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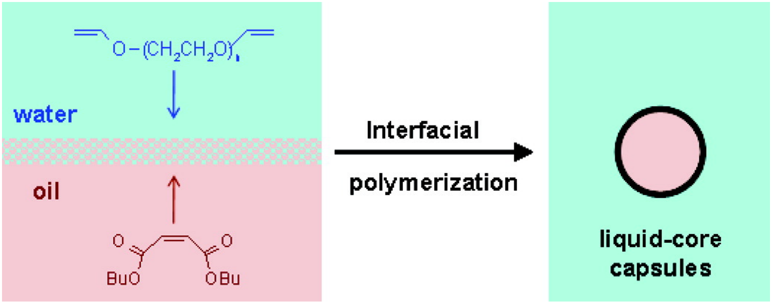

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Liquid-Core Capsules via Interfacial Polymerization: A Free-Radical Analogy of the Nylon Rope Trick

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Liquid-core capsules have wide-ranging applications in the high efficiency encapsulation and controlled delivery of drugs, dyes, enzymes, and many other substrates. These important applications have driven the rapid development of innovative techniques based on polyelectrolyte or colloidal self-assembly,[1] shell polymerization of particles or dendrimers followed by core removal,[2] microphase separation of core−shell latexes,[3] and vesicles,[4−7] to confine polymerization or assembly of encapsulants at the interface. Here, we demonstrate a direct approach to preparing submicrometer liquid-core capsules, eliminating procedures and materials, such as repeated centrifugation or filtration, sintering, core removal, microphase separation, vesicle templates, and block copolymers, that limit control of shell thickness, preclude direct encapsulation of substrates, or hamper large-scale practical application.

The interfacial free-radical alternating copolymerization, reported here for the first time, allows for precise control of the onset of reaction, leading to the direct encapsulation of submicrometer liquid drops within nanometer-thick polymer shells. Conceptually, this approach is analogous to interfacial condensation polymerizations, such as the classic "nylon rope trick" demonstration, but relies on the alternating free-radical copolymerization of hydrophobic maleate and hydrophilic vinyl ether monomers initiated by a surface-active azo-initiator to localize radical formation at the oil/water interface (Figure 1).

Miniemulsions used in these studies were prepared from a 10 wt % oil phase composed of hexadecane, 25 wt % dibutyl maleate (**1**) (hydrophobic monomer), and 5% paraffin wax (hydrophobe), and an aqueous phase containing PEG-1000 divinyl ether (**2**) (hydrophilic monomer with the concentration of vinyl groups fixed equimolar to **1**), and 1 wt % of dodecyltrimethylammonium bromide (DTAB) as surfactant. Following homogenization and high shear dispersion (sonication) of the oil/water mixture, the miniemulsion system was polymerized at 60 °C via injection of an interfacially active initiator, 2,2′-azobis(*N*-octyl-2-methyl-propionamidine)dihydrochloride (**3**) ($t_{1/2} = 10$ h at 59.5 °C), as an aqueous solution. The reaction was monitored by absolute heat-flow calorimetry (CPA 200, Chemisens AB) until completion after ∼4 h (Figure 2, ○). When 10 wt % of **2** is replaced with a cationic vinyl ether, *N*-ethyl-*N*,*N*-dimethyl-2-(vinyloxy)ethylammonium chloride (**4**), the reaction is retarded beyond 70% conversion, presumably due to the buildup of charge and reduced diffusion rate of monomers into the polymerizing interface (Figure 2, □).

The overall size of the capsules is set by the processing conditions used to form the initial miniemulsion. Under thermal reaction conditions (60 °C), the miniemulsion drops, formed at room temperature, are partially destabilized and coalesce, forming larger capsules. Number-size analysis of dynamic light scattering resulted in an average diameter of 218 ± 15 nm and a small population (27%) of larger capsules with an average diameter of 745 ± 41 nm. The slightly larger size (∼280 and ∼1200 nm for small and large capsules, respectively) observed with TEM (Figure 3, and Supporting Information Figures S5 and S6) is likely due to flattening and deformation of the capsules upon drying.

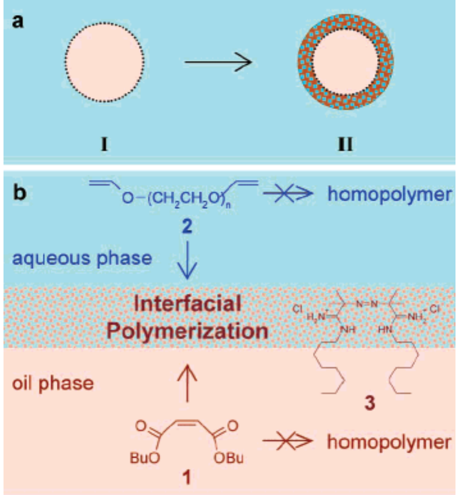

Figure 1. (a) Interfacial free-radical polymerization of miniemulsion oil drops (**I**) to form liquid-core polymer capsules (**II**) proceeds via (b) alternating copolymerization of dibutyl maleate (**1**) and hydrophilic PEG-divinyl ether **2**, initiated with surface active initiator **3** at the oil/water interface.

Destabilization and coalescence, encountered under thermal reaction conditions, may be avoided by conducting polymerizations at lower temperatures (35 °C), using 150 W UV irradiation at 365 nm (BIB-150P, Spectronics Corp.) to initiate the reaction. While the kinetic data (Figure 2, ◇) shows a significant decrease in the reaction rate, presumably due to the decreased propagation rate constant and the inability of light to deeply penetrate the opaque emulsion, analysis of the capsules formed by DLS shows a monomodal size distribution of capsules with an average number-weighted diameter of 186 ± 23 nm. This relatively monodisperse size distribution of liquid-core capsules is consistent with the typically narrow droplet size distribution of the starting miniemulsion.[8] As expected, imaging by TEM shows particles with an average diameter of ∼210 nm (Supporting Information Figure S7), slightly larger than that measured by DLS

Other approaches to the direct formation of liquid-core capsules have been conducted using monomers dissolved and initiated within a dispersed oil phase.[9] When the polymer formed is insoluble in the oil and specific wetting conditions at the polymer/oil and polymer/water interfaces are satisfied, the polymer precipitates to form an engulfing shell around the oil drops. However, the detailed studies of Tiarks et al.[9a] demonstrate that these approaches often yield nonuniform shell morphologies, solid particles, and intercapsule bridging, the extent of which are highly sensitive to the monomers, surfactants, and initiators used.

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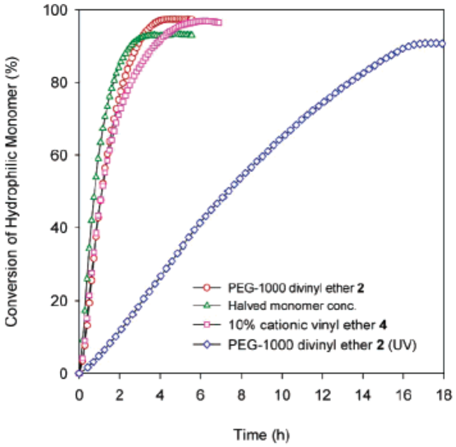

Figure 2. Kinetics of the interfacial copolymerization of hydrophobic monomer **1** with hydrophilic monomers under thermal and photochemical conditions.

Owing to the low solubilities of the hydrophilic monomers (**2** and **4**) in the oil phase and the hydrophobic monomer (**1**) in water, the free-radical polymerizations described here are constrained to the interfaces due to the alternating nature of the copolymerization and the reluctance of either monomer to radically homopolymerize. In contrast to other interfacial polymerizations that "grow" polymers out from surfaces, this approach leads to a polymerizing interface that grows from within. If this hypothesis is true, the position of highest radical activity within the polymerizing interface would be set by the relative diffusion rates of the hydrophobic and hydrophilic monomers to the active radical ends. The uniformity in shell thickness (Figure 3 and Supporting Information Figures S5, S6a–d, and S7) for capsules prepared using the approach may thus be the result of monomers diffusing, and reacting, more readily at thin portions of the shell compared to thicker portions.

No polymerization is observed when either the hydrophobic or hydrophilic monomer is absent; thus, the thickness of the polymer shell may be controlled by limiting the concentration of either monomer. Although the TEM images suggest a shell thickness on the order of ∼10 nm for the capsules shown in Figure 3 and Supporting Information figures, the diffuse polymer boundaries coupled with capsule deformation and electron beam damage preclude an accurate determination. Contrast variation SANS experiments are planned to measure more accurately the shell thickness of capsules in solution.

In conclusion, we have presented here the first demonstration of an interfacial free-radical alternating copolymerization and established its utility in forming liquid-core capsules. The principles and methodology behind this technique are readily scalable and have broad utility in the practical encapsulation and controlled-release of drugs, dyes, enzymes, cells, etc. Although this technique is limited to specific monomer pairs that alternately copolymerize at an oil/water interface, the ester and ether functionalities of the monomers used here are prime candidates for functionalization before or after polymerization, with an almost infinite variety of biologically or chemically active groups, allowing for a wide variety of potential applications. While the polymerization reaches high conversion, residual monomer is inevitable; thus for some applications, the less objectionable monomer should be added in slight excess or specific methods for removal must be developed. Experimental and modeling efforts are in progress to establish the relationships between polymerization conditions and the formation kinetics, size, shell thickness, and permeability of the capsules for both encapsulation and release.

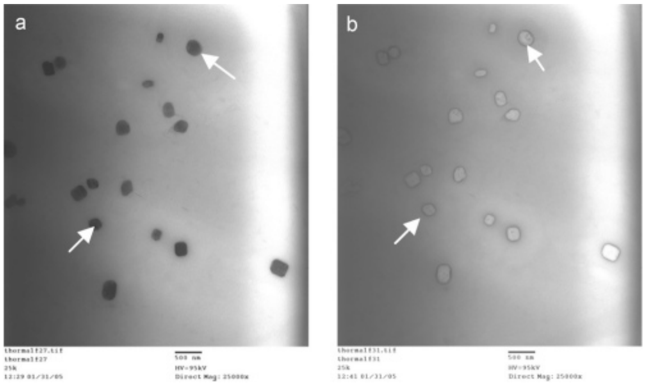

Figure 3. TEM images of liquid-core capsules following thermally initiated polymerization (Figure 2, circles). Originally intact (∼280 nm diameter) capsules (a) are damaged following 5 min of electron beam irradiation revealing hollow cores (b). Arrows point out the registration between the two images. Additional TEM images (Figures S5 and S6a–d) are included in the Supporting Information.

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Supporting Information Available: Materials and methods for monomer/initiator syntheses, polymerization and initiator kinetics, DLS measurements, and additional TEM images. This material is available free of charge via the Internet at http://pubs.acs.org.

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