Stimuli-Responsive Lipogel Capsules

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Introduction

- Lipogel capsules are a promising technology for controlled release of actives as they stabilise an impermeable lipid membrane shell onto a porous hydrogel core.
- If the hydrogel core comprises a stimuli-responsive polymer, expansion of the gel can trigger membrane pores to open, allowing the release of encapsulated actives.
- Alternatively, a shape change of the gel core due to shear may also cause membrane pores to open.
- Upon destretch, the pores close.
- The reversible formation of pores has been demonstrated on planar membranes supported on elastic sheets (Figure 1)[1].
- **The aim of this work is to employ this phenomenon into capsules that can be used for controlled release.**

Figure 1[1]: A planar bilayer on an elastic, hydrophilic PDMS substrate.

Upon biaxial expansion of the substrate, stable membrane pores are opened.

Substrate strain = 6%.
Scale bar = 50 µm.

Microgel Cores

Two methods of inverse emulsion templating are used to prepare microgel cores.

Shear Emulsification	Microfluidic Emulsification
High productivity but high size dispersity	Low size dispersity but low productivity
Size depends on volume fraction, surfactant, shear, etc.	Size depends on flow rates, geometry, viscosity, etc.

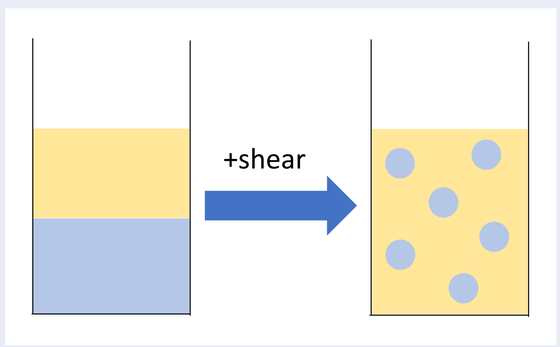

Figure 2a: Shear emulsification

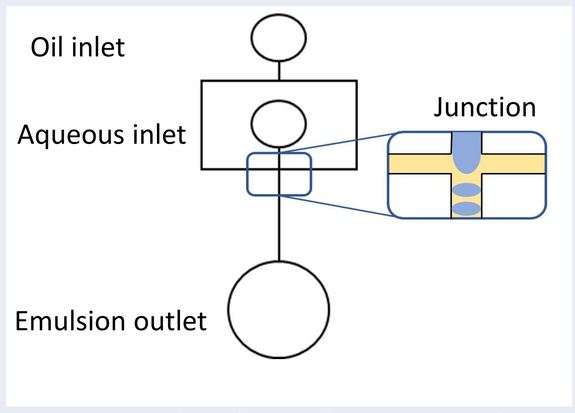

Figure 2b: Channel geometry for microfluidic emulsification

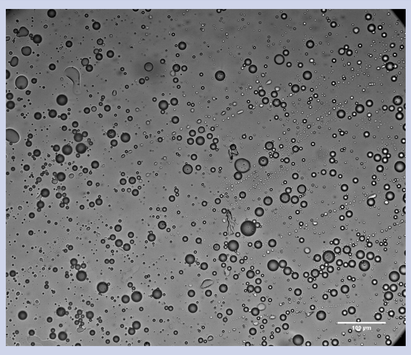

Figure 3a: Microgels viewed under bright field microscopy
Diameter = (9 ± 4) µm

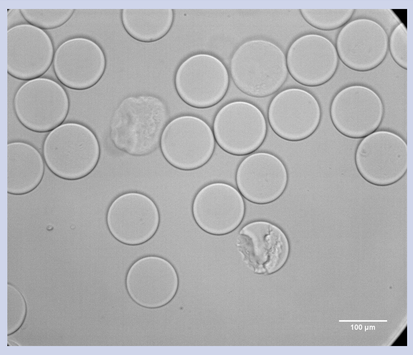

Figure 3b: Microgels viewed under bright field microscopy
Diameter = (96 ± 6) µm

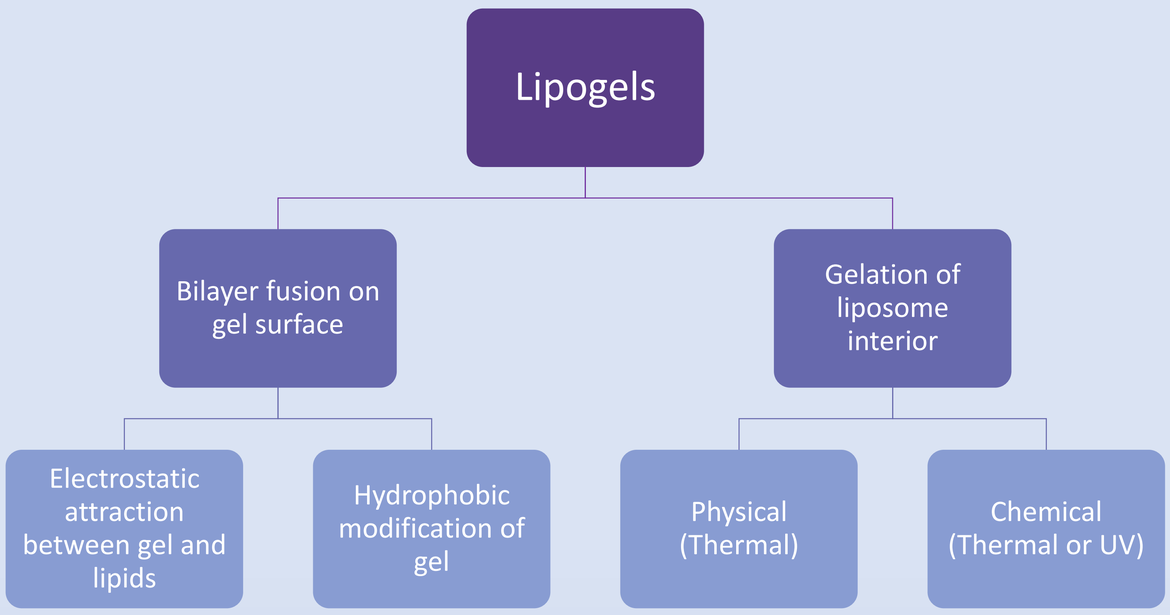

Figure 4: Methods of forming lipogels. This work focuses on the bilayer fusion method due to the ability to modify the lipid-gel interaction strength.

Lipid Bilayers

- The lipid bilayer is formed by fusion of small unilamellar vesicles (SUVs) at the gel surface.
  - This can be promoted by electrostatic attraction or hydrophobic modification (Figure 4).
- A combination of z-stack images and permeability tests were run using confocal microscopy (Figure 5).
  - There is a high, near-homogeneous adsorption of lipids onto the gel surface (Fig. 5a).
  - Fluorescein can permeate the adsorbed lipids which suggests that it is not a lipid bilayer.

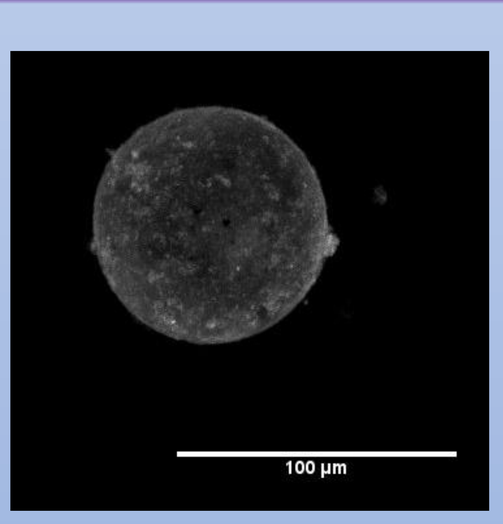

Figure 5a: Z-stacked image of a lipogel showing a near-homogeneous coating of lipids.
The gel is anionic polyacrylamide and the lipids are a 1:1 mixture of DOPC and DOTAP.

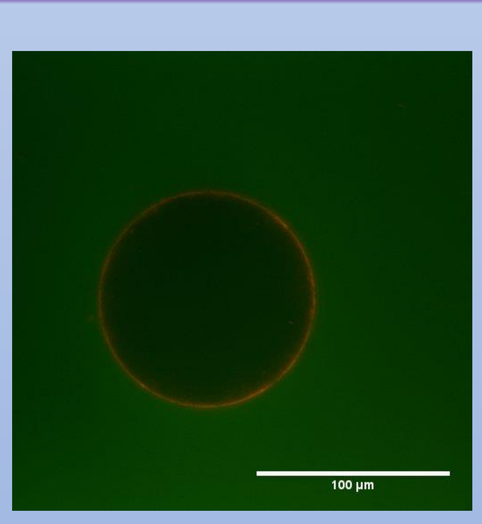

Figure 5b: Confocal image of a lipogel showing fluorescein within the gel.
Fluorescein in the solution is imaged in the green channel.
Rhodamine in the lipid membrane is imaged in the red channel.

Further Work

- Investigate other methods that promote fusion of SUVs onto the gel surface.
- Incorporate stimuli-responsive polymers into the gel core.

References:

1) L. Stubbington, M. Arroyo, M. Staykova, “Sticking and sliding of lipid bilayers on deformable substrates”, *Soft Matter*, 2017, **13**, 181

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