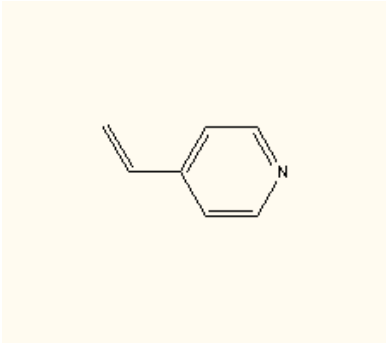
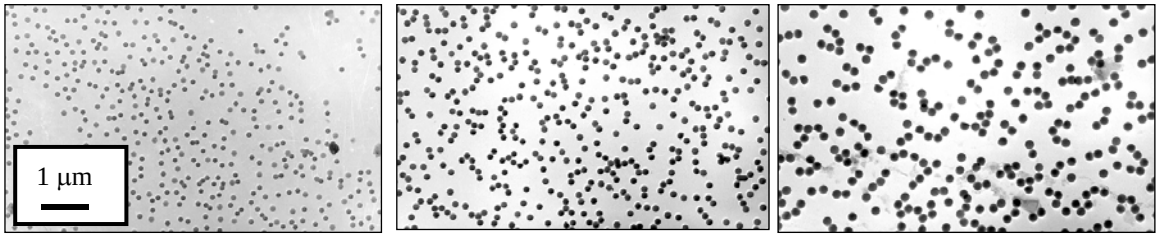
pH-sensitive Microgels

Microgels are chemically crosslinked submicron polymer particles prepared by emulsion polymerization. This water-based process leads to a product that is an aqueous colloidal dispersion. The microgel particles can be designed to swell with changes in solvent, temperature and / or pH. By varying the crosslink density and co-monomer ratios the degree and rate of particle swelling are readily controlled. This paper describes the preparation and properties of microgels prepared by copolymerization of the monomer 4-vinylpyridine (shown below) and styrene. Recipes used are also shown (4VP = 4-vinyl pyridine, ST = styrene, DVB = divinylbenzene crosslinker).

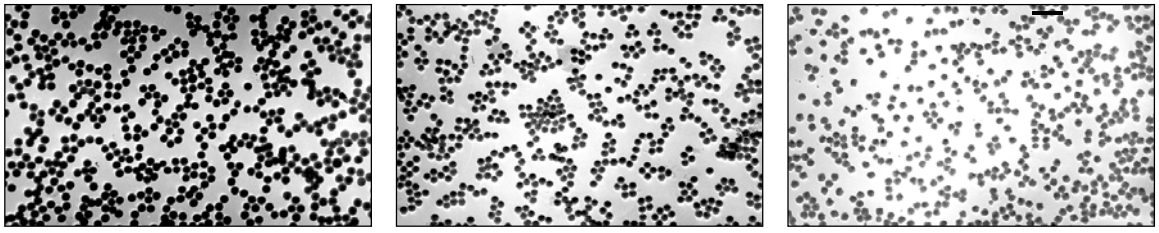


Ref	4VP	ST	DVB
A	99.75	0	0.25
B	99.00	0	1.00
C	98.50	0	1.50
D	89.75	10	0.25
E	79.75	20	0.25
F	59.75	40	0.25

Polymerization is carried out in hot water (80°C) with a small amount of a water-soluble free radical polymerization initiator, with a total monomer:water ratio of around 2:98 by mass.
After four hours of polymerization, the resulting particles are spherical, and nearly monodisperse. Transmission electron micrographs of the particles are shown below, all images are at the same magnification. Particles are around 200nm in diameter.

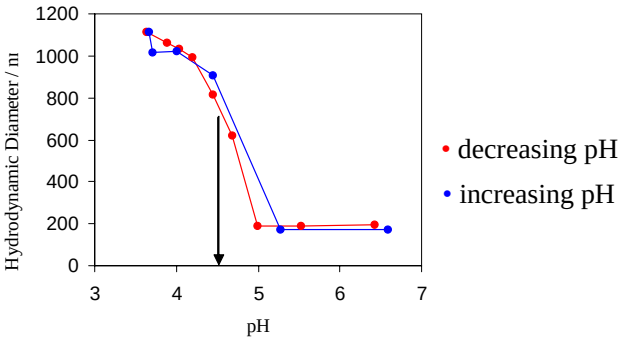


A B C



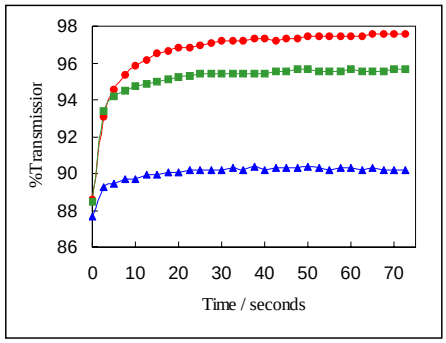
D E F

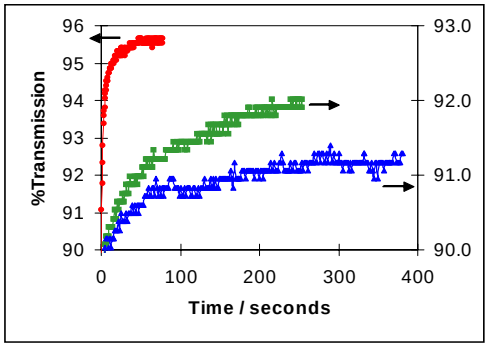
The nitrogen atom in the 4-vinylpyridine ring is basic due to its lone pair of electrons, and becomes protonated and charged when the pH is below it's pK_b (4.0). This makes the polymer chains hydrophilic, but since they are crosslinked to one another, they cannot freely dissolve and the particle swells instead. The degree of swelling as a function of pH is show in the graph below for the sample with 0.25% DVB crosslinker and no styrene in the copolymer. The particle size was determined by photon correlation spectroscopy after gradual acidification with HCl of a dilute dispersion. At their most swollen, the particles are 5 times their initial diameter (about 125 times their initial volume!).



The swelling process is fully reversible; one curve on the plot shows the changes in particle size on acidification, and the other shows the reverse process on stepwise elevation of pH with NaOH. This can only be repeated 4 times as the salt concentration eventually exceeds the critical coagulation concentration for the particles and the dispersion becomes unstable. The arrow indicates the pK_b of 4-vinyl pyridine – almost exactly at the midpoint of the particle swelling regime.

The second plot shows the rate at which the particles swell as a function of crosslinker level. This is followed by the change in dispersion opacity as the particles are mixed rapidly with buffer solutions of various pH in a stopped-flow turbimeter. The level of light transmitted through the dispersion is followed as the particles swell and become more transparent. The amount of crosslinker clearly affects the degree of swelling but not the rate at which final swelling is achieved, with all particles reaching their maximum transparency (maximum transmission of light) at around 30 seconds. On the other hand, the level of the hydrophobic monomer styrene changes the *rate* at which the particles swell, as well as their final swollen size. This can be seen in the next graph where particles comprising 0% ST have reached maximum swelling in around 30 seconds, and the time to plateau increases with higher ST content of the particles (200s for 10% ST, and 300s for 20% ST). Thus the swelling properties of these particles can be finely controlled by judicious choice of monomer and crosslinker ratios in the initial preparation.





This system has application to controlled release of entrapped molecules. If a drug for example is trapped within the matrix of the collapsed particles, diffusion out of the particle will be limited. When the particle reaches a location of reduced pH (such as the stomach) rapid expansion would cause the release of the drug,. Using another approach, and leveraging the controlled swelling of crosslinked poly(4-vinyl pyridine) larger microcapsules with liquid cores and pH-responsive shells can be prepared which show controlled release of marker molecules from within the core as a function of pH. This is discussed in a separate technical note on microcapsules. By varying the monomer feed, pH-controlled release could be finely tuned to meet specific drug delivery demands.

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