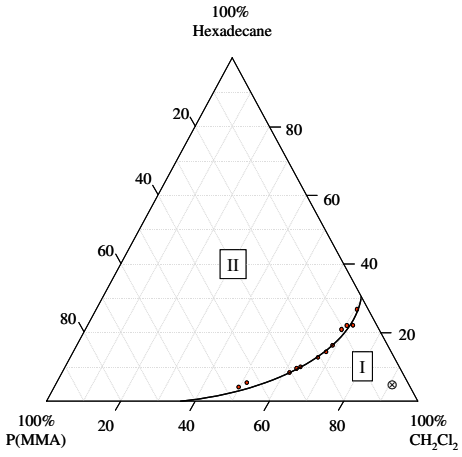
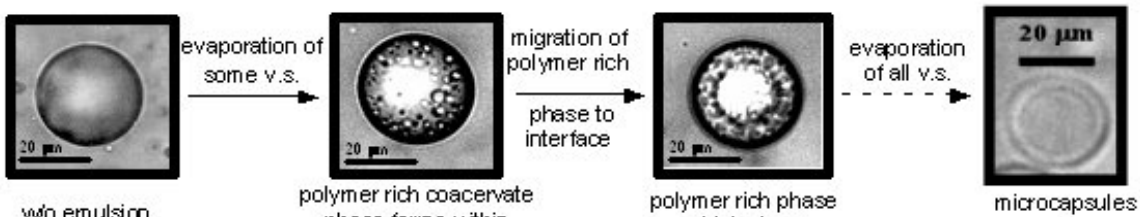
Microcapsules With Liquid Cores And Polymer Shells Made By Solvent Evaporation

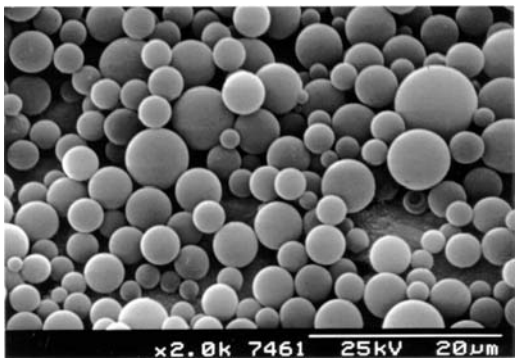
Microcapsules having liquid cores and polymer shells were prepared by a simple physical process. The morphology of the resulting particles depends upon materials, and can be controlled to yield spherical core-shell type microcapsules. The thickness of the shell is readily varied from 1% to 10% of the microcapsule radius.

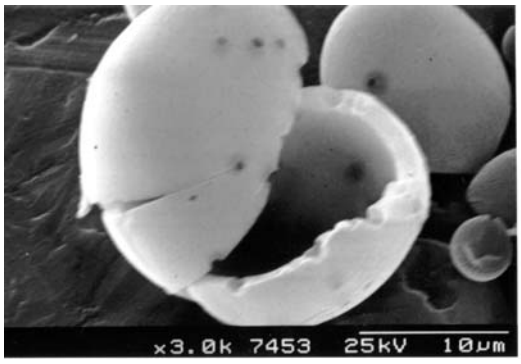
A three-component solution containing a polymer, a good solvent for the polymer (dichloromethane, DCM) and poor solvent (hexadecane) was emulsified into an aqueous phase containing an appropriate emulsifier to yield droplets of ~10μm mean diameter. By controlled evaporation of the DCM, the polymer-solvating power of the solvent mixture within the droplets is reduced until eventually the polymer phase-separates and forms a complete shell around each droplet. A typical phase diagram for the 3-component droplet phase is shown in figure 1. The region where the ternary mixture is a single phase is denoted I and is in the dichloromethane rich corner of the diagram. The line separating this region from the region where the polymer is in a separate phase (denoted II in the figure) is called the bimodal line and was determined experimentally by observation of the turbidity of various mixtures (clear = one phase, cloudy = two phases). The initial polymer solution used to make the present microcapsules was formulated to have the composition indicated by the dot in the one-phase region. By removing DCM from the droplets of an emulsion made with oil of this composition, the oil droplet composition moves toward one that is on the bimodal line, at which point the polymer in solution begins to separate as a phase rich in solvent and so quite fluid and mobile. This mobile fluid appears in the droplets as smaller droplets which move to the droplet surface to form capsules as illustrated in figure 2 [ref]).



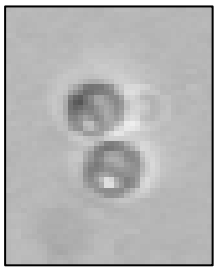


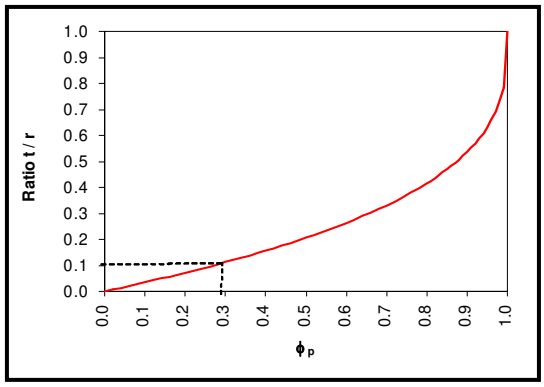
morphology, one particle was fractured under liquid nitrogen to reveal the internal structure as shown in figure 3b.



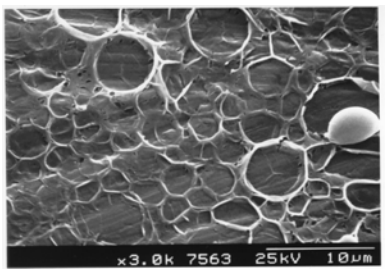


This core-shell morphology is not guaranteed for all materials, and careful selection of the emulsifier used at the emulsification step is critical. If the emulsifier is not chosen correctly, the morphology shown in figure 4 is more likely to result, where the phase separated polymer has left the droplet and aggregated to form a localized lobe of material on the droplet surface.

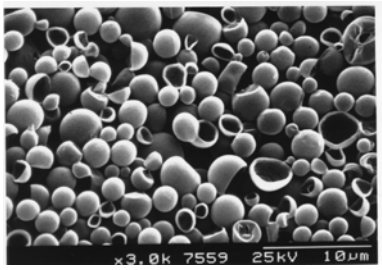




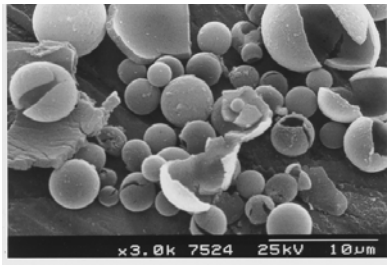
The thickness of the shell wall depends on the concentration of polymer in the initial solution, and the functional form of the dependence is shown in figure 5. The ratio of wall thickness to capsule radius has been plotted as a function of the volume fraction of polymer in the microcapsule (which is set by the initial oil-phase composition). The dashed line shows that to make a microcapsule with a wall thickness that is 10% of the microcapsule radius, it is necessary to have the polymer:hexadencane ratio at 30:70 in the initial oil phase. By varying this ratio, microcapsules with a range of shell thicknesses were prepared and scanning electron microscope images of the various products are shown in figure 6.



Polymer:hexadecane 2:98



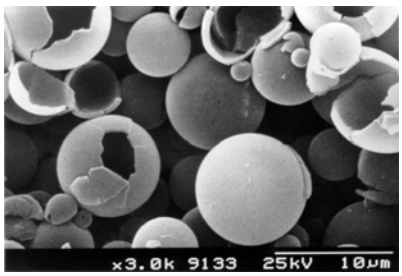
Polymer:hexadecane 12:88



Polymer:hexadecane 32:68

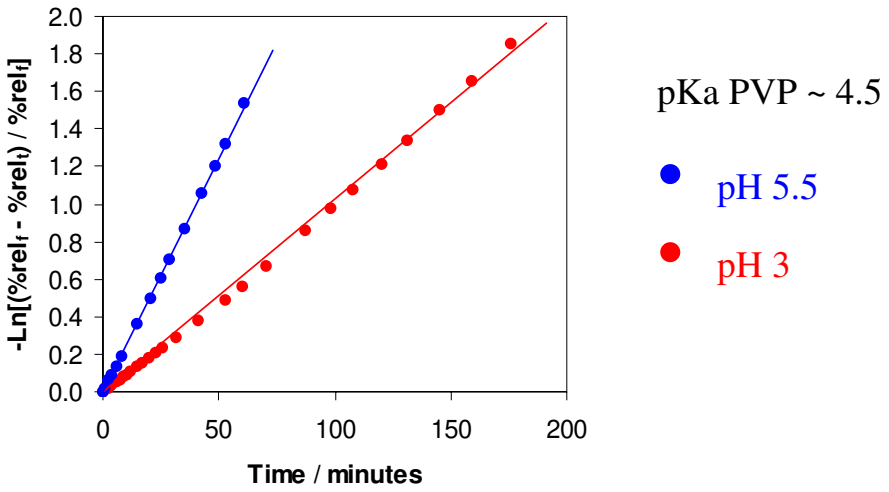
Microcapsules with walls less than about 10% of the particle radius tend to be too fragile to maintain their form on the severe drying required for sample preparation, and the electron micrographs show partially collapsed particles, or in the case for very thin walls, no microcapsules are visible at all. The microcapsules with the thickest walls shown here were very robust, and intentionally fractured under liquid nitrogen to demonstrate the wall thickness to be ~10% of the microcapsule radius.

These microcapsules were prepared with poly(methylmethacrylate) shells, though a variety of polymers can be used. Microcapsules that demonstrated pH-controlled release of a compound dissolved in the liquid core were made with poly(4-vinylpyridine) shells, and show the same morphology as the P(MMA) microcapsules (as shown in the figure below).



The pH-responsive nature of poly(4-vinylpyridine) presents an opportunity to develop site-specific drug-release formulations based on these microcapsules. In initial studies, a first-order diffusion model fit the release data well, and a two-fold change in release rate was observed when the pH was adjusted from 5.5 (above the pH_b for the vinylpyridine repeat unit) to 3 (below the pH_b for the vinylpyridine repeat unit). The kinetic data are shown in the figure below:

It is also possible to use pharmacologically-accepted polymers such as biodegradable PLGA



for the shell. In this case oily materials could be encapsulated and handled as dry powders that revert to oily materials *in vivo*. Alternatively, the slow dissolution of the shell could be used to control the release of an oil-soluble drug molecule dissolved in the microcapsule core.

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