Introduction

The micellar self-assembly of AB diblock copolymers in selective solvents was first recognized almost 40 years ago.\(^ 1\) In aqueous solution the driving force for micellization is usually the presence of a permanently hydrophobic block based on, say, polystyrene or polymethyl methacrylate.\(^ 2,3\) More recently, there has been increasing interest in the use of tunably hydrophobic blocks, since the resulting copolymers are stimuli-responsive.\(^ 4\) However, this is not the only approach to micelle formation: Kataoka's group,\(^ 5\) Kabanov and co-workers,\(^ 6\) and Gohy et al.\(^ 7\) have each reported that polymer complexation between oppositely charged polyelectrolytes leads to ionic micelle cores. These polymer complexes offer some potential for biomedical applications, since synthetic cationic diblock copolymers can form compact supramolecular structures with the pendent anionic phosphate residues on DNA.\(^ 8\) Such colloidal "packets" of DNA are small enough to be transported across cell membranes, which is a prerequisite for genetic engineering.

An alternative mechanism for achieving complexation between polymer chains is hydrogen bonding, which has recently received renewed attention. Scranton and co-workers have shown that high molecular weight statistical copolymers based on poly(methacrylic acid) (PMAA) and monomethoxy-capped poly(ethylene oxide) methacrylate can act as pH-responsive emulsifiers at low pH since hydrogen bonding occurs between the poly(ethylene oxide) side chains and the PMAA backbone, leading to hydrophobic patches.\(^ 9\) Meijer's group has shown that two homopolymers can form a hydrogen-bonded diblock copolymer in nonaqueous media if the end group of each homopolymer contains a sufficient number of hydrogen bond donor/acceptor sites.\(^ 10\) More pertinent to this work, Jiang's group has developed a novel route to polymeric micelles in aqueous media. A poly(styrene-co-methacrylic acid) statistical copolymer (MAA content varying from 4 to 13 mol %) formed a micelle core with a stabilizing corona of poly(N-vinylpyrrolidone) chains, with the latter binding to the MAA residues via hydrogen bonding.\(^ 11\)

Within the past 5 years, the synthesis of so-called "schizophrenic" AB diblock copolymers has been described. Here both the A block and the B block are stimuli-responsive; hence this new class of copolymer surfactants is capable of forming two types of micellar structures in aqueous solution.\(^ 12\) Recent examples include a purely pH-responsive diblock copolymer reported by Liu and Armes\(^ 13\) and purely thermoresponsive diblock copolymers reported by both Laschewsky and co-workers and Weaver et al.\(^ 14\)

Herein we describe the remarkable reversible self-assembly behavior of a binary mixture of a neutral–cationic diblock copolymer and a simple anionic polyelectrolyte at room temperature (see Figure 1). Judicious adjustment of the solution pH leads to the formation of a "holy trinity" of micellar/colloidal aggregates due to hydrophobic forces, polyelectrolyte complexation, and hydrogen bonding; as far as we are aware, such complex self-assembly behavior in aqueous solution is unprecedented.\(^ 15\) This is also the first example of a homopolymer being used to produce "schizophrenic" behavior in a diblock copolymer.

Experimental Section

Materials. Monohydroxy-capped poly(ethylene oxide) (PEO–OH; \(M_n = 5000; M_w/M_n = 1.10\)) was kindly donated by Cognis Performance Chemicals (Hythe, UK). 2-(Diethylamino)ethyl methacrylate (DEA) was purchased from Aldrich, and its
Inhibitor was removed by treatment with a basic alumina column prior to use. Sodium 4-styrenesulfonate (NaStS), Cu(II)Br, 2,2'-bipyridine (bpy), and isopropyl alcohol (IPA) were also obtained from Aldrich and were used as received. Deionized, doubly distilled water was used in all experiments. Poly(sodium methacrylate) (PNaMAA; PMAA is used to denote its homopolymer) was obtained from Aldrich and was used as received. Deionized water was used to prepare aqueous solutions at 20 °C (see Supporting Information).

**Figure 1.** Variation of intensity-average particle diameter with solution pH for a 1:1 binary mixture of PEO_{113}–PDEA_{50} and PMAA as determined by dynamic light scattering studies at 20 °C (○, PEO_{113}–PDEA_{50} with PNaMAA; ●, PEO_{113}–PDEA_{50} alone). A schematic representation of the three types of aggregates that are formed is also depicted. The vertical dotted lines correspond to the approximate phase boundaries between the micelles/colloidal aggregates and unimer states.

Aldrich as a 30 wt % aqueous solution. According to the literature, the molar mass of the poly(sodium methacrylate) homopolymer was determined to be 9500. Silica (silica-60 gel) was purchased from E. Merck (Germany).

**Diblock Copolymer Synthesis.** The poly(ethylene oxide–block-2-(diethylamino)ethyl methacrylate) (PEO–PDEA) was synthesized via atom transfer radical polymerization (ATRP) in a 2:1 v/v IPA/water mixture at 20 °C using a poly(ethylene oxide) macroinitiator and a Cu(II)Br catalyst, using 2,2'-bipyridine as a solubilizing ligand. After 1.5 h the DEA conversion was more than 95%.

**Aqueous Solution Characterization.** Dynamic light scattering (DLS) measurements were made on 1% w/v aqueous solutions at 20 °C using a Brookhaven BI-9000AT instrument equipped with a 125 mW laser operating at 488 nm. A scattering angle of 90° was used in all DLS studies of the micellar/colloidal aggregates. However, a scattering angle of 30° was used for the determination of the molecularly dissolved PEO–PDEA copolymer chains at pH 5.6 in order to avoid problems caused by short correlation times. Intensity correlation data were analyzed by the cumulants method to produce the average decay rate (Γ) (Γ = qD, where D is the diffusion coefficient). The intensity-average hydrodynamic diameter was calculated from the measured diffusion coefficients using the Stokes–Einstein relation and assuming the viscosity of the dilute aqueous solution to be that of pure water. TEM studies (see Supporting Information) indicate that broad size distributions for these micellar/colloidal aggregates. Thus, the hydrodynamic diameter measured at a scattering angle of 90° is almost certainly an underestimate of the true hydrodynamic diameter due to polydispersity effects. A full angular dependence study is required for more rigorous DLS characterization, but this is beyond the scope of the present study.

Static light scattering (SLS) studies were carried out at 25 °C using a Brookhaven Instrument Corp. (B19000) instrument equipped with a Lexel 2 W argon ion laser operating at 488 nm. The scattering angle, θ, was varied from 30° to 150° to produce Zimm plots. The dn/dc values for aqueous solutions of the PEO_{113}–PDEA_{50} diblock copolymer alone at pH 11 and its binary mixture with PMAA at pH 7.3 and pH 2.2 were determined to be 0.250, 0.236, and 0.211, respectively, using an Optokem differential refractometer operating at λ = 488 nm. To ensure accurate dn/dc measurements, stock solutions of each type of micelle/colloidal aggregate were diluted with water at constant pH to maintain a constant ionic strength. The resulting multipoint calibration plots at pH 11, 7.3, and 2.2 are provided as Supporting Information. We estimate that the error in such dn/dc determinations is around ±2%, which normally leads to an approximate error in the micelle molecular weight of around 10%. Measurement of the angular dependence of the excess absolute time-averaged scattered light intensity, known as the Rayleigh ratio, of a series of dilute polymer solutions allows determination of the weight-average molar mass (M_w,app) and the root-mean-square z-average radius of gyration (R_g) (see Supporting Information).

**Results and Discussion.** In 1999, we reported the pH-induced micellization of a PEO–PDEA diblock copolymer that had been synthesized by oxyanionic polymerization. In the present work a similar PEO–PDEA diblock copolymer was prepared using ATRP chemistry. The diblock composition was determined to be PEO_{113}–PDEA_{50} (i.e., M_w,app = 14 300) by 1H NMR spectroscopy in d_4-methanol using PEO as an “end group”. Gel permeation chromatography studies indicated a polydispersity of 1.25 for the final PEO_{113}–PDEA_{50} diblock copolymer. A phase diagram showing the three types of micelles formed by the binary mixture of the PEO–PDEA diblock copolymer and the PNaMAA homopolymer on varying the solution pH was constructed from DLS studies (see Figure 1). Control experiments were also conducted on the PEO_{113}–PDEA_{50} diblock copolymer in the absence of any PNaMAA homopolymer.
dissolved molecularly at low pH due to protonation of
the tertiary amine groups on the PDEA chains (con-
firmed by 1H NMR and DLS studies). Above pH 7.5, the
PDEA block becomes hydrophobic and PDEA-core mi-
celles were obtained with PEO coronas, as described by
Vamvakaki et al.18 Inspection of the 1H NMR spectrum
recorded at pH 11.8 (not shown) confirmed that the
PEO signals were no longer visible. If the PNaMAA
homopolymer is added to this alkaline solution, it simply
remains molecularly dissolved as an anionic polyelec-
trolyte (methacylate backbone signals due to PNaMAA
appear in the 1H NMR spectrum recorded for the binary
mixture) and does not interact with the diblock copoly-
mer micelles at this pH (see Figure 2). Regardless of
whether the PNaMAA is present or not, DLS studies
indicate the formation of micelles with an intensity-
average micelle diameter of 25 nm and a polydispersity
of 0.08.

Formation of Micelles with Mixed Polymer Cores
(pH 6–8.5). On lowering the solution pH of the above
binary solution to around pH 8.5, the PDEA block
becomes partially protonated and hence cationic,
while the PNaMAA chains lose some of their anionic
character. Under these conditions, efficient charge
compensation occurs, and micelles are formed that
comprise PNaMAA and PDEA mixed ionic cores with
the PEO chains forming the micelle coronas (see Figure
2). These “polyion complex” micelles have an intensity-
average mean diameter of around 32–35 nm and a
narrow size distribution (polydispersity = 0.03). On
further lowering the solution pH to below pH 6, charge
imbalance occurs. Given the dramatic decrease in the
scattered light intensity, it appears that the polyion
complex micelles begin to dissociate. However, the
observed particle diameter of 10 nm at pH 5.6 suggests
that there is still some weak interaction between the
highly protonated PEO–PDEA diblock and the near-
neutral, weakly hydrophilic PMAA chains rather than
true molecular dissolution. In contrast, control experi-
ments conducted in the absence of any PNaMAA
confirmed that the PEO–PDEA diblock copolymer mi-
celles formed in alkaline media simply dissociate below
around pH 7.3 to give unimers, with no supramolecular
assemblies being observed. The hydrodynamic diameter
estimated for a 10.0 g/L unimer solution at pH 5.6 was
3 nm. Finally, it is noteworthy that, if the solution pH is
raised from pH 7.6 to pH 11, the anionic PNaMAA
chains are released from the polyion complex micelles,
which become simple PEO–PDEA micelles with hydro-
phobic cores (see Supporting Information for NMR
evidence).

Formation of Micelles with Hydrogen-Bonded
Cores (pH < 3). Below pH 3, the degree of ionization
of the PMAA chains is essentially zero, and hydrogen
bonding of these neutral chains with the PEO blocks
can occur. Intuitively, micelles comprising hydrogen-
bonded PMAA/PEO cores and cationic PDEA coronas
were expected. However, DLS measurements indicated
the formation of colloidal aggregates of around 120 nm
diameter with low polydispersities (0.01–0.08).

The estimated contour length of a single PEO–PDEA
diblock copolymer chain is around 60 nm, but this
theoretical upper limit is calculated for the fully stretched
chains, which is physically unrealistic. Thus, the DLS
diameter is clearly too large for simple core–shell
micelles. Vesicle formation is an alternative explanation,
but the calculated density of these aggregates (0.057 g
cm–3) is probably too low to support this hypothesis.
The polyelectrolytic nature of the PDEA chains at low pH
is expected to produce bigger aggregates than the
micelles obtained at neutral or high pH. Moreover, 1H
NMR studies indicate that the PEO chains are merely
attenuated rather than completely suppressed (see Figure
2).19 This suggests a relatively high degree of
hydration for these aggregates. However, the combina-
tion of these two factors is not sufficient to account for
the observed hydrodynamic diameter. Another possible
explanation is that micellar aggregates or compound
micelles are formed, as described by Zhang and Eisen-
berg.20 In summary, we believe that the hydrogen-
bonded structures formed at low pH are more compli-
cated than simple core–shell micelles, and further work
is in progress to investigate this aspect.

Static Light Scattering Studies. Allowing for the
effect of dilution, the addition of PNaMAA to the DEA-
core diblock copolymer micelles at pH 11 had no
significant effect on the scattering intensity at all
angles, since the anionic homopolyelectrolyte

<table>
<thead>
<tr>
<th>Parameter</th>
<th>PEO113–PDEA50 alone at pH 11</th>
<th>Binary mixture at pH 7.3</th>
<th>Binary mixture at pH 2.2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrodynamic diameter (nm)</td>
<td>25</td>
<td>33</td>
<td>120</td>
</tr>
<tr>
<td>Polydispersity</td>
<td>0.16</td>
<td>0.03</td>
<td>0.08</td>
</tr>
<tr>
<td>M_0 (g mol⁻¹)</td>
<td>6.25 x 10⁶</td>
<td>2.08 x 10⁶</td>
<td>3.09 x 10⁷</td>
</tr>
<tr>
<td>Navg</td>
<td>35</td>
<td>152</td>
<td>2430</td>
</tr>
</tbody>
</table>

* The polydispersity, P_{2,1}^Γ, is defined as the ratio of the second
  moment of the cumulant fit (Γ2) to the first moment (Γ1) squared.
* These aggregation numbers were calculated assuming 1:1 stoi-
  chiometry between the PEO113–PDEA50 diblock copolymer and the
  PNaMAA (or PEO).
light very weakly compared to the much larger diblock copolymer micelles. Static light scattering (SLS) studies yielded weight-average micelle masses of approximately 6.25 × 10^6, 2.08 × 10^6, and 3.09 × 10^7 g mol⁻¹ for the PEO₁₁₃–PDEA₅₀ micelles at pH 11, polyion complex micelles at pH 7.3, and hydrogen-bonded aggregates at pH 2.2, respectively (see Table 1 and also the three Zimm plots in Figures 1–3 of the Supporting Information). On the basis of the respective weight-average molecular weights of the diblock copolymer and the homopolymer, the micelle aggregation numbers \( N_{agg} \) can be calculated. For the simple diblock copolymer micelles formed at pH 11, there are 35 copolymer chains per micelle. The diblock copolymer/homopolymer binary mixture was optimized to promote formation of a polyelectrolyte complex at pH 7.3 with a 1:1 DEANaMAA molar ratio; this assumed charge-compensated composition leads to a calculated micelle aggregation number of 152. In the absence of any other data it is also assumed, though with less justification, that the same 1:1 stoichiometric complex is formed via hydrogen bonding between the PEO and PMAA chains at pH 2.2, which leads to an aggregation number of 2430. This latter value is relatively high; if correct, it may indicate the presence of compound micelles.\(^\text{20}\)

**Aqueous Electrophoresis Data.** Aqueous electrophoresis studies (see Figure 3) indicated weakly negative zeta potentials (−3 to −7 mV) for the PDEA-core micelles above pH 8.5. On lowering the pH, the PDEA block becomes protonated and the anionic PNaMAA chains are incorporated into the micelle cores due to electrostatic attraction, leading to charge compensation. An isoelectric point is observed at pH 7.0, which is approximately the midpoint between the pKₐ of the PMAA and the conjugate acid form of the PDEA. On decreasing the pH further, the zeta potential remains almost zero. Below pH 3.5, when the PEO block forms a hydrogen-bonded complex with the neutral PMAA chains, the PDEA chains become highly cationic and the zeta potential increases dramatically to +29 mV, as expected.

**Effect of Additives on Micelle Formation.** It is well-known that polyelectrolyte complex micelles cannot be formed at high salt concentrations, since electrostatic interactions are substantially attenuated under these conditions.\(^\text{76}\) To test the hypothesis that the micelles formed at pH 6–8.5 comprised polyelectrolyte complex cores, \( \chi \) and additional DLS studies were carried out in the presence of added electrolyte (0.50 M NaCl). The presence of salt did not affect the formation of either hydrophobic DEA-core micelles in alkaline media or hydrogen-bonded aggregates below pH 3. However, no polyelectrolyte complex micelles were observed at intermediate pH, as expected.

In summary, the reversible formation of three types of micelles/aggregates in aqueous solution is reported for the first time. This unprecedented self-assembly behavior is readily achieved by adjusting the solution pH of a simple binary mixture of a judiciously selected neutral–cationic diblock copolymer and an anionic polyelectrolyte at ambient temperature. The driving force for aggregation is different in each case: conventional micelles are formed by hydrophobic interactions at high pH, polyelectrolyte complexation occurs at intermediate pH, and hydrogen-bonded complexes are produced at low pH.

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**Supporting Information Available:** The dn/dc calibration plots for (a) the PEO–PDEA diblock copolymer alone at pH 11, (b) the binary mixture of this diblock copolymer and the PMAA homopolymer at pH 7.3, and (c) the binary mixture of this diblock copolymer and the PMAA homopolymer at pH 2.2; three Zimm plots for the PEO₁₁₃–PDEA₅₀ diblock copolymer at pH 11 in the absence of PNaMAA, for the 1:1 binary mixture of PEO₁₁₃–PDEA₅₀ and PNaMAA at pH 7.3, and for the 1:1 binary mixture of PEO₁₁₃–PDEA₅₀ and PMAA at pH 2.2; representative transmission electron micrograph of the PEO–PDEA micelles formed at pH 11 in the absence of any PNaMAA homopolymer; NMR studies of the effect of pH cycling between the polyelectrolyte complex micelles formed at pH 7.6 and the hydrophobic PDEA-core micelles formed at pH 11. This material is available free of charge via the Internet at http://pubs.acs.org.

**References and Notes**


(15) During the preparation of this manuscript, we became aware of a recent paper by Gohy and co-workers (see ref 7b), who examined the self-assembly behavior of a binary pair of asymmetric diblock copolymers based on a near-monodisperse poly(2-vinylpyridine)–poly(ethylene oxide) (P2VP–PEO) and a highly polydisperse poly(methacrylic acid)–poly(ethylene oxide) (PMAA–PEO). At high pH the P2VP–PEO diblock formed P2VP-core micelles, with the PMAA–PEO remaining molecularly dissolved, at intermediate pH a mixed polyion complex micelle comprising charge-compensated P2VP and PMAA residues was formed, and at low pH the PMAA–PEO blocks formed micelles due to intrachain hydrogen bonding between the short PMAA and the long PEO blocks. Thus, there are certainly some similarities between this work and the present study.


(19) Assuming that the PDEA chains are fully solvated, an apparent EO/DEA block ratio of 1.45 can be calculated. Since the actual EO/DEA block ratio is 2.26 (determined from the diblock copolymer’s 1H NMR spectrum recorded in d4-methanol), this indicates that the PEO chains are less solvated/mobile at low pH, which is consistent with the formation of hydrogen bonding between the PEO and PMAA chains. Hydrogen bond complexation between PEO and PMAA was also postulated by Scranton and co-workers (see ref 9).


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