ENCAPSULATION BY MEMBRANE EMULSIFICATION

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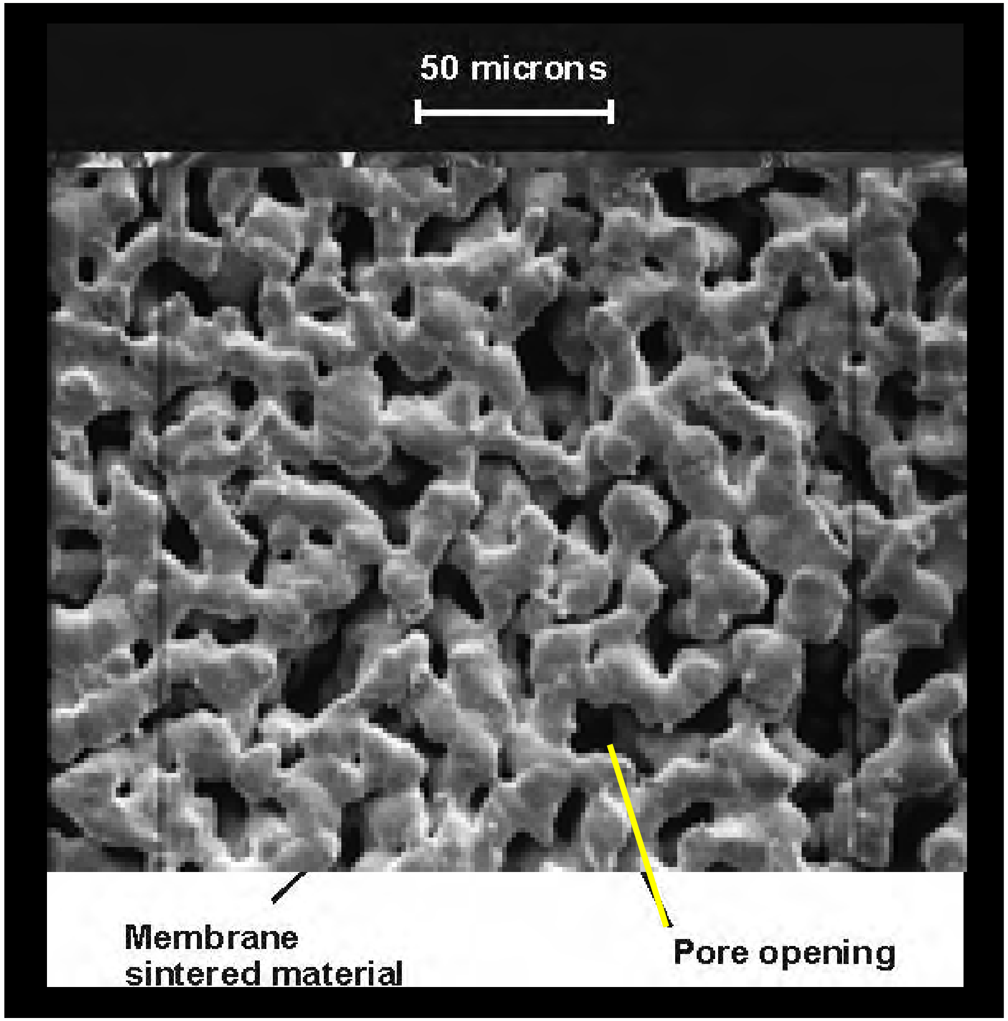
PRESENTATION LAYOUT

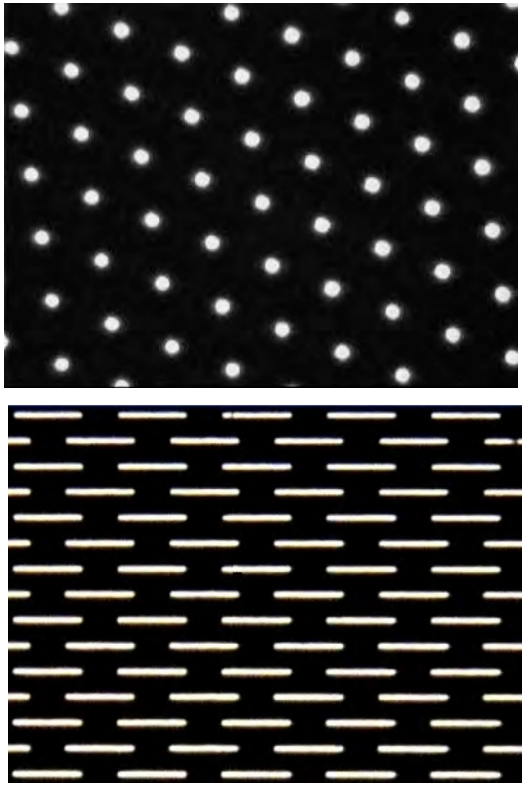
- Produce drops (convert to encapsulated particles)
- Membrane surface, what makes a good membrane?
- Membrane emulsification – shear and size
- Examples – from drops to particles, including surfactant free drops and yeast encapsulation

CONVENTIONAL MEMBRANES

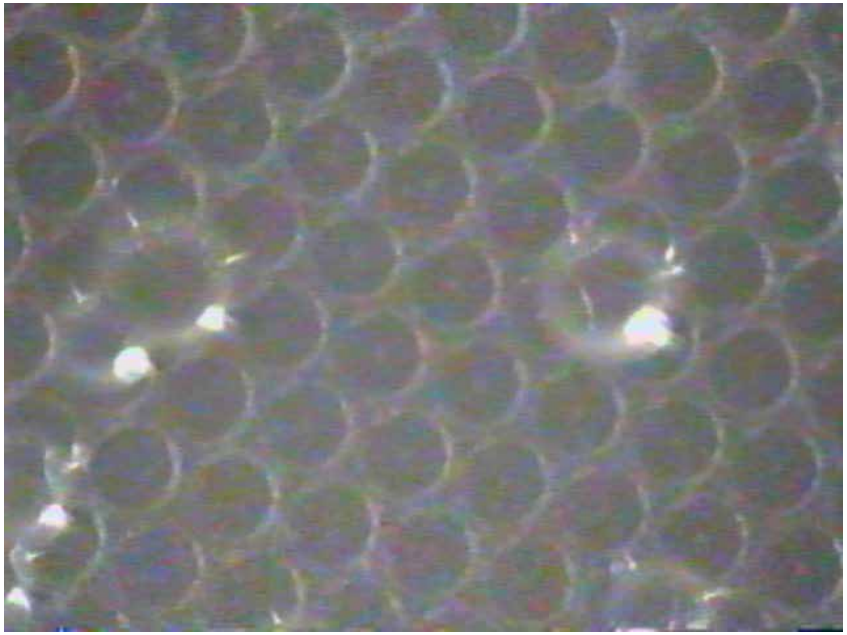


MEMBRANE EMULSIFICATION

NO SHEAR STRESS ON THE MEMBRANE SURFACE



TOP VIEW



Hydrophilic membrane

D_{50}=200 μm

Kosvintsev et al. 2008

Scaling up – possible

Productivity – high

SHEAR STRESS ON THE MEMBRANE SURFACE

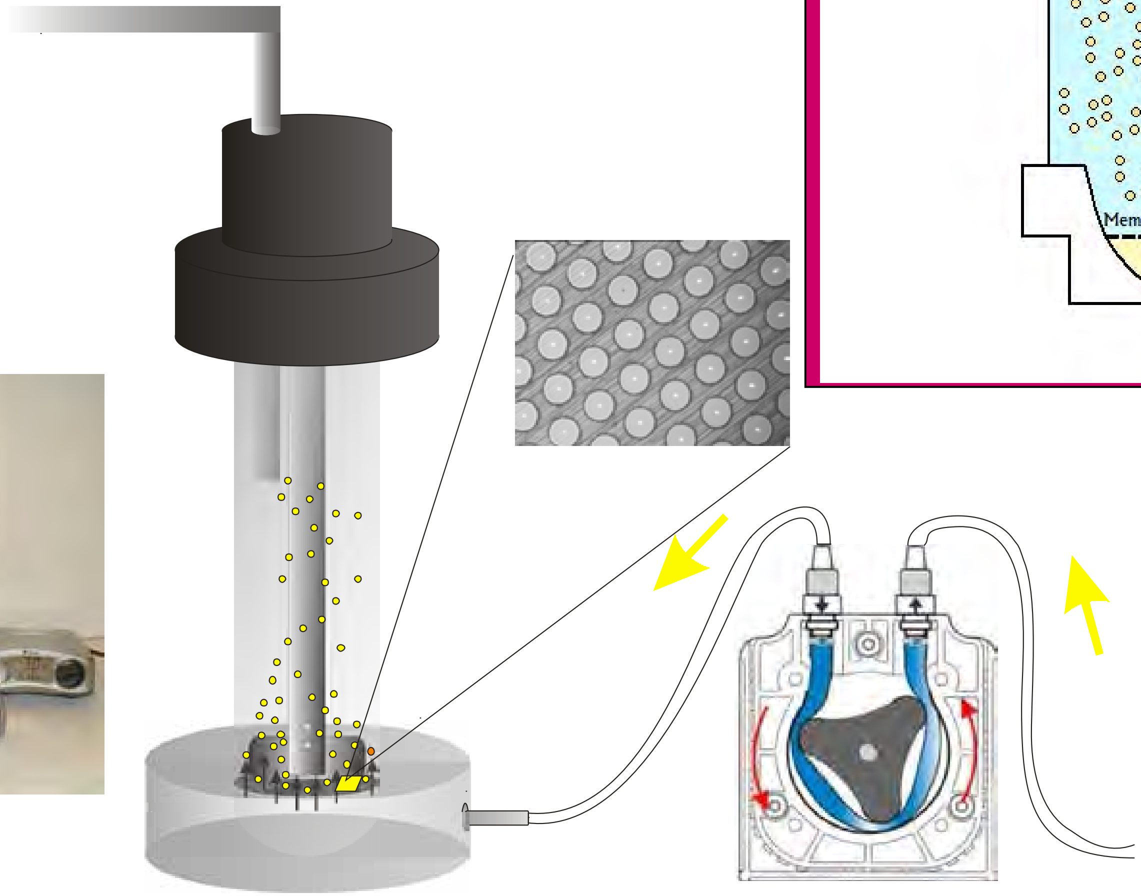
Movements of continuous phase:

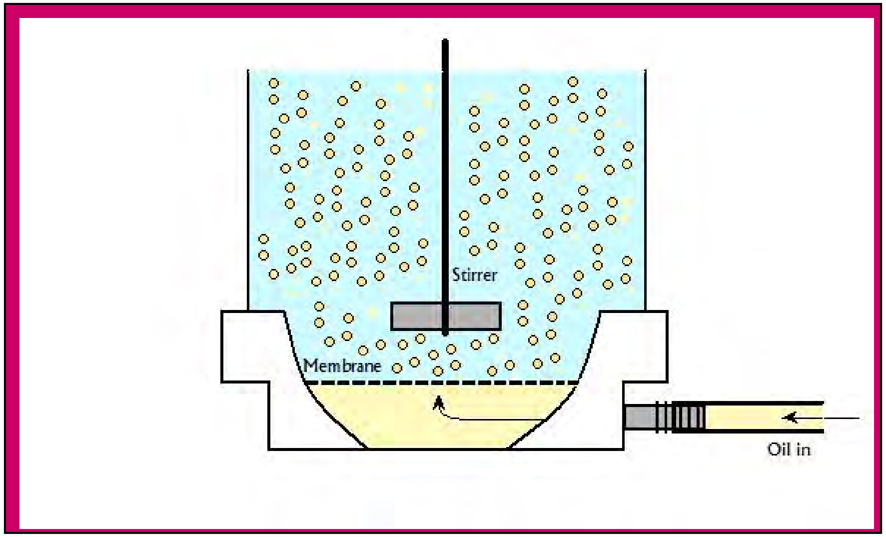
- **STIRRING**
- **CROSS FLOW**
- **PULSING THE CONTINUOUS PHASE**

Movements of the membrane:

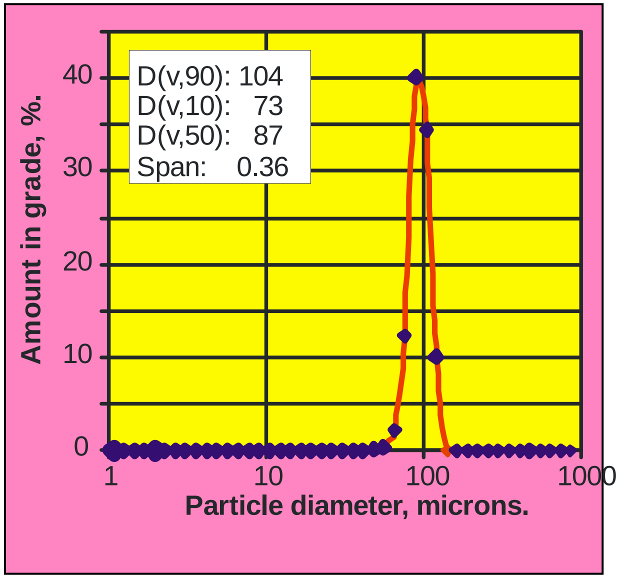
- **VIBRATION (axial oscillation)**
- **ROTATION**
- **AZIMUTHAL (TORSIONAL)**

STIRRING – DISPERSION CELL

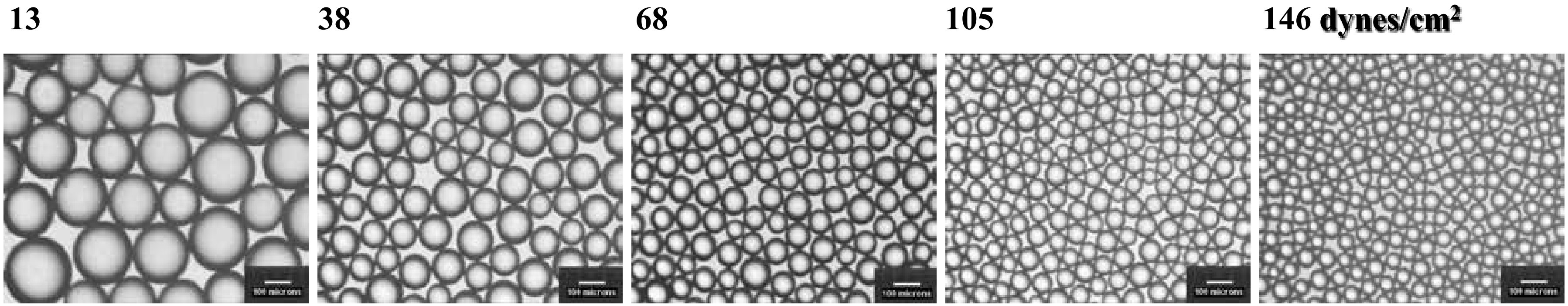




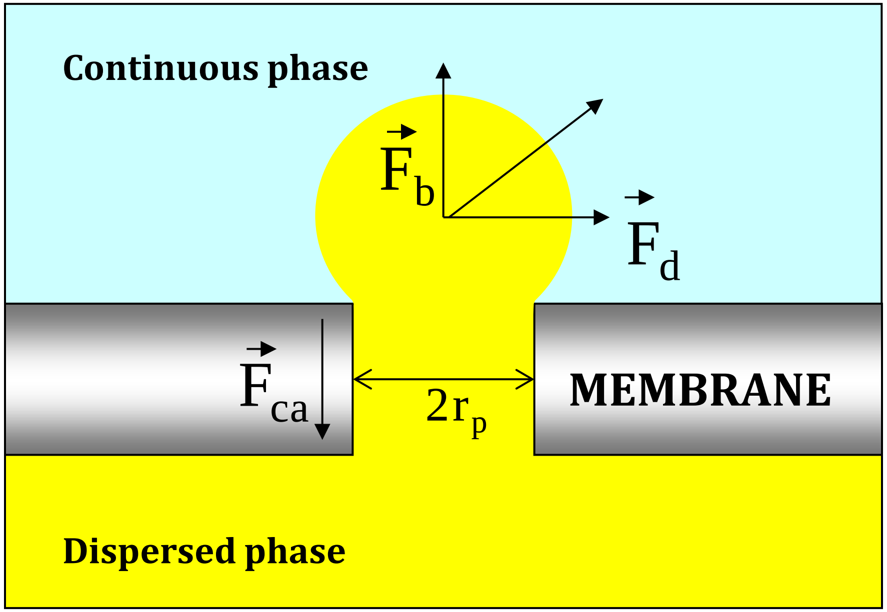
STIRRING – DISPERSION CELL

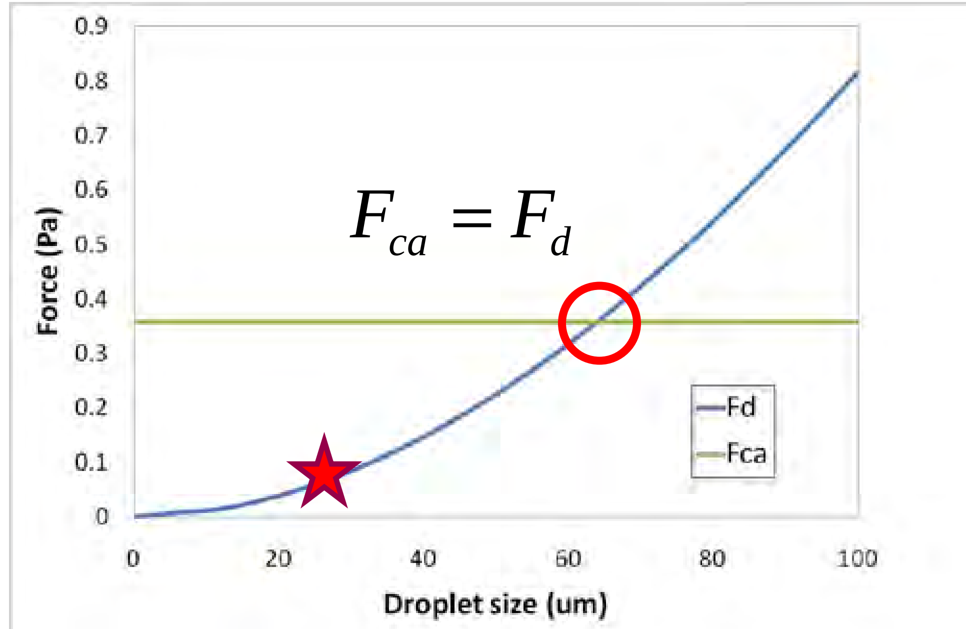


pressure drop is very low, due to the membrane design, the shear is low and emulsification conditions are gentle



FORCE BALANCE MODEL





F_{ca} - Capillary force

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

F_d - Drag force

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

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

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

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

Kosvintsev et al. 2008

Dragosavac et al. 2008

STIRRING – DISPERSION CELL

$$x = \frac{\sqrt{18t^2 r_p^2 + 2\sqrt{81t^4 r_p^4 + 4r_p^2 t^2 g^2}}}{3t}$$

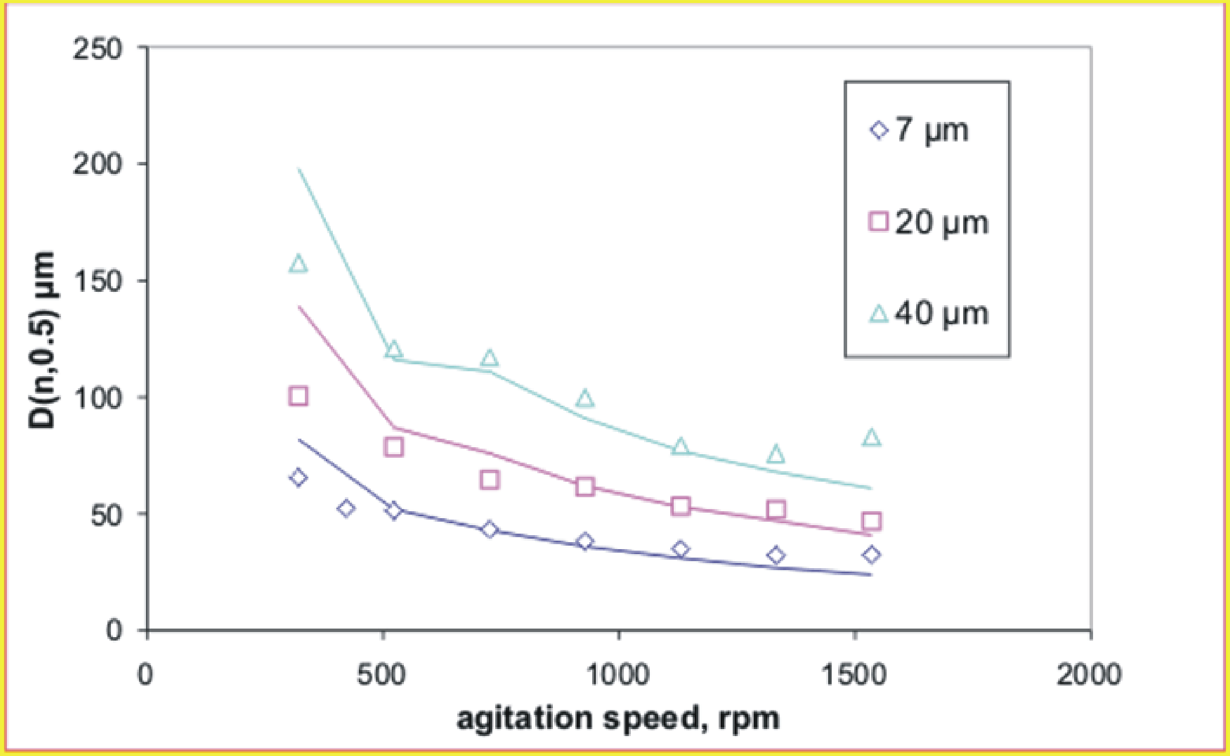
Drop diameter

Shear stress

Pore radius

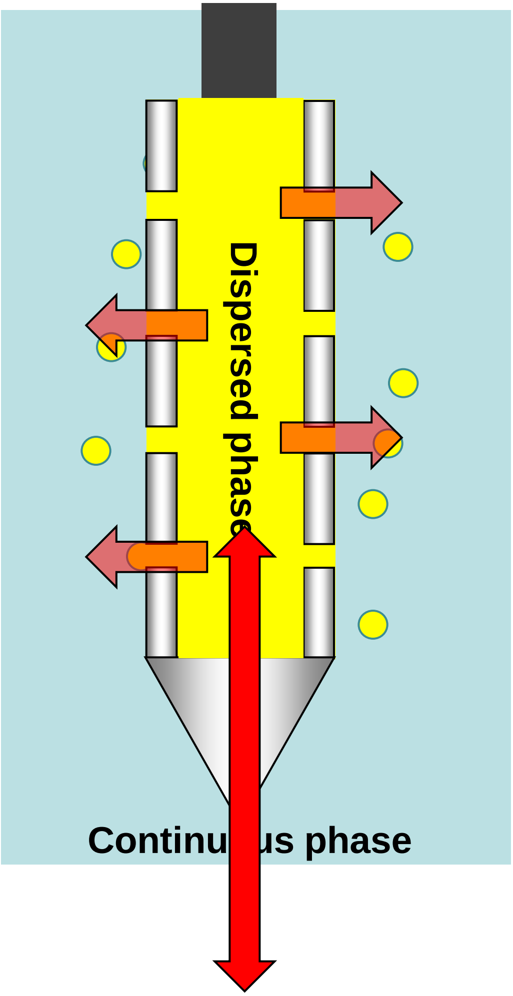
Interfacial tension

STIRRING – DISPERSION CELL

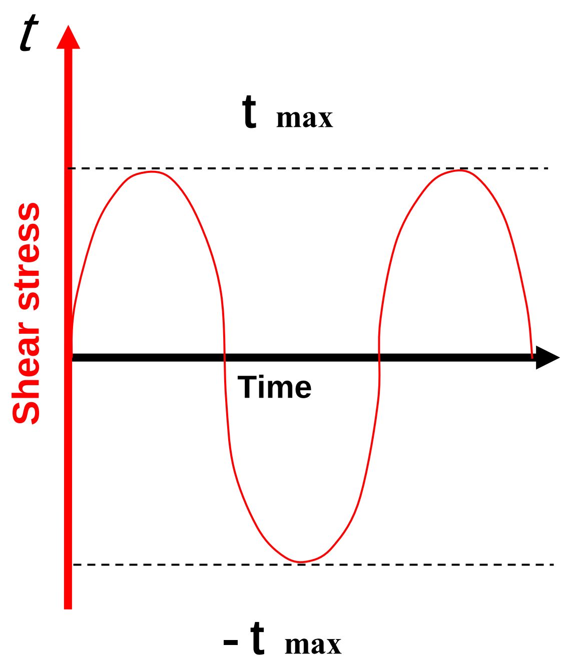


SHEAR STRESS ON THE MEMBRANE SURFACE

OSCILLATION AXIAL SYSTEM



Holdich R. G. et. al. 2010



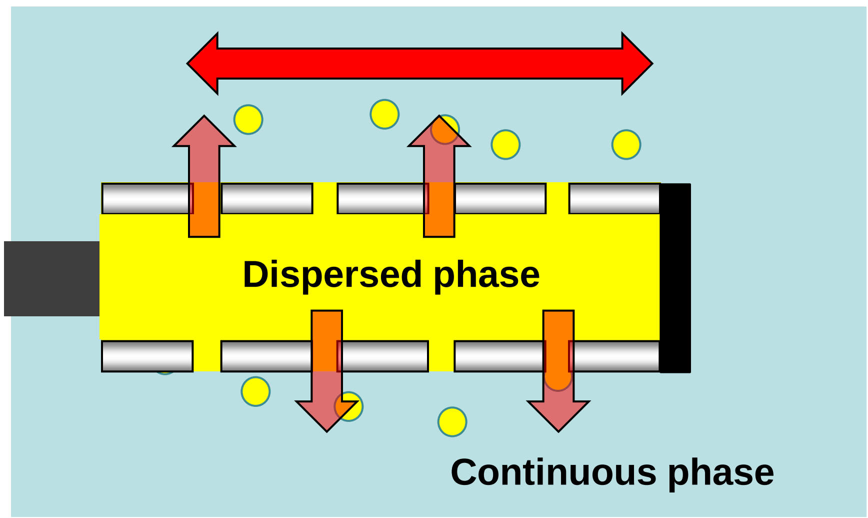
Shear stress

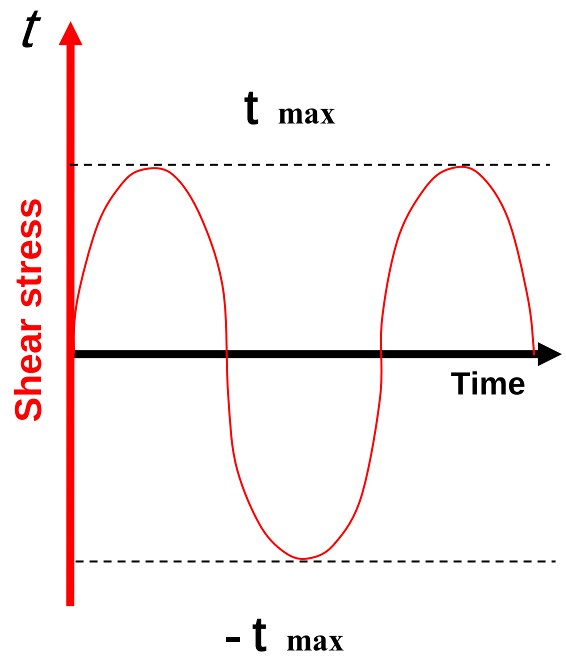
$$t\ \max = f\left(h, f, a\right)$$

DOES CHANGE WITH TIME AND IT DOES NOT CHANGE OVER THE MEMBRANE AREA

SHEAR STRESS ON THE MEMBRANE SURFACE

PULSING THE LIQUID FLOW





Holdich R. G. et. al. 2010

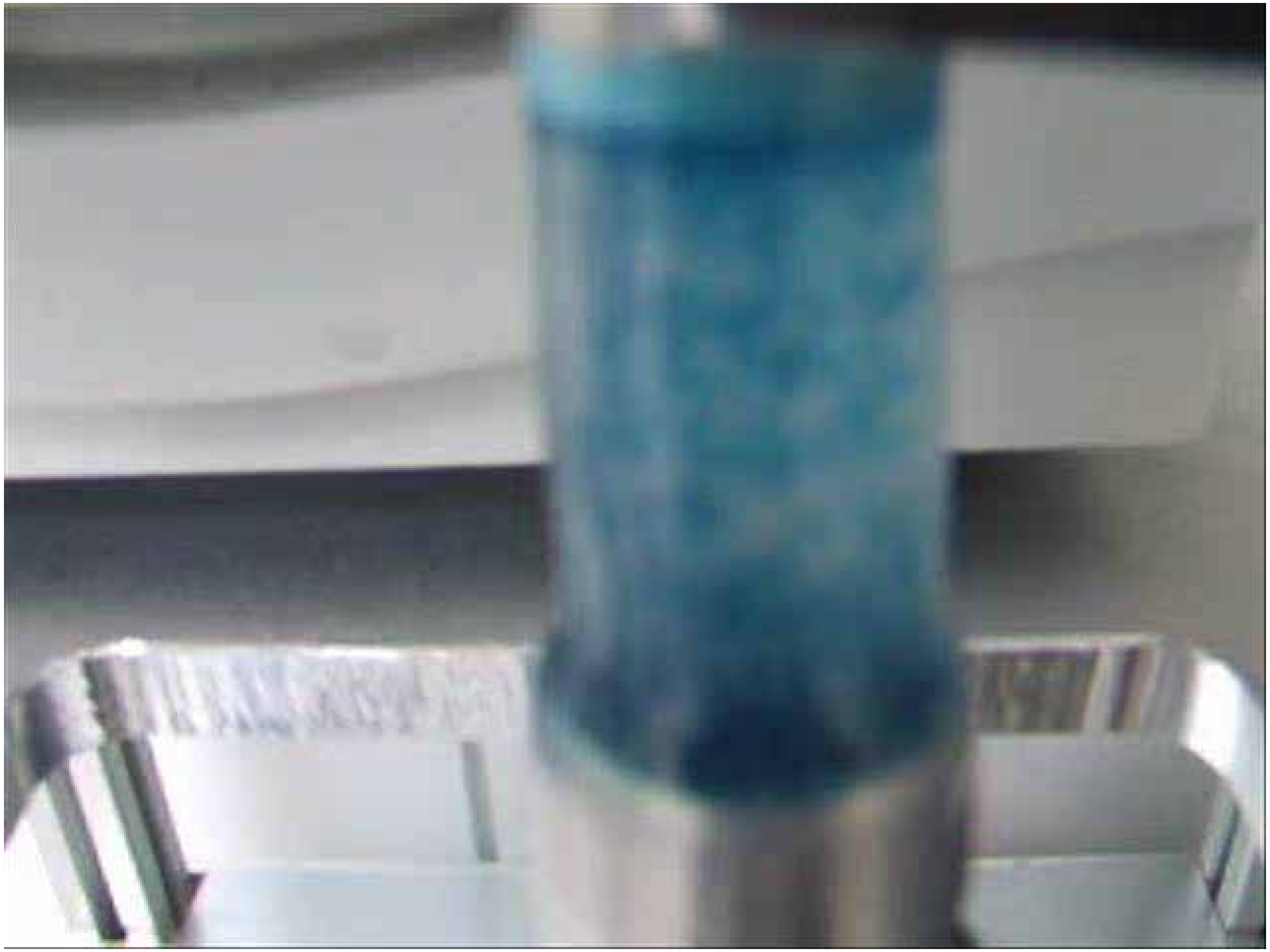
Piacentini. et. al. 2014

Shear stress

$$t \max = f(h, f, a)$$

SHEAR STRESS BY PULSING LIQUID FLOW

coacervates dyed with blue food colouring:



SHEAR STRESS ON THE MEMBRANE SURFACE

OSCILLATING (AZIMUTHAL) SYSTEM

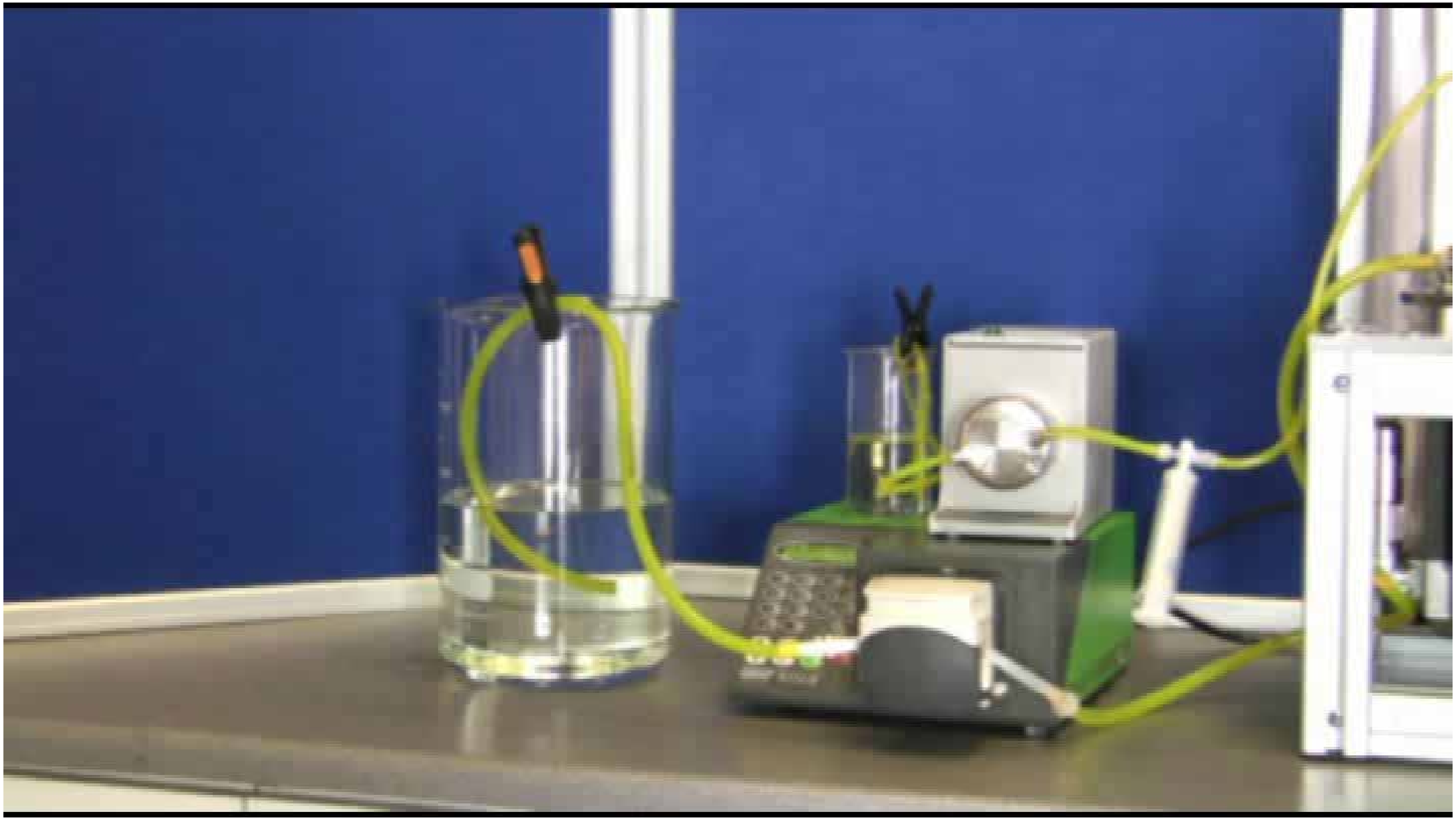
Oscillating Membrane Emulsification

- **Pharma / high value**
  - **Current capacity: 4 kg/hour,**

- **FMCG market**
  - **Current capacity: 100 kg/hour,**

SHEAR STRESS ON THE MEMBRANE SURFACE

OSCILLATING (AZIMUTHAL) SYSTEM



EXPERIMENTAL RESULTS

FORMULATIONS

1. COMPLEX COACERVATION
2. POLYMER PARTICLES FOR DRUG DELIVERY
3. INORGANIC SILICA PARTICLES
4. SURFACTANT FREE STABILISATION
5. YEAST ENCAPSULATION

1. COMPLEX COACERVATION
O/W emulsion

Please see poster:
Alix Barton

1. COMPLEX COACERVATION

O/W emulsion

Motivation for the work:

Currently batch production

High polydispersity of the product and usually too big droplet size

Need for pig gelatine alternative

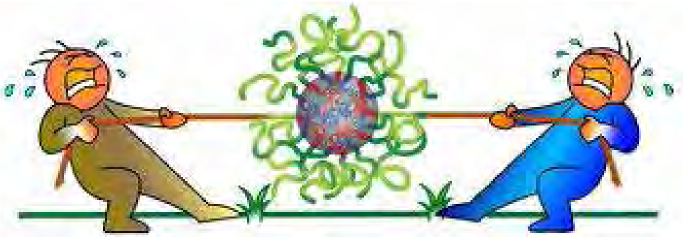
1. COMPEX COACERVATION

1. **Drop production** in hydrocolloids solution

2. Coacervation (phase separation) implying the formation of a coacervate phase – **pH adjustment**

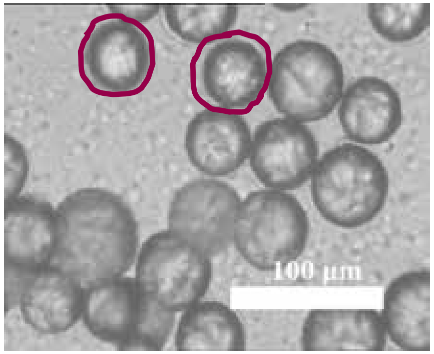
3. Wall formation by aggregation of the hydrocolloid around droplets of the emulsified hydrophobic material – **time, room temperature**

4. **Wall-hardening**, which is generally achieved by cross-linking the hydrocolloid forming the wall

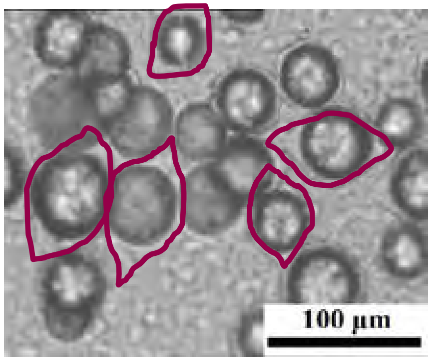


1. COMPLEX COACERVATION – Oil encapsulation

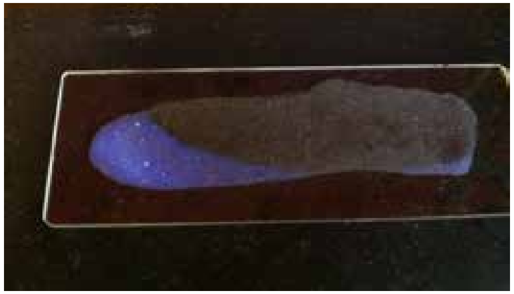
LIQUID CRYSTALS



Fast cooling



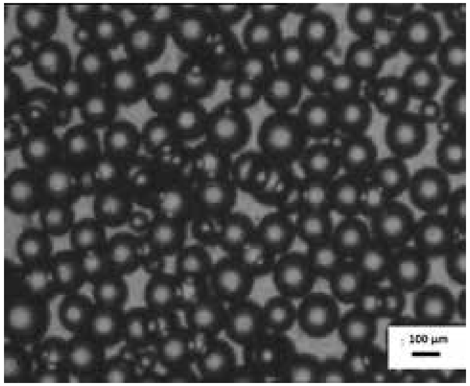
Slow cooling



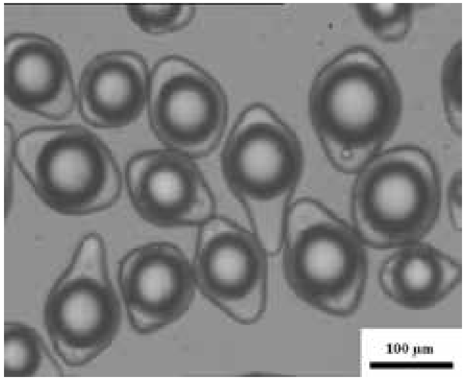
Dragosavac 2012, Unpublished material

Optimising drying methods – longer storage

ENCAPSULATION OF ESSENTIAL OILS



ENCAPSULATION OF PARAFFIN OIL



Dragosavac 2012, Unpublished material

1. COMPLEX COACERVATION – Oil encapsulation

FISH GELATINE CAPSULES

WHY FISH GELATINE?

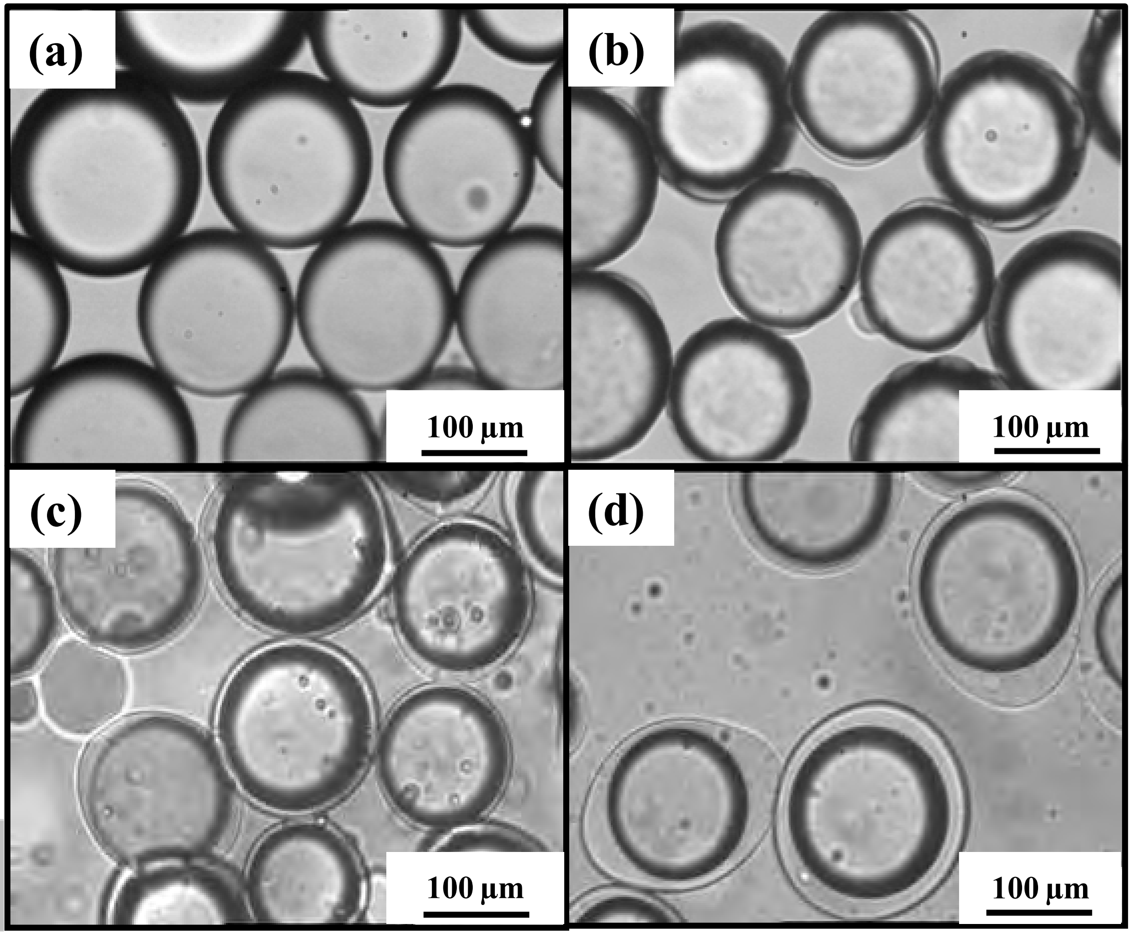
- **ROOM TEMPERATURE** - less energy compared to alternative gelatine types and £££
- New possibilities for encapsulation of **VOLATILE COMPOUNDS**
- Increased **CONSUMER** consent for religious or diet reasons and health safety

Piaccentini et al., 2013

ITM-CNR @ University of Calabria, Rende

DIFFERENT RATIOS OF FG:GA FOR MICROCAPSULES

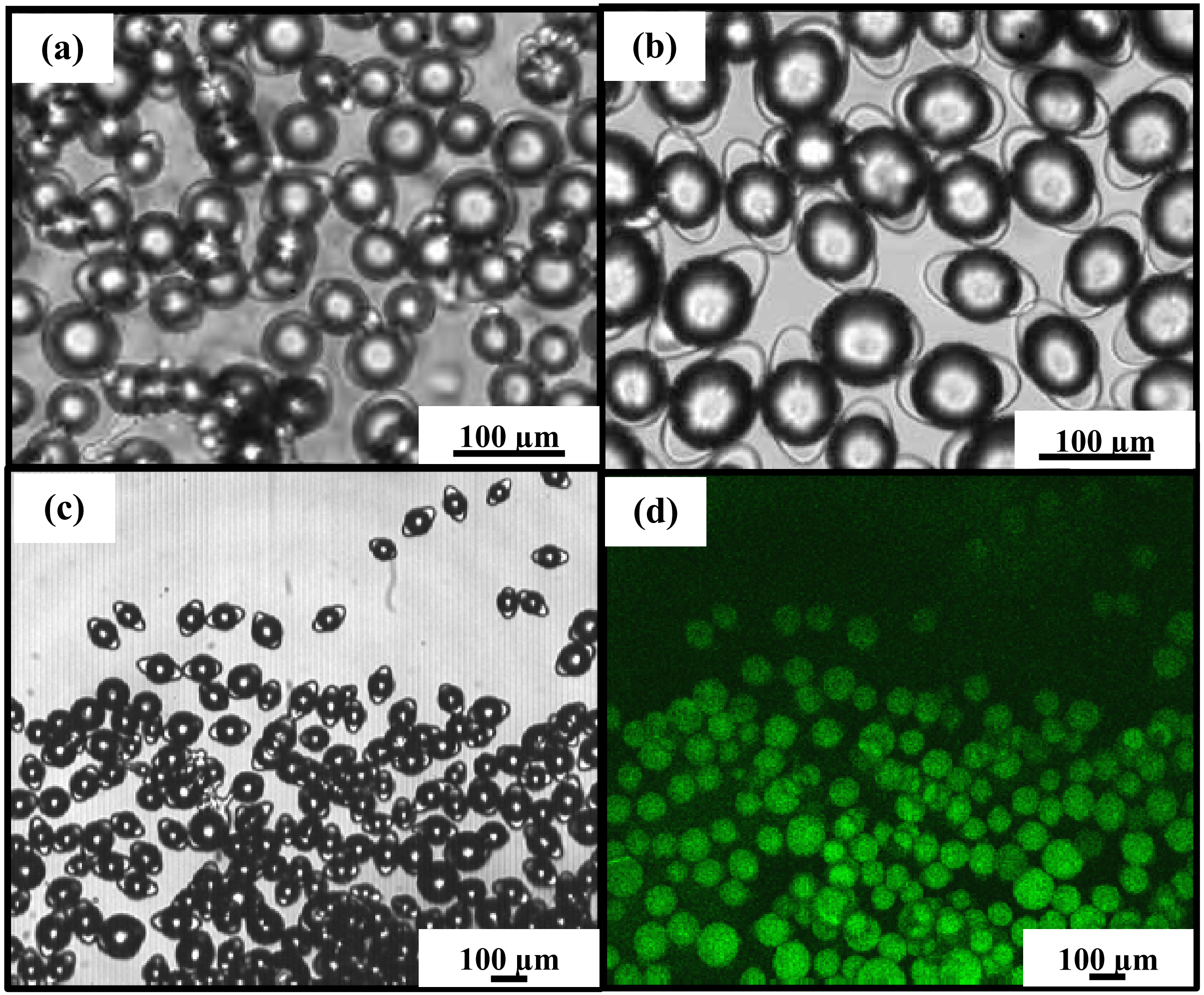
ROOM TEMPERATURE



Piaccentini et al., 2013

FG:GA **(a) 30:70; (b) 40:60; (c) 80:20; and (d) 50:50.**

OIL ENTRAPMENT



Freeze dried particles (to enable future volatile compound encapsulation)

Silica particles added to produce free flowing particles

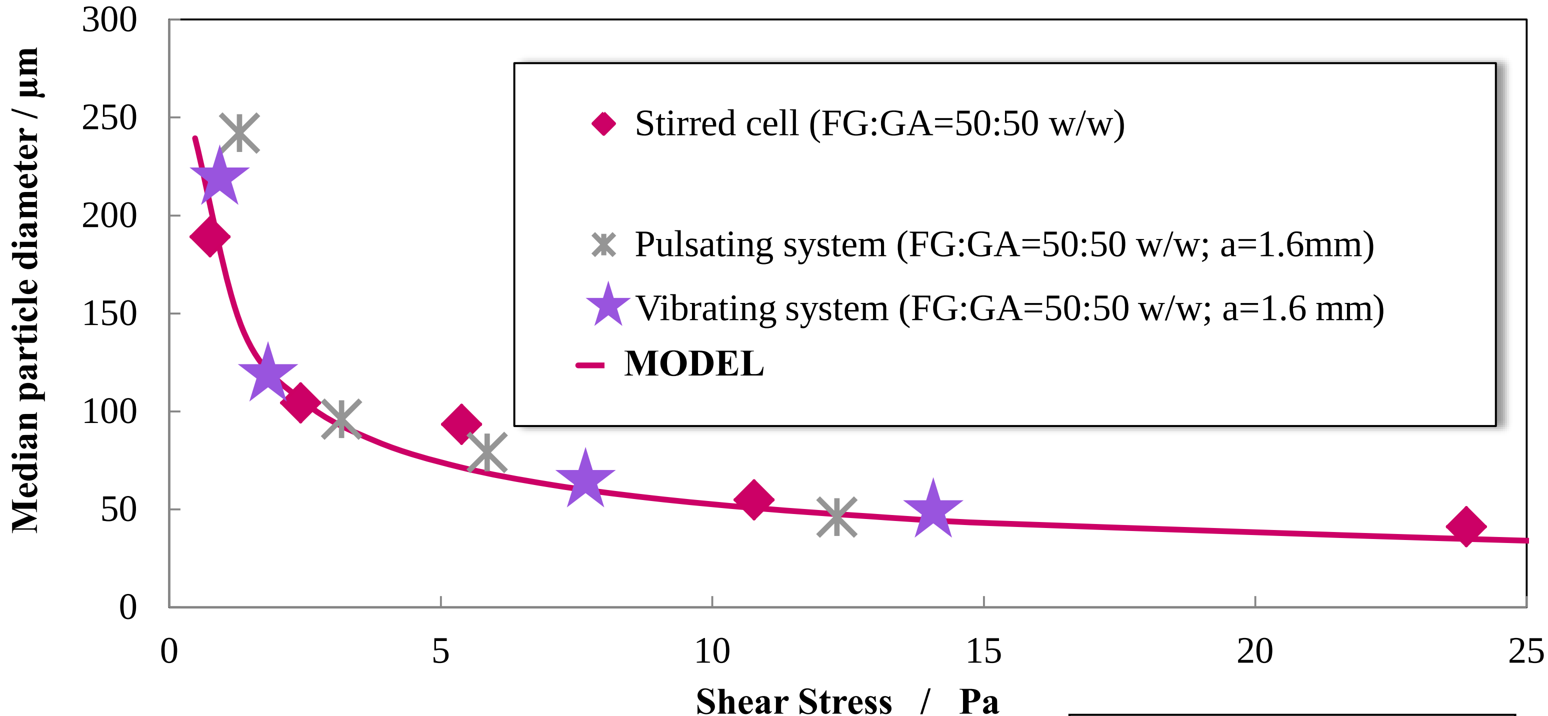
Piaccentini et al., 2013

1. COMPLEX COACERVATION

DISPERSION CELL, PULSING & VIBRATING SYSTEMS

Dispersed phase: **Sunflower oil**
Continuous phase: **Fish gelatine (FG) and Gum Arabic (GA)**

20 µm MEMBRANE



Piaccentini et al., 2013

Flux through the pulsed membrane up to 30 L h^{-1}

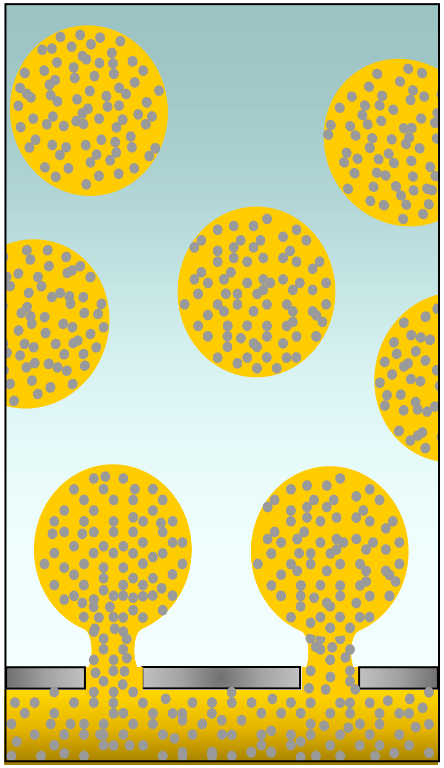
2. ANTICANCER DRUG ENCAPSULATION

Aim to encapsulate water soluble peptide

2. Poly (D,L-Lactic-Glycolic Acid): PLGA

- FDA approved biocompatibility
- Complete degradation
- Current applications:
  - Anticancer drug carrier
  - Human growth deficiency treatments
  - Protein and gene delivery
  - Scaffolds for bone repairing
  - Suture material

Secondary emulsion W/O/W



2. ANTICANCER DRUG ENCAPSULATION
O/W & W/O/W

Motivation for the work:

Currently batch production

Low uniformity of the produced particles using conventional emulsification methods, *expensive losses of product*

Need for higher encapsulation efficiency

Anticancer drug - extremely expensive & shear/temperature sensitive

2. ENCAPSULATION OF WATER SOLUBLE PEPTIDE USING BIODEGRADABLE POLYMER

SOLVENT EVAPORATION

1. **Dispersion phase – polymer (PLGA) mixed with DCM (volatile oil phase)**

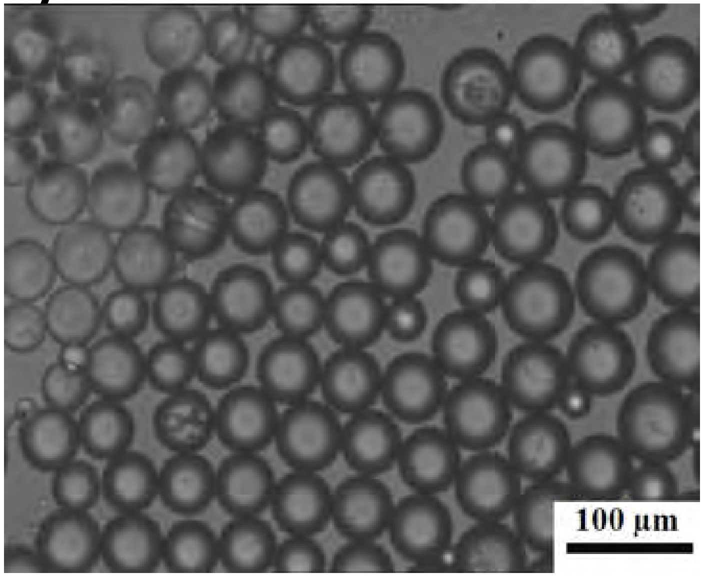
2. **Mixing the peptide with previously prepared dispersion phase**

3. **Injecting through the membrane into 1% PVA solution**

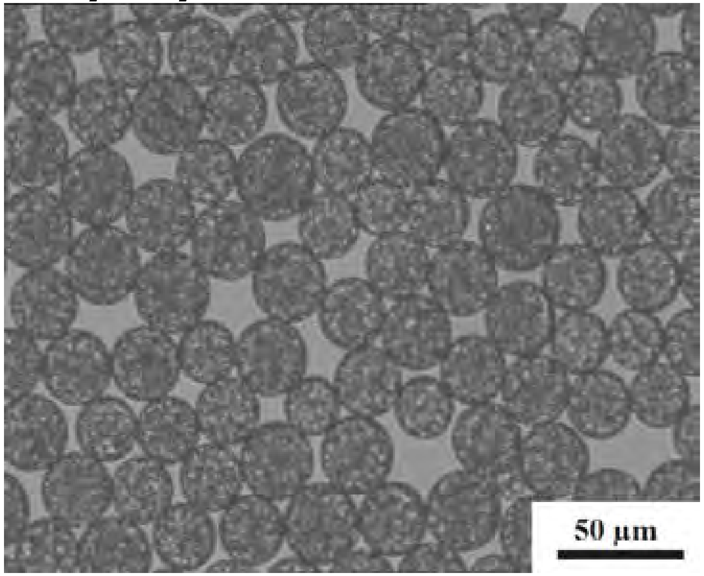
4. **DCM will evaporate from the particles leaving only peptide within the spherical PLGA particles**

2. ENCAPSULATION OF WATER SOLUBLE PEPTIDE USING BIODEGRADABLE POLYMER

O/W EMULSIONS



W/O/W EMULSIONS



HPLC - ENCAPSULATION EFFICIENCY (EE) OF PEPTIDE

ü Cancer treatment	POLYMER CONCENTRATION (%)	EE (%)
COSOLVENT METHOD (O/W)	10	40
	20	50
W/O/W	10	70
	20	85

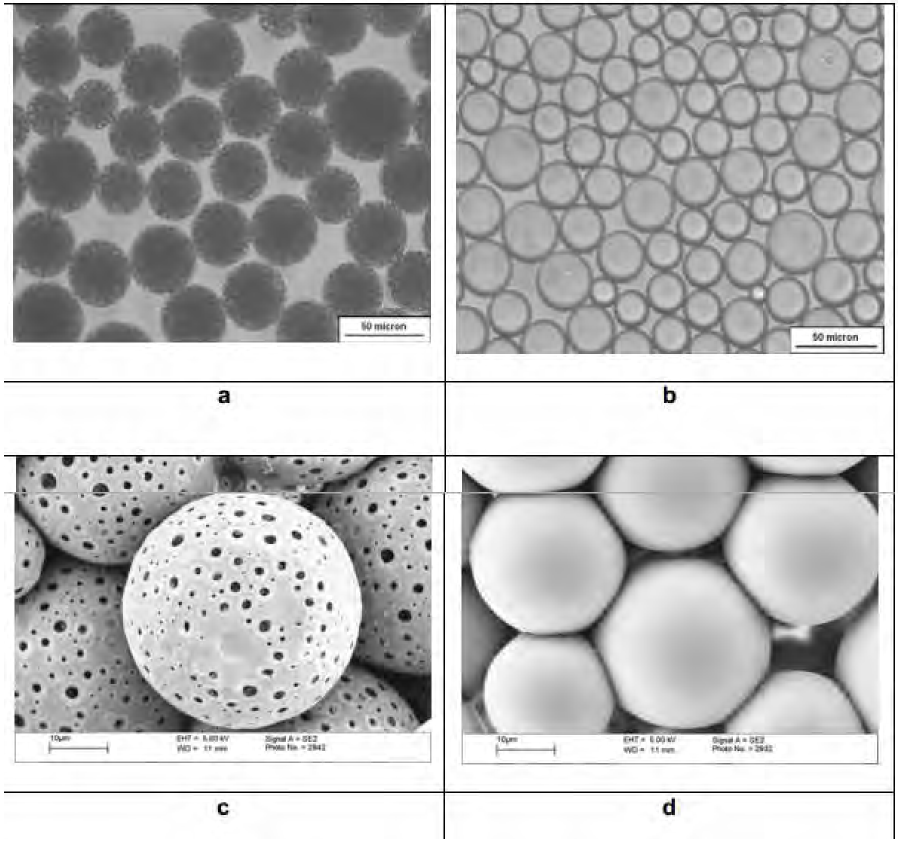
Commercially available
14 day kit
(~1g particles/ 70mg peptide)

~200£

Dragosavac 2012, Unpublished material

2. ENCAPSULATION OF WATER SOLUBLE PEPTIDE USING BIODEGRADABLE POLYMER

W/O/W EMULSIONS **O/W EMULSIONS**



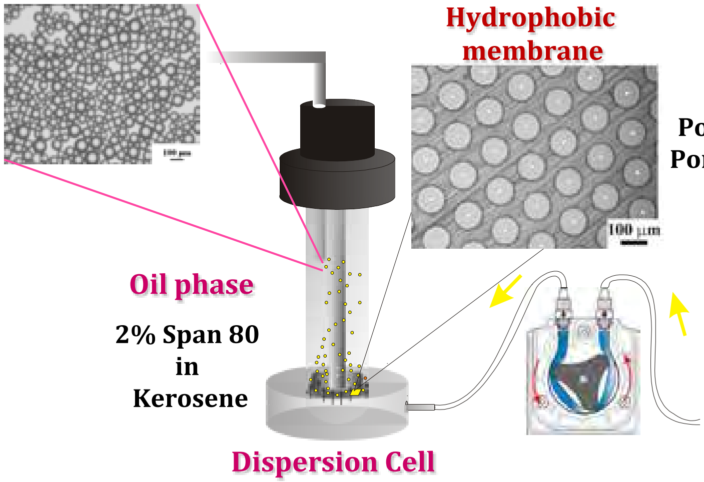
G. Gasparini et. al, 2010, Colloids and Surfaces B: Biointerfaces

W/O/W emulsions encapsulation efficiency close to 100%

3. SILICA PARTICLES
W/O emulsion

Aim to produce spherical silica particles with high surface area and internal structure

3. SILICA PARTICLES

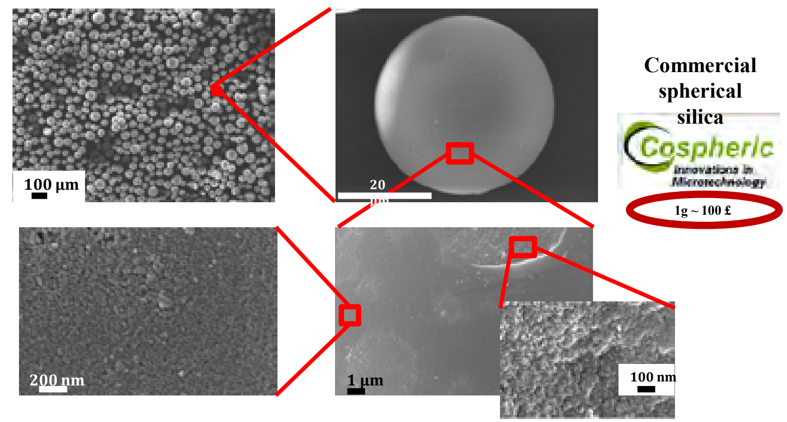


Pore size 15 µm
Pore spacing 200 µm

5% Sodium silicate
1M H_2SO_4
Final solution had pH=3.5

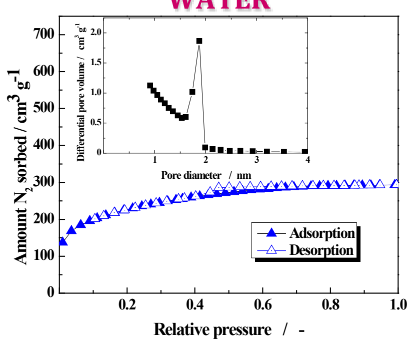
SILICA PARTICLES WITH D_{50}=40µm AFTER DRYING

SEM at Loughborough Materials Characterization Centre



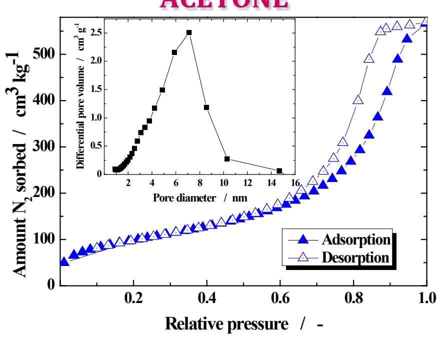
AGING OF THE HYDROGEL IN DIFFERENT SOLVENTS

WATER



Spec. surface area - 750 m^2 g^{-1}
Av. pore size - 1.3 nm

ACETONE



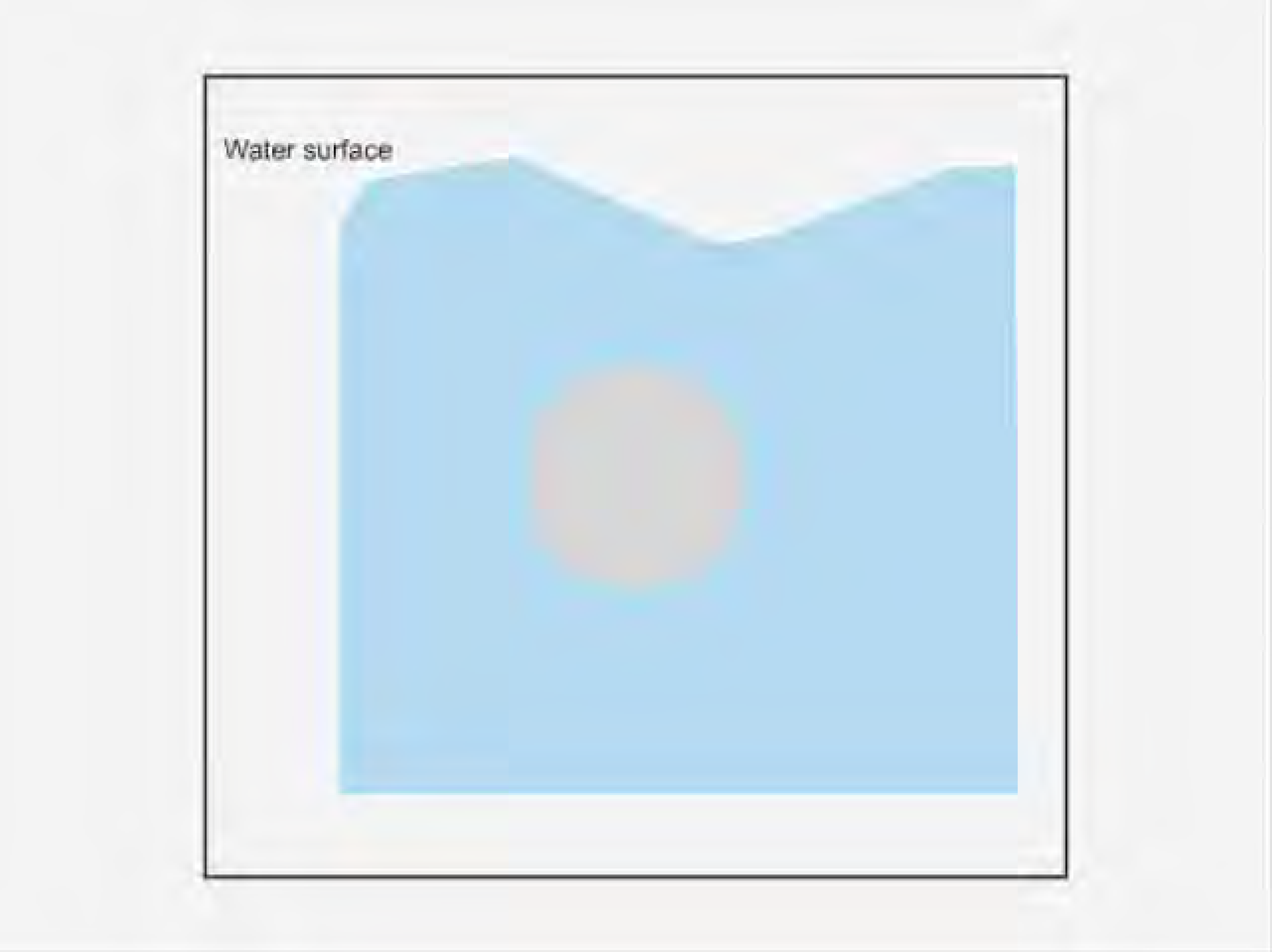
Spec. surface area - 320 m^2 g^{-1}
Av. pore size - 6 nm

$$Na_2SiO_{3\ (aq)} + H_2SO_{4\ (aq)} \rightarrow SiO_{2\ (s)} + Na_2SO_{4\ (s)} + H_2O_{\ (aq)}$$

4. SURFACTANT FREE PARTICLES
O/W emulsion

Aim to produce encapsulated and functional particles for photocatalysis

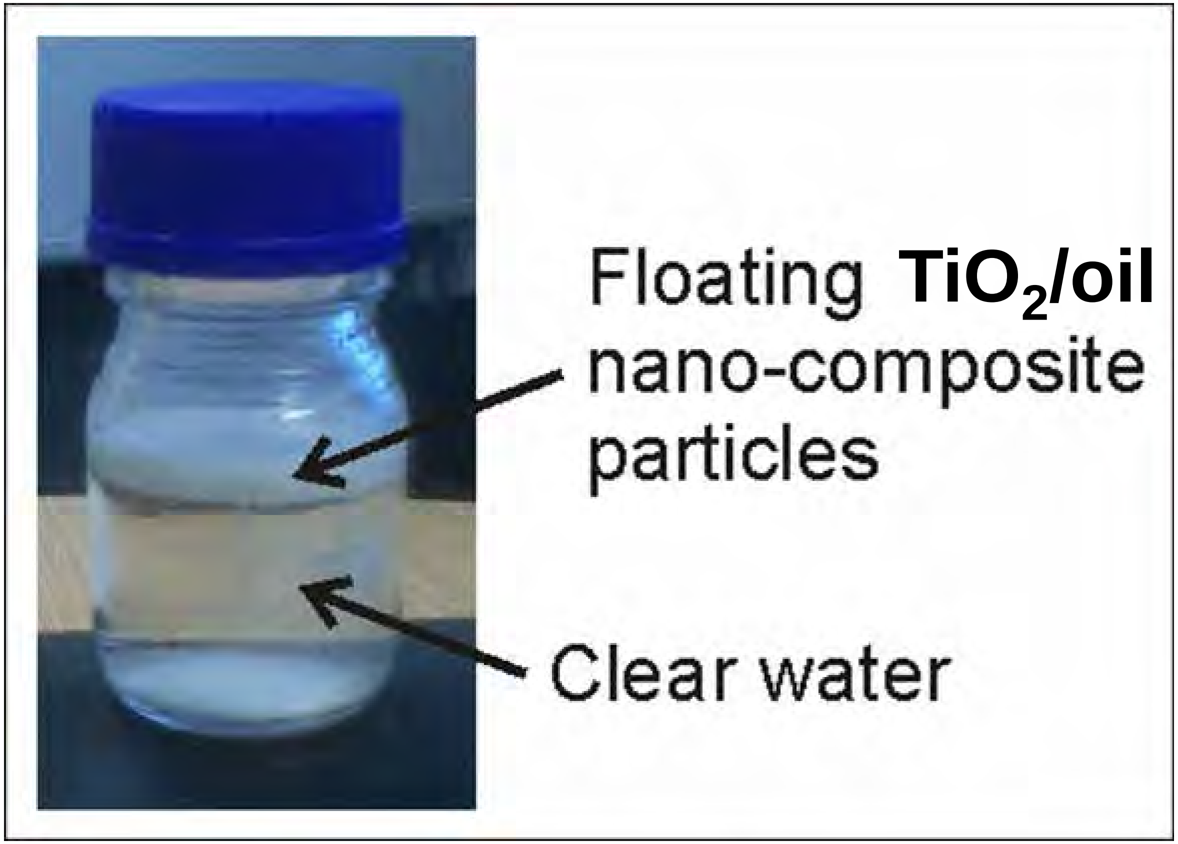
4. SURFACTANT FREE STABILISATION



A Pickering emulsion (Ramsden)

surfactant free

4. SURFACTANT FREE STABILISATION

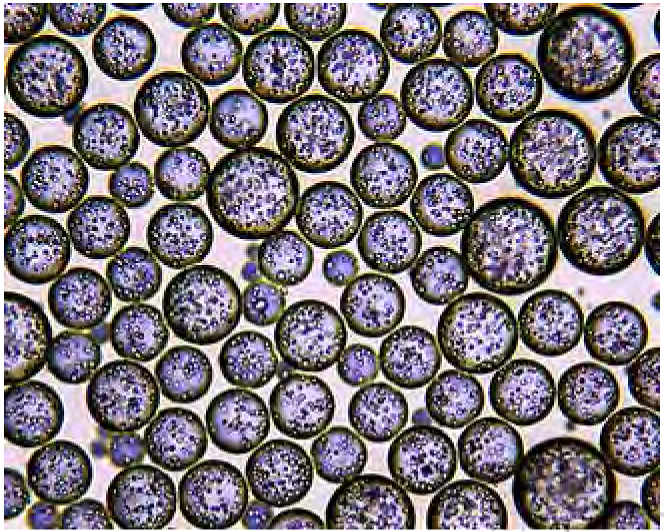


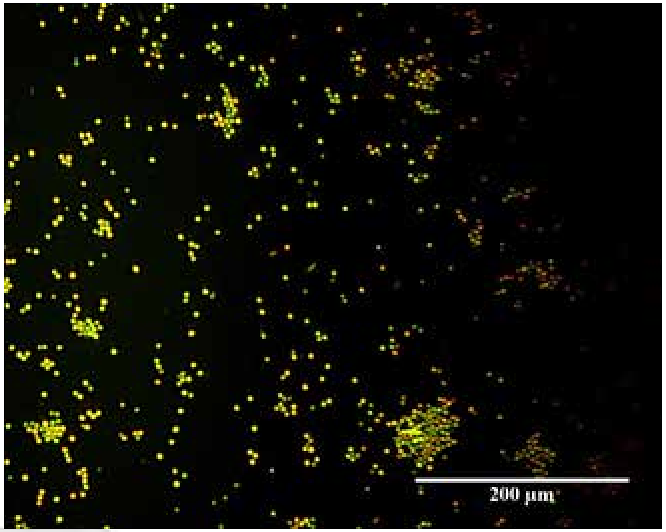
surfactant free

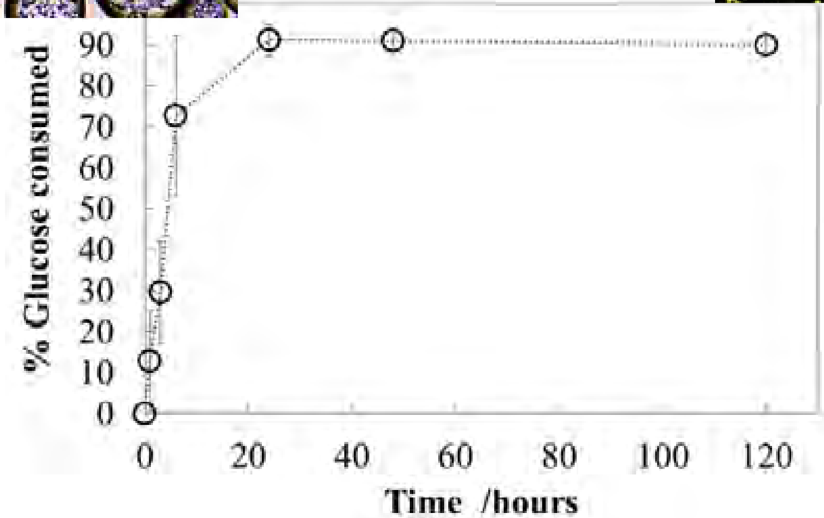
5. YEAST ENCAPSULATION
W/O emulsion

Aim to produce encapsulated particles capable of drug delivery surviving gastric juices

5. YEAST ENCAPSULATION







Please see poster: Serena Morelli

WHY MEMBRANE EMULSIFICATION?

- Low energy process
- Low pressure process
- Formulation is <u>still</u> key
- Small-scale through to production
- Variety of shear techniques:
  - Mainly stirred cell and oscillation/pulsation
- Good for multiple emulsions and continuous production
- Small & large drop: encapsulation and functionalised particles
- Good encapsulation of shear/temperature sensitive compounds

Micropore Technologies

Loughborough University

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Alessandra Imbrognio, CNR Italy

Miguel Angel Suarez Valdes, UNIDAV, Spain

For the membranes:

Micropore Technologies

http://www.micropore.co.uk/

Micropore Technologies Ltd. UK

Current Research Students & PostDocs:

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Alix Barton,

Rahimah Othman,

Konstantin Loponov…

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