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Supramolecular microcapsules: *directing self-assembly*

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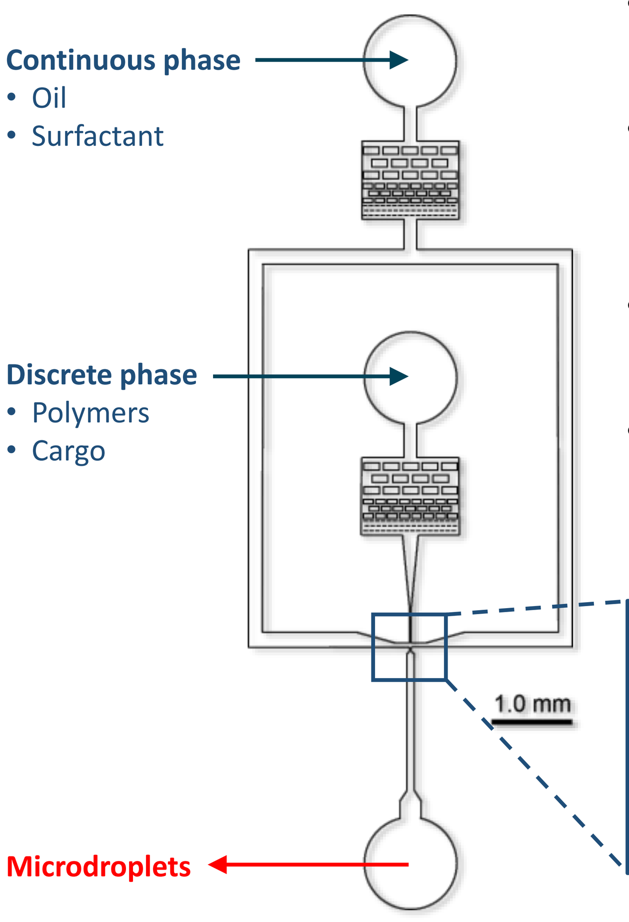
Supramolecular Microencapsulation

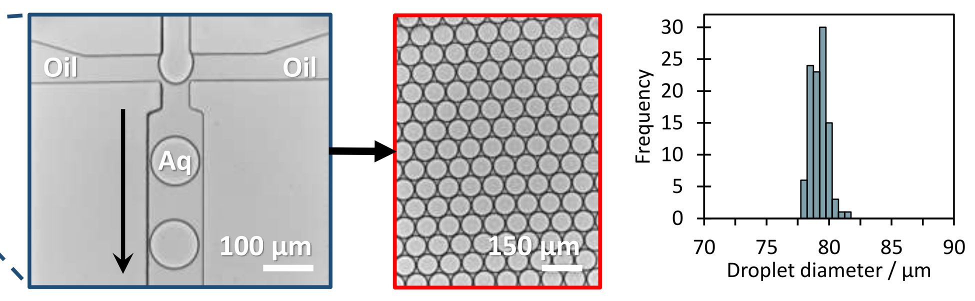
Microencapsulation refers to a very wide range of technologies that encapsulate, protect and release active cargo when needed. The annual global market is estimated at $40 billion in 2015 with applications across a wide range of products; from detergent and perfume, to paints and pesticides. It also has potential in other areas, including: targeted drug delivery, cell encapsulation, catalysis and self-healing concrete.

Directing both the micro-scale accumulation and molecular-scale self-assembly of components at the interface of sub-millimetre aqueous 'microdroplets' offers a powerful route to monodisperse 'microcapsules' with identical composition, in a *single step*. These microcapsules are uniquely assembled by dynamic molecular "handcuffs" that can be triggered to dismantle when exposed to a specific stimulus (e.g. light), releasing the protected cargo *on demand*.

Droplet-based microfluidics



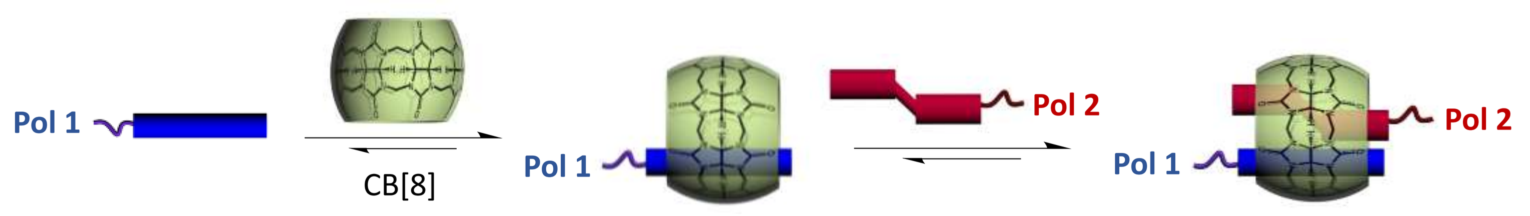
- Droplet-based microfluidics is a rapidly growing field of interdisciplinary research.
- Applications range from fast analytical systems and biological cell assays, to crystallisation and the synthesis of advanced materials.
- Uniform microdroplets are generated in a single step as an aqueous emulsion in oil.
- The microdroplets are used to template microcapsule formation, enveloping the droplet contents.



(left) *Aqueous microdroplets generated at a 60 µm diameter microfluidic flow-focusing junction.*

(right) *Monodisperse microdroplets with a diameter of 79.0 ± 0.7 µm*

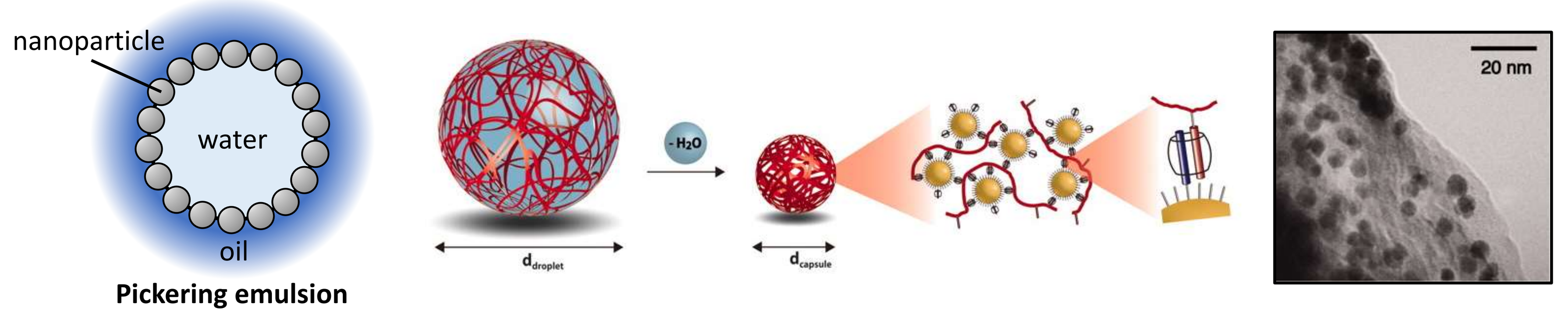
Ternary Host-Guest complex



Supramolecular microcapsules are assembled *via* a dynamic ternary complex between cucurbit[8]uril (CB[8]) and guest molecules on the substrates.

Nanoparticle-driven assembly [1,2]

Supramolecular *nano-composite* microcapsules and colloidosomes self-assemble by first forming a 'Pickering emulsion' of nanoparticles at the oil/water droplet interface.



(left) *Nanoparticle-composite microcapsules were formed at the interface of aqueous droplets.*

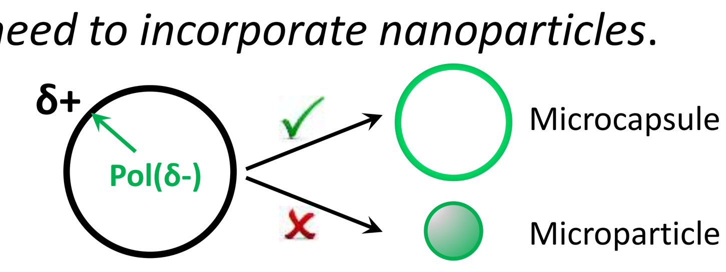
(right) *Image of the capsule skin, showing gold nanoparticles embedded within a polymer mesh.*

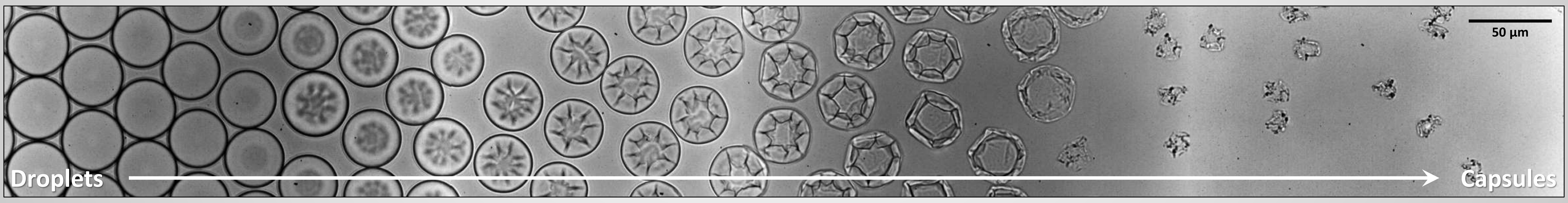
Polymer-only microcapsules

To expand the versatility of the supramolecular platform it is necessary to generalise microcapsule fabrication away from the need to incorporate nanoparticles.

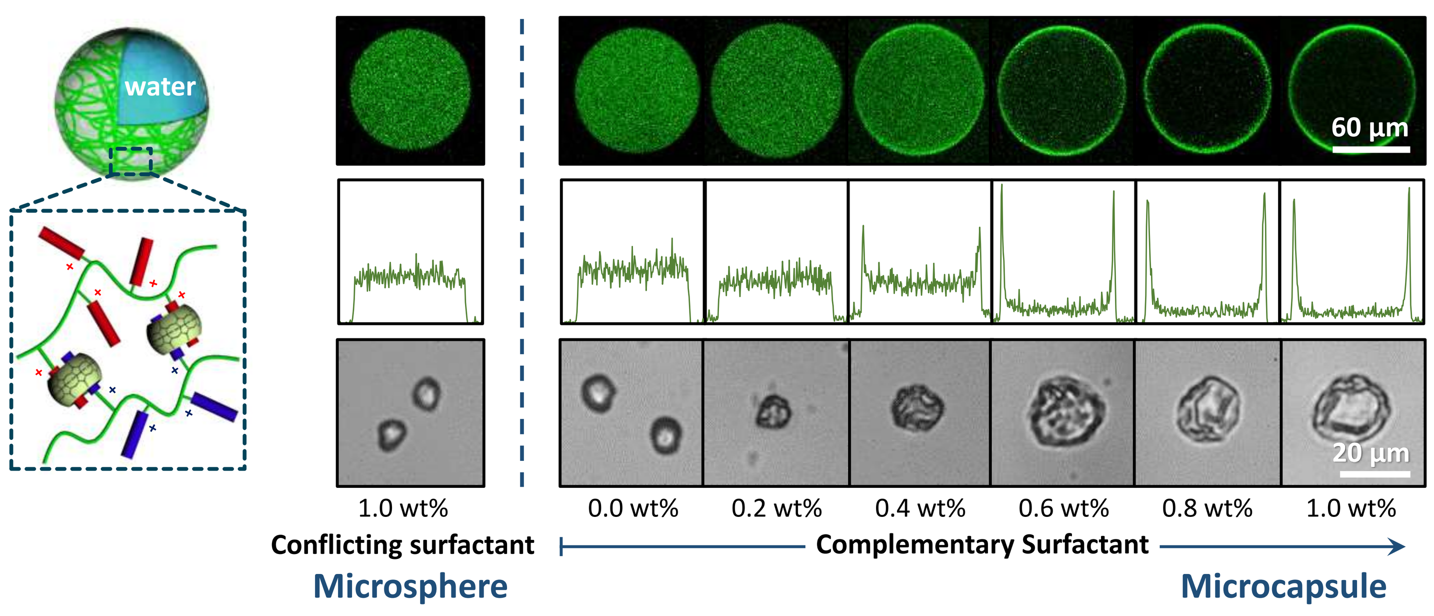
The assembly of *supramolecular microcapsules* from *aqueous microdroplets* is driven by electrostatic interactions, whereby charged polymers are selectively accumulated at the microdroplet interface by a complementary-charged surfactant (*patent filed and licensed*).

This is both dynamic and reversible, with the location of polymers within the droplet able to be externally manipulated through the carrier oil.

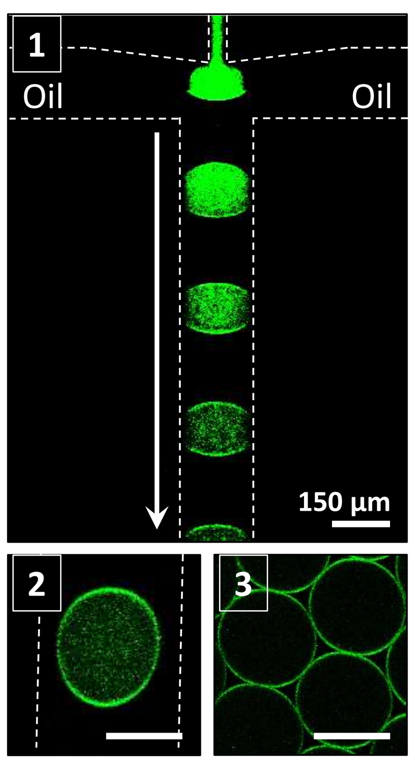




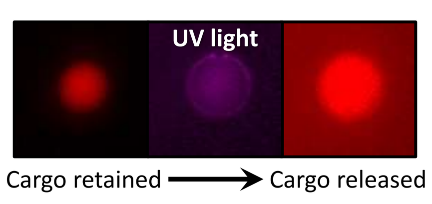
Directing self-assembly [4]



(top) *Increasing the amount of complementary-charged surfactant results in an accumulation of polymer at the interface, leading to a switch from microparticle to microcapsule formation.*



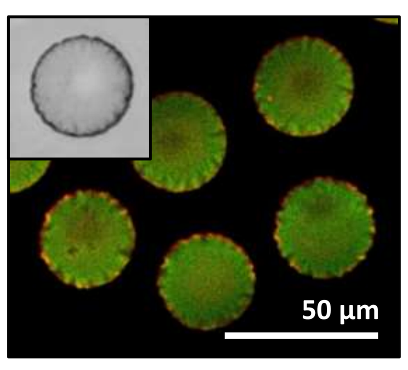
- The distribution of polymer within the microdroplet directly correlates with the resultant micro-structure upon evaporation.
- ***Conflicting charge:*** microdroplets contain a uniform distribution of polymer throughout the droplet, forming a smooth *microparticle*.
- ***Complementary charge:*** partitioning of all polymers to the droplet interface leads to the formation of an ultrathin, hollow *microcapsule*.
- Partitioning of charged polymers to the droplet interface is both rapid (<3 s) and dynamic.



(left) *Tracking the accumulation of charged polymer at the interface as the droplet flows along the microfluidic channel from* **1** *to* **3** *(~10 s), by fluorescence.*

(bottom) *Triggered release of capsule cargo (red) with UV light.*

Core-shell capsules [4]

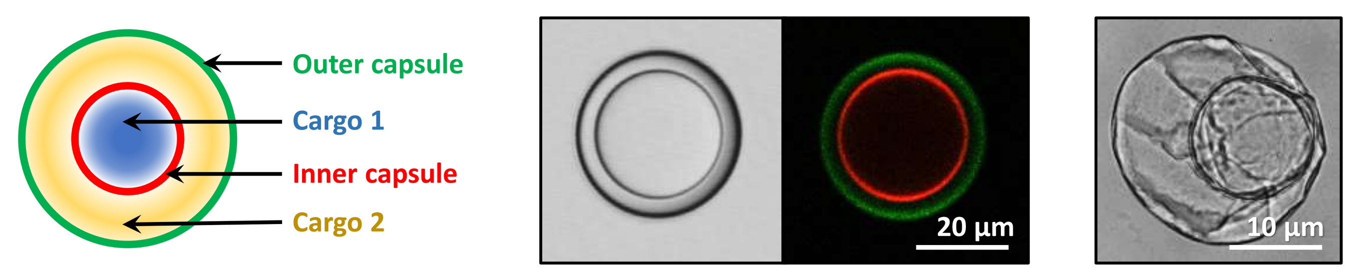


- Control over the location of individual components within the droplet allows for the design of complex structures.
- A mixed solution of oppositely-charged polymers results in the formation of core-shell capsules (*left*):
  - **red polymer** forms the outer capsule wall
  - **green polymer** forms the solid core

'Capsules-in-Capsules'

Electrostatics can be extended to multiple interfaces within a nested microdroplet to form capsules within capsules. Here orthogonal charges allow for distinct compartments.

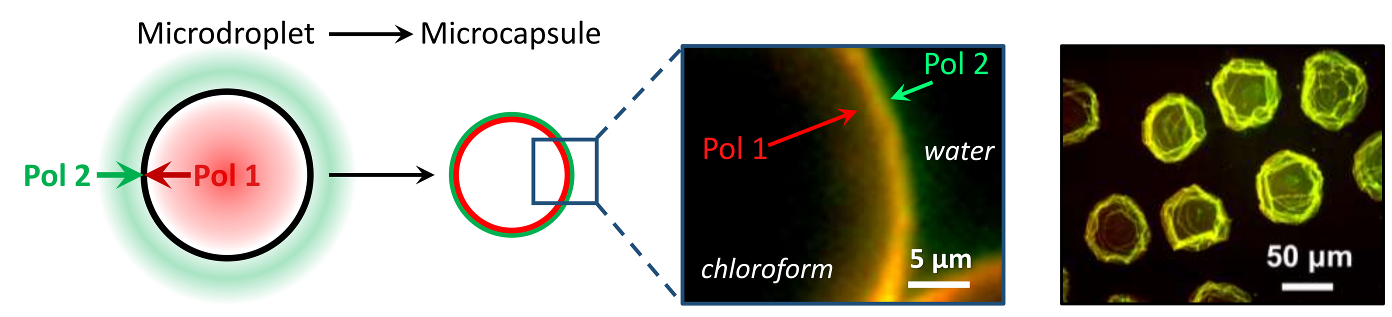
- Capsule architecture is externally controlled.
- Unique chemistry at each interface ('bespoke').
- Precise, multi-step or multi-trigger release.
- Segregated carriage of multiple cargos.
- Synergistic delivery with controlled dosages.
- Study of chemistry in a controlled environment.



(left) *Schematic of a compartmentalised 'Capsule-in-Capsule' with segregated cargo.*

(right) *Partitioning of a mixture of oppositely-charged polymers to specific interfaces within the nested droplet results on evaporation in the formation of two distinct capsule skins.*

Alternative approach: Interfacial assembly [3]



Complementary polymers self-assemble at the microdroplet interface through the supramolecular "handcuff" (*left*), forming a polymer microcapsule (*right*).

REFERENCES

[1] J. Zhang, R.J. Coulston, S.T. Jones, J. Geng, O.A. Scherman, C. Abell, *Science*, 2012, **335**, 690–694.

[2] G. Stephenson, R.M. Parker, Y. Lan, Z. Yu, O.A. Scherman, C. Abell, *Chem. Commun.*, 2014, **50**, 7048–7051.

[3] Y. Zheng, Z. Yu, R.M. Parker, Y. Wu, C. Abell, O.A. Scherman, *Nat. Commun.*, 2014, **5**, 5772.

[4] (a) R.M. Parker *et al.*, *Adv. Funct. Mater.*, 2015, **25**, 4091. (b) Z. Yu, *et al.*, *Chem. Sci.*, 2015, **6**, 4929.