Orthogonal Self-Assembly of Low Molecular Weight Hydrogelators and Surfactants

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The self-assembly of partially incompatible molecular components leading to (micro-) phase separation comprises a powerful approach toward the fabrication of complex nanoarchitectures and new materials and plays an essential role in nature, for example, in protein folding and the formation of biological membranes.1–3

Phase-separated systems are so far usually based on the immiscibility of block-copolymer segments4 or fluorinated compounds with hydrocarbons,5 and this toolbox has only very recently been extended by low molecular weight organogels in liquid crystalline phases.2b Here, we report on the concurrent self-assembly of new low molecular weight hydrogelators6,7 and various surfactants in water, leading to self-assembled fibrillar networks with encapsulated micelles. This prototype system presents an example of orthogonal self-assembly, that is, the independent formation of two different supramolecular structures, each with their own characteristics that coexist within a single system.

Recent progress in the design of low molecular weight gelators has emphasized the importance of self-complementary and highly anisotropic interactions for the gelation ability.6,8–10 In the present work, we employed the 1,3,5-triamide cyclohexane11 moiety because it can self-assemble into 1D arrays stabilized by six hydrogen bonds. We have extended this moiety with hydrophobic amino acids to shield the amide groups from competitive interactions with water and have thereby enforced the anisotropic self-assembly of the gelator molecules in water due to the concurrent action of hydrogen bonding and hydrophobic effects. A similar combination of interactions stabilizes secondary protein structures, which are stable in the presence of weakly interacting surfactants and lipids.3

Compounds 1–3 are examples of gelators12 (Chart 1) that fulfill these requirements and are easily prepared by coupling of the corresponding (C-derivatized) amino acids with 1,3,5-tris(carbamoyl chloride)cyclohexane. Compounds 1–3 all form thermoreversible gels in water at very low concentrations.13,14 The very low critical gelation concentrations (cgc) and the high gel−sol phase transition temperatures (TGS) of the gels clearly indicate that self-assembly of 1–3 is driven by strong intermolecular interactions. FTIR spectroscopy of xerogels and of hydrogels of 1 showed amide I vibrations typical for hydrogen-bonded amides at almost the same position of 1639 and 1635 cm−1, respectively.15 This indicates that the amide moieties participate in a similar hydrogen-bonded network in hydrogels and their corresponding xerogels. Hydrogels of 1–3 tolerate NaCl concentrations up to at least 100 mM and are stable for at least 3 months. Transmission electron microscopy (TEM and cryo-TEM) of the gels in water revealed that 1–3 self-assemble into elongated fibers (diameters for 1, 20−150 nm; 2, 10−50 nm;

Table 1. Gelation of Water by 1–3 in the Presence of Surfactants

<table>
<thead>
<tr>
<th>gelator</th>
<th>anionic (SDS)</th>
<th>cationic (CTAB)</th>
<th>nonionic (OG)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>cgc (mM)</td>
<td>TGS (°C)</td>
<td>cgc (mM)</td>
</tr>
<tr>
<td>1</td>
<td>4.6</td>
<td>35</td>
<td>16</td>
</tr>
<tr>
<td>2</td>
<td>0.5</td>
<td>16</td>
<td>0.9</td>
</tr>
<tr>
<td>3</td>
<td>13.6</td>
<td>34</td>
<td>8.1</td>
</tr>
</tbody>
</table>

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1 SDS, sodium dodecyl sulfate (cgc = 8.1 mM); CTAB, cetyltrimethylammonium bromide (cgc = 0.9 mM); OG, n-octyl-β-D-glucopyranoside (cgc = 25 mM); G, gel; p, precipitation.  ‡ Concentration of surfactant in mM.

3, 10−200 nm), which in turn form an entangled fibrillar network, thereby immobilizing the solvent.

The compatibility of hydrogel formation by 1–3 with various types of surfactants was investigated by dissolving 1–3 in surfactant solutions below and above the critical micelle concentration (cmc)16 at T > TGS and by subsequently examining the samples for gelation after they had been cooled to room temperature (Table 1). Gels of 1 are formed in combination with nonionic (OG) or anionic (SDS) surfactants either by temperature-induced gelation or by the lowering of the pH from 7 to 3.5,13 but with cationic CTAB immediate precipitation occurred, due to salt formation. Most interestingly, cryo-TEM showed no significant differences between hydrogels of 1 alone and in the presence of OG (Figure 1), and furthermore the melting temperatures of hydrogels of 1 are not changed by the presence of OG up to concentrations well above the cmc (35 mM). The gelation behavior of the nonionic gelators 2 and 3 is even more tolerant toward the presence of surfactants, and transparent gels are obtained in the presence of SDS, CTAB, or OG below and well above the cmc of the surfactants. These results clearly indicate that the self-assembly of 1–3 leading to the gelation of water is not markedly affected by the presence of surfactants or surfactant assemblies, except when strong interactions between surfactant and gelator are possible, like electrostatic interactions between acidic gelator 1 and the cationic surfactant CTAB.
speculate that the orthogonal self-assembly of our hydrogelators and surfactants is due to their different molecular architectures as well as the in part different driving forces for self-assembly, that is, hydrogen bonding and hydrophobic effects versus hydrophobic effects alone, respectively. The straightforward design of 1,3,5-trisamide-cyclohexane-based gelators and the thermoreversibility and pH-sensitivity\(^1\) of the hydrogels make them ideal model systems to investigate the factors controlling self-assembly and phase separation in gelator–surfactant systems and employ them as cytoskeleton mimics in liposomes.

Supporting Information Available: Experimental details on the preparation and characterization of 1–3, and cryo-TEM (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

References

12. A full report on the synthesis and gelation properties of 1,3,5-trisamide-cyclohexane gelators is in preparation.
13. Interestingly, reversible gelation and dissolution of water by 1 is observed by changing the pH from 7 to 3.5 and back.
14. Cge at 25 °C for 1, 1.7 mM; 2, <3 mM, and 3, 1.3 mM; and Tcg of gels of 1, 73 °C (6.4 mM); 2, 104 °C (3.5 mM); and 3, 118 °C (1.7 mM).
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