Synthesis and aqueous solution properties of a well-defined thermo-responsive Schizophrenic diblock copolymer

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1 J. V. M. Weaver et al., Chem. Commun., 18, 2122, 2002
A brief history of “Schizophrenic” micelles

First Generation: Salt and pH responsive  
- **S. Liu et al, Angew. Chem., 40, 2328, 2001**
- PPO-core micelles at 40 °C, pH 6.5, $N_{agg} = 760$
- PPO-DEA unimers at 5 °C, pH 6.5
- DEA-core micelles at 5 °C, pH 8.5, $N_{agg} = 650$

Second Generation: Purely thermo-responsive  
- $1.0 \text{ M} \text{Na}_2\text{SO}_4$, pH 6.7
- Dialysis or pH < 6.7
- MEMA-DEA
- pH 8
- pH < 7

Third Generation: Purely pH-responsive  
- **S. Liu et al, Angew. Chem., 41, 1413, 2002**
Thermo-responsive, schizophrenic diblock copolymers

Laschewsky and co-workers have reported the labour-intensive RAFT synthesis of a sulfobetaine-block-N-isopropylacrylamide copolymer

Conversion of the first block was allowed to reach only 27 % for efficient blocking and purification was tedious. Mw / Mn = 1.35

BUT

This was the first example of an entirely thermo-responsive schizophrenic (forms micelle and inverted-micelles) diblock copolymer.

Synthesis of the “schizophrenic” diblock copolymers

1,3 propane sultone, THF, 20 °C, 3 days

DMA content = 35 or 51 mol %

Selective betainisation of DMA residues give the thermo-responsive diblock copolymers

Aqueous solution properties of poly(SBMA)

Poly sulfobetaines often show Upper Consolute Solution Temperatures (UCST) in aqueous solution

At low temperature, in the absence of electrolyte, attractive inter-chain electrostatic interactions prevent dissolution of the polymer in water.

- At elevated temperatures, the thermal energy becomes enough to break the relatively weak inter-chain ionic interactions. The polymer becomes water-soluble. This is a fully reversible process.

- In the presence of salt, polymer chains preferentially complex the electrolyte and reduce the attractive inter-chain interaction. The polymer becomes water-soluble. This is a reversible process (requires dialysis against pure water).
Aqueous solution properties of poly(MEMA)

Poly (2-((N-morpholino)ethyl methacrylate) is a weak polybase, which is water-soluble at both neutral and acidic pH at ambient temperature.

Poly MEMA precipitates from neutral or basic aqueous solutions at elevated temperatures (32-53 °C, depending on molecular weight).

- At elevated temperatures, the thermal energy breaks the extensive hydrogen bonding network with the water. The polymer phase-separates from water. This is a fully reversible process.

- Addition of as little as 0.2 M \( \text{M}_2\text{SO}_4 \) salts out the polymer under neutral or basic conditions.

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4 V. Butun et al., *Polymer*, 42, 5993, 2001
DLS for SBMA-MEMA diblock copolymer

Temperature / °C

< 20 °C
Loose, SBMA-core micelles

20-50 °C
Molecularly dissolved

> 50 °C
Compact, MEMA-core micelles

1.0 w/v % aqueous solution
$^1$H NMR spectra of the thermo-responsive, ‘schizophrenic’ SBMA-MEMA diblock copolymer

$^1$H NMR in D$_2$O at pH 6.5
Mn = 44,000 g mol$^{-1}$
Mw/Mn = 1.10
SBMA content = 35 mol %

$\Leftarrow$ Molecules dissolved, SBMA-MEMA unimers

$\Leftarrow$ Hydrated SBMA-core micelles

$\Leftarrow$ Dehydrated MEMA-core micelles
Conclusions

1. Near-monodisperse diblock copolymer precursors are readily synthesised in high yield by GTP
2. Molecular dissolution occurs at around 20-50 °C
3. Hydrated, polydisperse SBMA-core micelles at below 20 °C
4. Relatively dehydrated, monodisperse MEMA-core micelles at above 50 °C
5. This is only the second example of a purely thermo-responsive, schizophrenic diblock copolymer
6. Continuing studies by SANS and SLS in collaboration with Alice Gast’s group (Stanford University/MIT)

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