Supramolecular Microcapsules from Microfluidic Droplets.

Coulston R., Zhang J., Abell C., Scherman O. A.
Melville Lab for Polym Synthesis, Dept of Chem, Univ of Cambridge, UK (rc517@cam.ac.uk)

INTRODUCTION

We are investigating the use of host-guest complexes and self-assembly in microfluidic droplets to generate controlled polymer architectures and inorganic nanoparticle assemblies (Zhang, 2012). Within the microdroplets it is possible to build porous microcapsules with quantitative loading efficiencies, customizable functionalities, and on-demand encapsulant release. The shell materials comprise a gold nanoparticle-copolymer composite that is held together by cucurbit[8]uril host-guest complexes. We have also made progress into assembling gold nanoparticle aggregates using cucurbit[n]urils in bulk solution as molecular-recognition-based SERS assays. When these nanoparticle assemblies are examined in the microfluidic droplet environment it is possible to study the real-time assembly and achieve high plasmonic enhancements.

MATERIALS AND METHODS

Nanoparticles and Np polymers were synthesised according to the literature (Coulston, 2011). Cucurbit[8]uril was prepared according to Kim, 2002.

RESULTS AND DISCUSSION

Cucurbit[8]uril (CB[8]) (Ruawald, 2008) is used as the host molecule because it is capable of forming stable yet dynamic complexes with guest compounds in water with extremely high affinity. Moreover, this larger CB homolog is capable of simultaneously accommodating two guests to form a 1:1:1 ternary complex in water (Appel, 2010) [with an association constant (K_a) up to 10^{15} M^{-2}] through multiple noncovalent interactions with an electron-deficient first guest such as methyl viologen (MV^{2+}) and an electron-rich second guest, such as naphthol (Np) derivatives (Fig. 1A). The ability of CB[8] to act as a supramolecular "handcuff " was further exploited by modifying gold nanoparticles (AuNPs) and water-soluble copolymers with complementary functionalities, thereby achieving a controlled dispersion of AuNPs in a polymer network held together by CB[8] (Coulston, 2011).

During microcapsule preparation, microdroplets were first generated in a microfluidic device, using a simple T-junction geometry (Fig. 1B). The oil carrier phase was directed perpendicular to the aqueous dispersed phase, which consisted of three inlets for the aqueous solutions of CB[8], MV2+-AuNPs (1a), and Np-containing copolymer (2a). Droplets were generated as the oil phase sheared off the aqueous phase, before passing through a winding channel designed for thorough mixing of the three reagents (Fig. 1C). With an oil:water flow rate ratio of 2:1, droplets were generated at a frequency of 300 Hz and exhibited a high level of monodispersity when collected on a microscope slide, as indicated by the narrow size distribution with a mean diameter of 59.6 mm (Fig. 1D) and a low coefficient of variation of 1.3%.

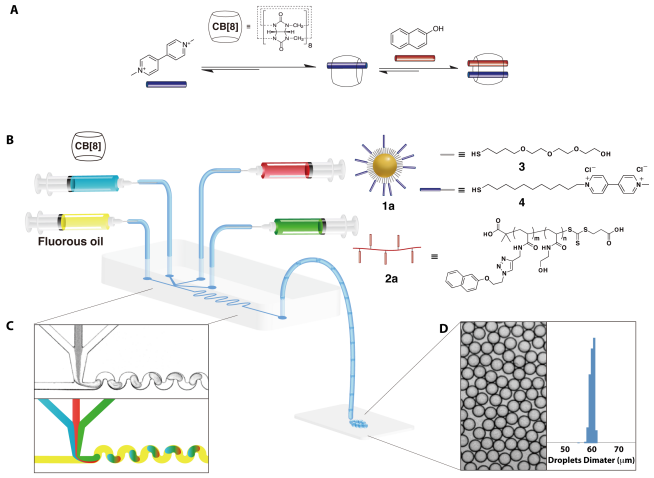

Figure 1 : Formation of the CB[8] ternary complex in water with MV2+ (blue) and Np (red). (B) Schematic representation of the microdroplet generation process. (C) Microscopic image and the schematic of the T junction and a wiggled channel for rapid mixing of reagents online. (D) The high monodispersity of microfluidic droplets is demonstrated by the narrow size distribution (diameter 59.6 ± 0.8 mm).

Individual stable microcapsules were observed immediately after dehydration of the microdroplet precursor. After 150 s, the spherical shape of the droplet was slightly distorted (Fig. 2A), until the capsules eventually collapsed on a glass surface. The individual microcapsules (Fig. 2B) can be easily isolated after the evaporation of the oil phase. By merely varying QOIL/QAQ, stable droplet precursors and microcapsules could be generated with a ddroplet of 42 to 67 mm and a dcapsule of 10 to 24 mm, with polydispersities of 0.9 T 0.4%. A transmission electron microscopy (TEM) image (Fig. 2C) shows that the capsule shell consists of a supramolecular self-assembled network of AuNPs 1a and copolymer 2a, where individual AuNPs are interlinked via a mesh of the polymer. The formation of a supramolecular microcapsule is schematically represented in Fig. 2D.

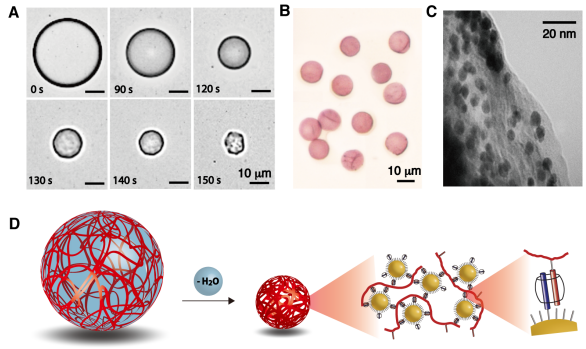

Figure 2 : (A) microscope images of the capsule dehydration process and of (B) Isolated capsules. (C) TEM of the capsule shell wall. (D) Schematic illustration of the microcapsules.

The microdroplet-assisted loading of water soluble cargo was investigated by simultaneously incorporating a rhodamine-B functionality onto the polymer backbone (Rho-B Np-polymer) and a fluorescein isothiocyanate–labeled dextran (FITC-dextran) into the capsule cavity. Aqueous solutions of Rho-B Np-polymer and FITC-dextran were injected into the microfluidic device with solutions of CB[8] and 1a (Fig. 3, A and B). Droplets were collected in a reservoir, and fluorescence images were recorded with a laser scanning confocal microscope (LSCM). The integrity of the capsule shell was not compromised by such loading, as shown by a clearly defined layer of rhodamine fluorescence confined to the water/oil interface of the droplets, whereas the interior of the capsule was filled evenly with FITC-dextran, as is apparent from the FITC fluorescence (Fig. 3B). The fluorescence intensity plot clearly shows that the rhodamine exterior is distributed in the "shell" forming outside the "cargo," whereas the FITC fluorescence is only observed inside the microcapsules. Other types of cargo were also similarly encapsulated, including *Escherichia coli* cells (Fig. 3C).

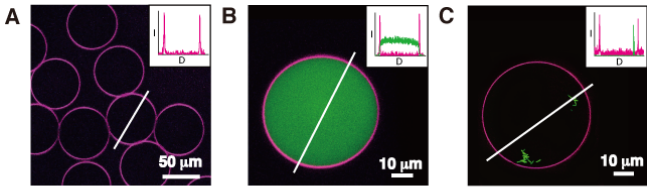

Figure 3 : (A) LSCM image of empty capsules containing Rho-B labeled polymer in the shell. (B) LSCM image of capsules containing aqueous solutions of CB[8], 1a, Rho-B Np-polymer, and FITC-dextran. (C) LSCM image of a capsule containing aqueous solutions of CB[8], 1a, Rho-B Np-polymer, and green fluorescent protein–expressing *Escherichia coli* cells.

CONCLUSION

We have described the preparation, characterization, and application of a microcapsule held together by supramolecular host-guest 1:1:1 ternary complexes of CB[8], MV2+-AuNPs, and a Np-containing copolymer at the liquid/liquid interface of microfluidic droplets. These microcapsules are produced from microdroplets in one step with high frequency and monodispersity. Upon dehydration, stable microcapsules with a hollow interior can be isolated within minutes. When an additional aqueous stream is incorporated, a wide variety of materials can be quantitatively encapsulated during capsule formation. Stimulus-triggered on-demand release of the encapsulated cargo is achieved as a result of the supramolecular host-guest chemistry incorporated in the capsule shell. Additionally, these microcapsules exhibit strong plasmonic properties on account of the AuNPs present and can be used as a SERS substrate for the encapsulated materials.

REFERENCES

- Appel E. et al. (2010) *Supramolecular cross-linked networks via host-guest complexation with cucurbit[8]uril* J. Am. Chem. Soc. (132) 14250.
- Coulston R. et al. (2011) *Supramolecular gold nanoparticle-polymer composites formed in water with cucurbit[8]uril* Chem commun. (47) 164.
- Rauwald U. & Scherman O. (2008) *Supramolecular block copolymers with cucurbit[8]uril in water.* Angew. Chem. Int. Ed. (47) 3950.
- Zhang J. et al. (2012) *One-Step Fabrication of Supramolecular Microcapsules from Microfluidic Droplets*. Science (335) 690.

ACKNOWLEDGMENTS

This work was supported by Engineering and Physical Sciences Research Council Basic Technology Translational grant EP/H046593/1, a European Research Council Starting Investigator Grant (ASPiRe) ERC-2009-StG-240629, and a European Union NanoSci-E+ (CUBiHOLE) grant EP/H007024/1. The authors thank X. Liu, C. A. Smith, S. Mahajan, E. Appel, J. J. Baumberg, and W. T. S. Huck for the helpful discussions.