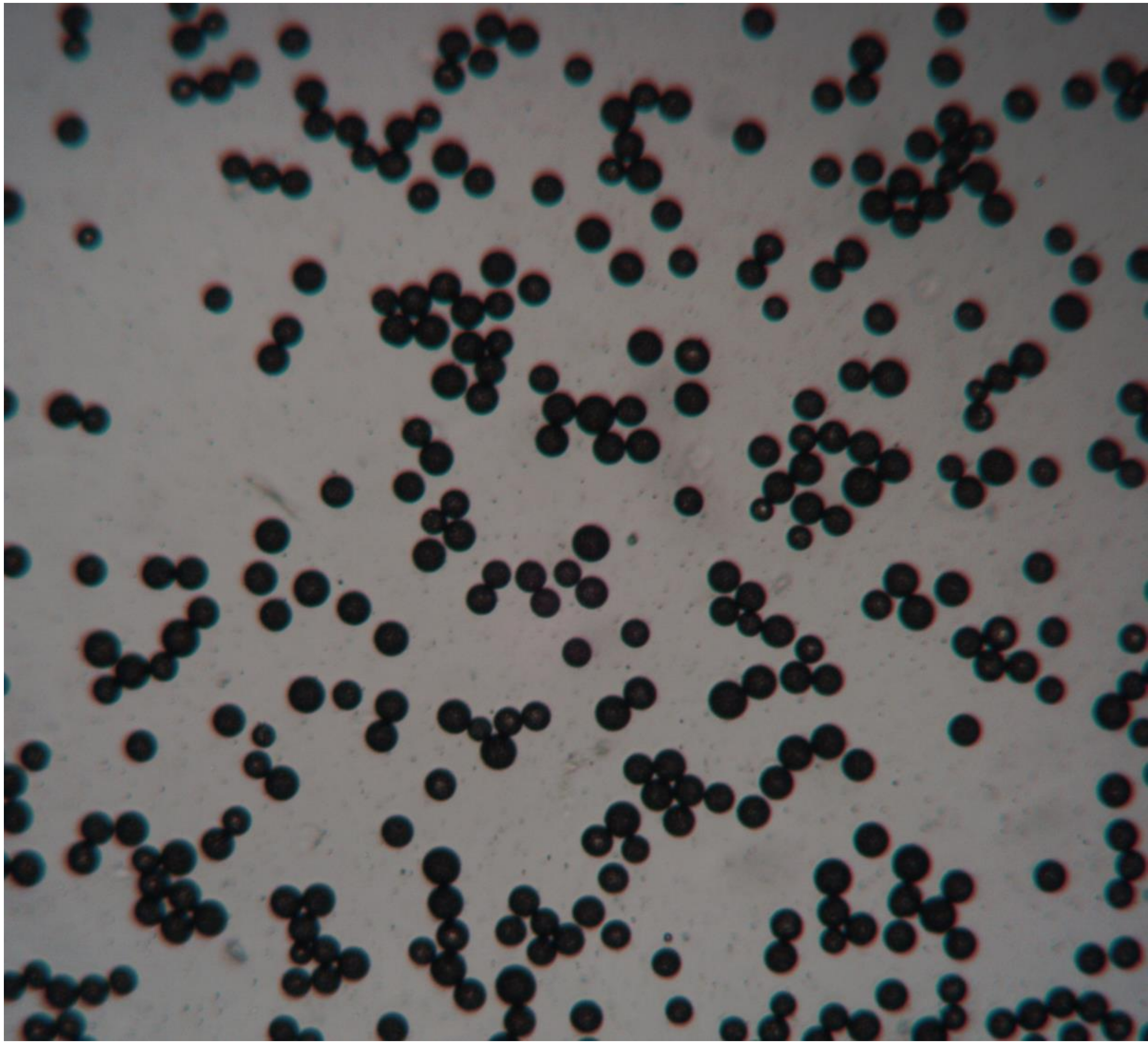
Interfacial Polymerisation



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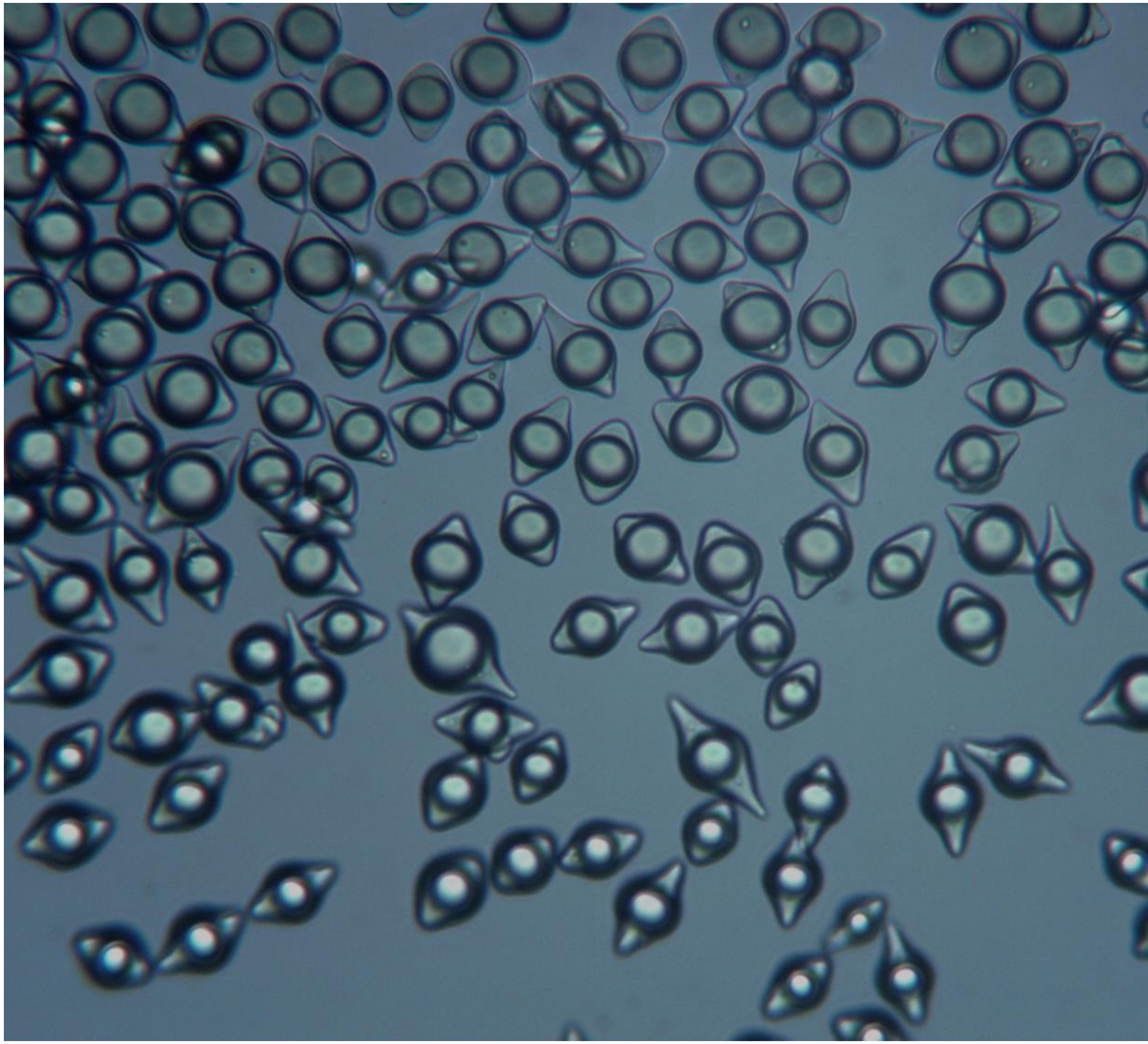
Coacervate Capsules



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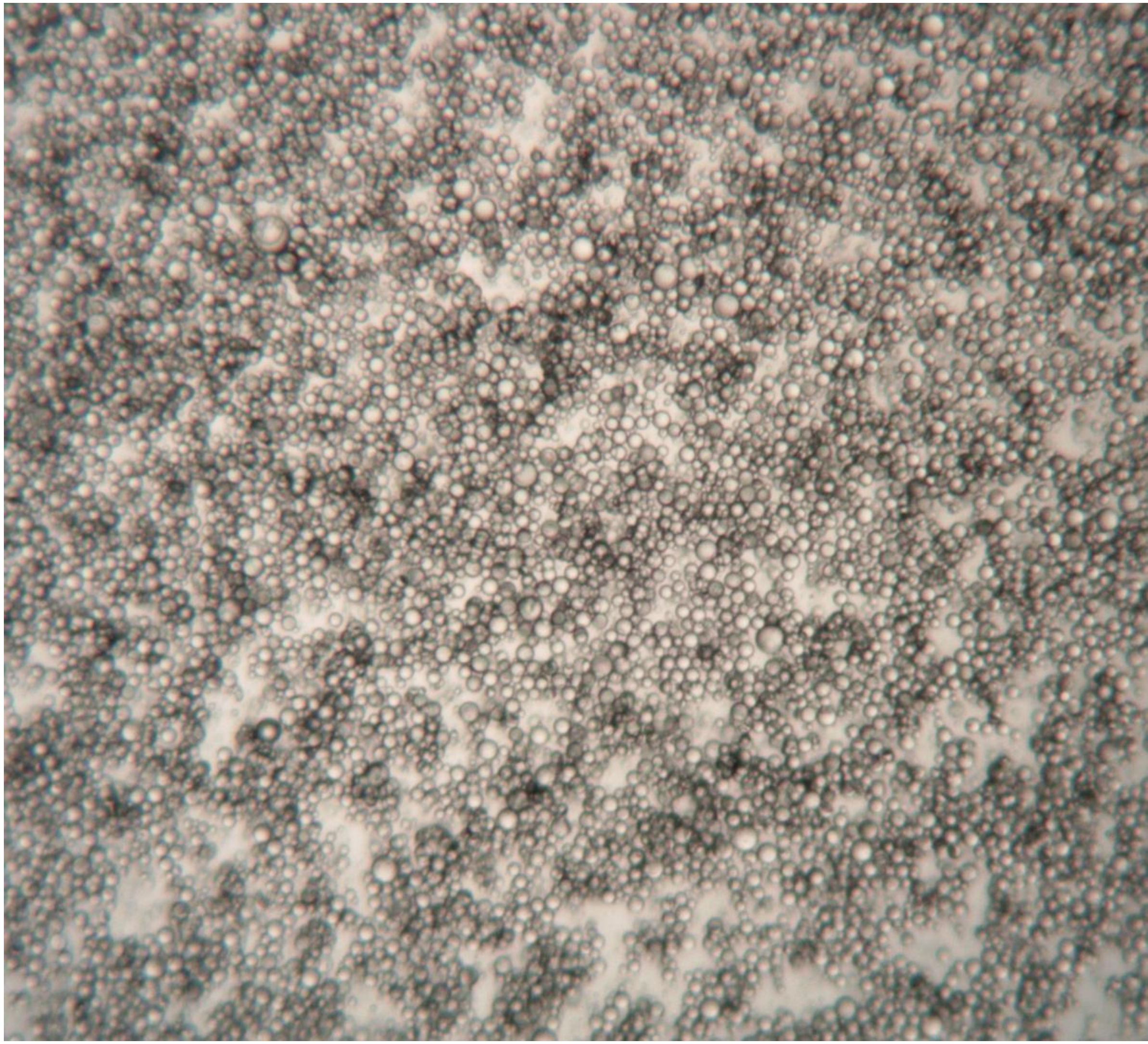
Melamine Formaldehyde Capsules



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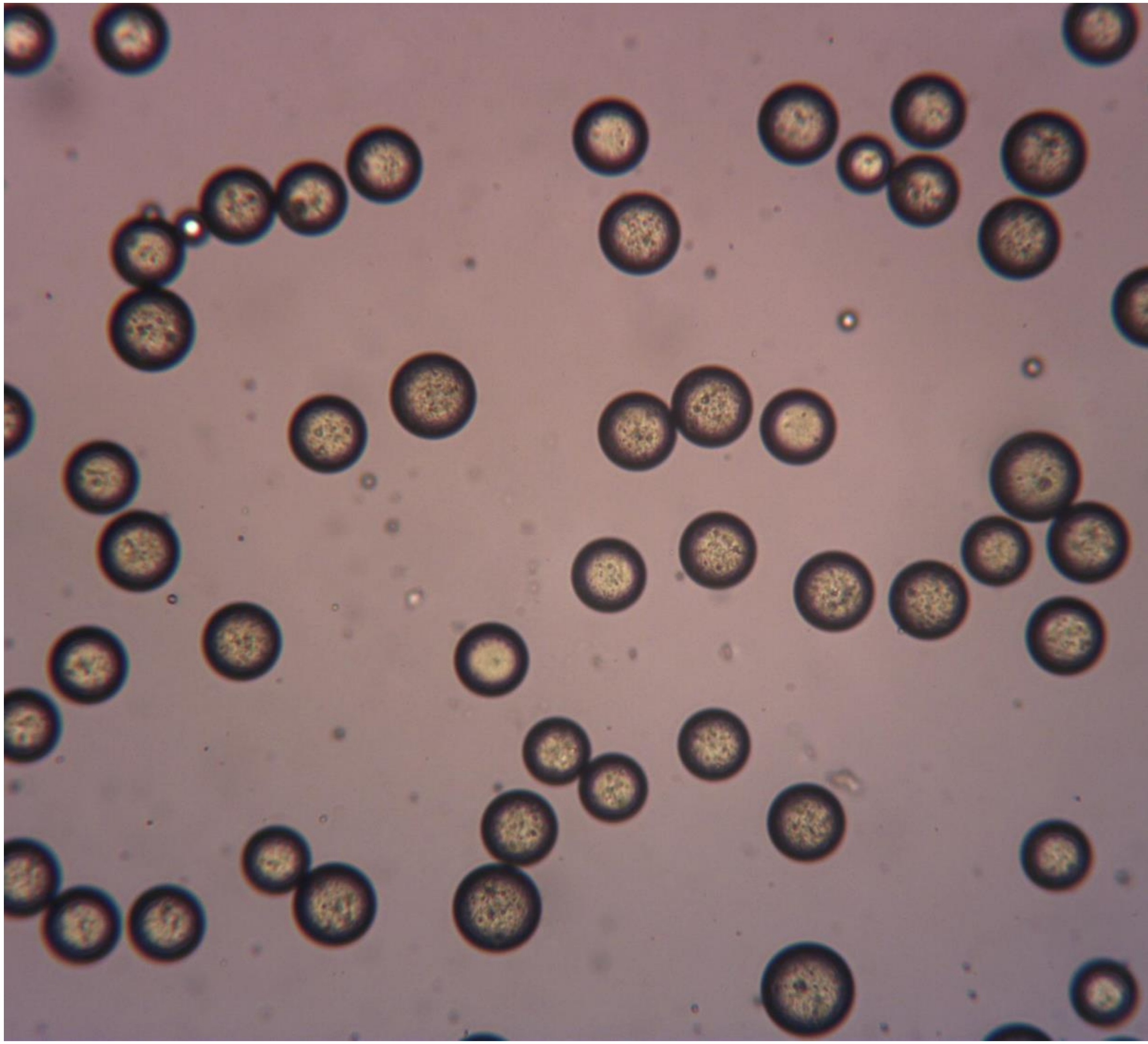
Double Emulsion Polymer Beads



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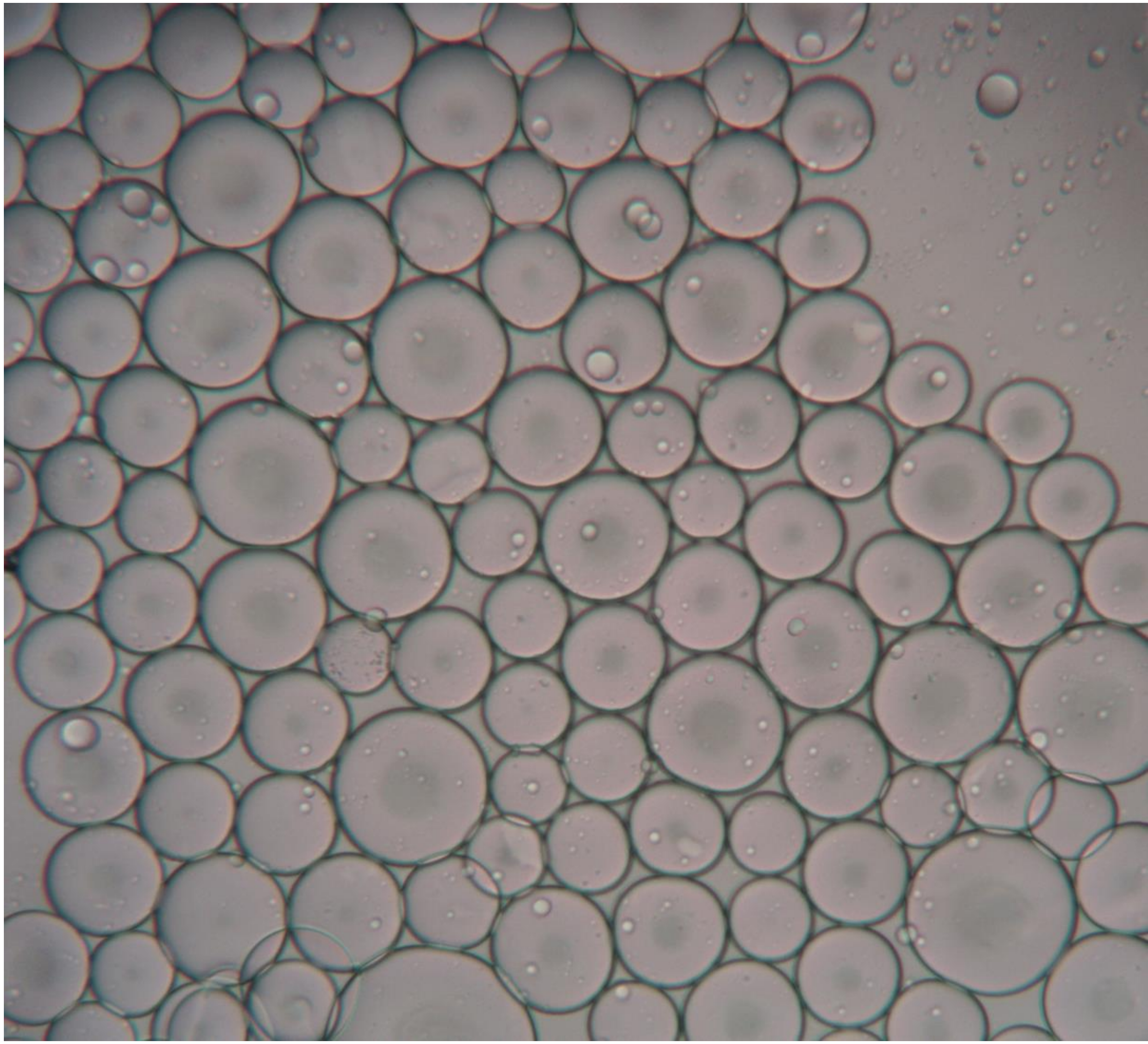
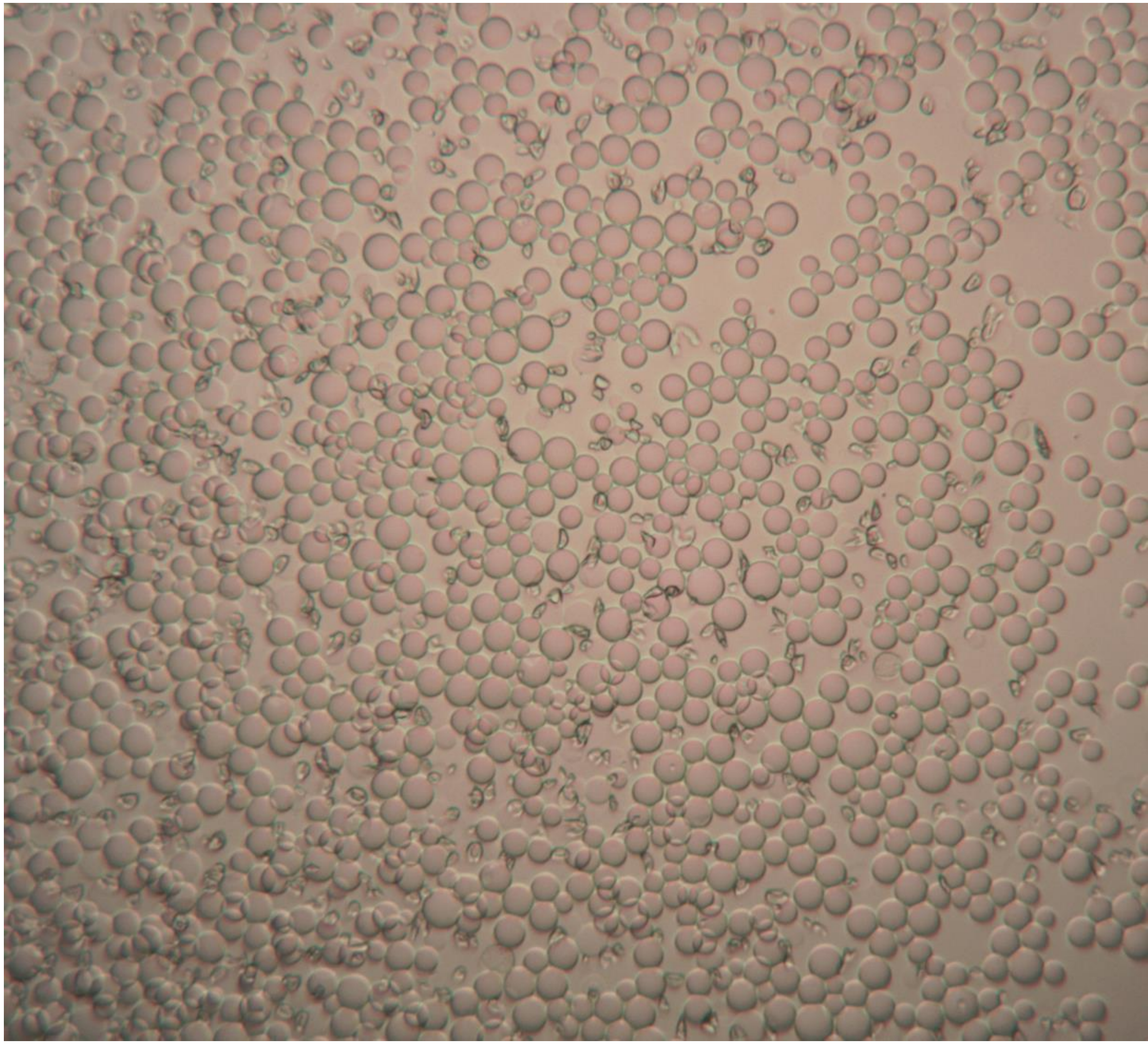
PVA Beads



Silica Beads



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Agarose Beads

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Encapsulation - Benefits

Micropore have an array of controlled release technologies that…

- Can act as delivery systems.
  - Isolate, stabilise, protect and release.
- Can enhance product functionality.
  - Improve processability by reducing unwanted interactions between formulation components.
- Provide a narrow particle size distribution.
  - Meaning that every particle behaves in exactly the same way.

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Summary

We have the technology…

- to manufacture uniformly sized emulsions
- with controlled size characteristics
- at high production volumes
- under favourable process conditions
- which can be used to make microcapsules

…using **membrane emulsification** techniques.

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Thank you for your attention!

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"Partners in Particle Production"

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