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Stimuli-responsive surfactants

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Recent progress in stimuli-responsive surfactants is reviewed, covering control of both interfaces and bulk solution properties. Particular attention is devoted to potential future directions and applications.

Introduction

Surfactants are frequently employed in Materials Science to generate self-assembly structures over nanometre to micron length scales; these added surfactants stabilize interfaces and nanostructures to affect solubilisation, morphology, biological, physical, optoelectronic and chemical properties.[1] The ability to tune self-assembly in a predictive and controllable way is also used in Organic Chemistry, where surfactants introduce compartmentalization and structuring for control in catalysis.[2] Conventionally, surfactant properties and self-assembly is manipulated by varying temperature, pH and ionic strength, often leading to irreversible changes in system composition, phase stability and structure. A more sophisticated approach is to use external stimuli to activate changes in molecular structures with responsive surfactants, hence it is possible to affect surface activity, aggregation structure, viscosity, (micro)emulsion stability and solubilisation.

This review covers currently available stimuli-responsive surfactants, categorized in terms of sensitivity to changes in pH, CO_2 levels, electrical potential, light, magnetic field, as well as surfactants sensitive to added enzymes and chemically labile systems which undergo bond cleavage. The focus is on reversible/switchable surfactants, and certain amphiphilic polymers, all of which having been chosen to highlight new types of stimuli and potential nanotechnological applications. It is envisaged that switchable surfactants will be primarily utilized for high-end materials science applications, but possibilities for using stimuli responsive surfactants in everyday applications are also covered.

General factors affecting surfactant self-assembly and cmc

The fundamental physical chemistry underpinning the behaviour of surfactants and (micro)emulsions has been extensively covered.[3–5] From a chemical structural viewpoint, the primary factors determining surfactant properties such as surface activity (adsorption), critical micelle concentration (cmc) are molecular structure and design; for example types and lengths of the hydrophobic tails, nature of the hydrophilic head-groups, and for ionic surfactants, counter-ion identity. Obviously, these factors are essentially “fixed” by surfactant chemistry, with no scope for variations or changes *in situ*, except by varying pH, salt concentration, temperature, pressure, *etc.* For example, with ionic surfactants added electrolyte tends to decrease cmc by screening electrostatic headgroup repulsions. For the same reason, at the oil–water interface (emulsions) salt can also alter the hydrophile–lipophile balance (HLB), which affects the phase inversion temperature (PIT), where emulsions invert from oil-in-water (o/w) to water-in-oil (w/o). As an example, replacing pure water by a 5% NaCl solution a PIT reduction in the order of 10 °C may be observed.[5]

Temperature (T) has major effects on surfactant solubility (Krafft point temperature where solubility rapidly increases), phase instabilities such as cloud points, and for polymeric surfactants on the cmc.[3] However, the influence of temperature on micellization is relatively weak, reflecting subtle changes in bonding, heat capacity and volume accompanying the transition. In thermodynamically stable microemulsions the effect of T may be significant, and may be due to a combination of changes in surfactant solubility and system Gibbs energy. To a first approximation, the Gibbs energy of (micro)emulsification (ΔG_{disp}) can be expressed in terms of the energy for creating new interface, $\Delta A\gamma$, and configurational entropy, ΔS_{conf}:

$$\Delta G_{\mathrm{disp}} = \Delta A\gamma - T\Delta S_{\mathrm{conf}} \quad (1)$$

where ΔA is the change in interfacial area A and γ is the interfacial tension between two phases (*e.g.* oil and water).

Obviously, with traditional inert surfactants the effects of temperature, pH and electrolyte are reversible, however, with responsive surfactants external stimuli can be applied, affording a finer level of control and reversibility over system characteristics.

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pH-responsive surfactants

Surfactants responsive to pH have been subject to increasing interest owing to their wide potential in novel applications where pH variations can be utilized to control self-assembly.[6] A new series of pH-responsive gemini surfactants with 2-pyrrolidone headgroups, *N*,*N*′-dialkyl-*N*,*N*′-di(ethyl-2-pyrrolidone)ethylenediamine (Di-C_nP, where $n = 6$, 8 10, 12) have recently been studied by Dong *et al.*[7] The group used surface tension to characterize surface activity and micellization behaviour in acidic, neutral and basic conditions, finding a pH dependence of aqueous solutions due to the protonated state of the surfactant molecule when pH was varied (Table 1, Fig. 1). In addition to this the group employed Di-C_nP to solubilize cyclohexane and demonstrated that the solubilization capacity of the surfactant could also be tuned using pH, suggesting potential applications in enhanced oil recovery, demulsification, contaminants remediation and textile treatment.

However, Di-C_nP, like many other responsive surfactants, is synthetically complex, and so recently there have been attempts to create amphiphiles with pH-responsive functional groups more easily and with greater yields. One of the simplest pH responsive surfactants is *N*-dodecyl-1,3-diaminopropane (C12NC*n*N, Fig. 2), which possesses a single hydrophobic carbon chain, coupled to a readily tunable diamine hydrophilic function.[8,9] Here, the diamine has two distinguishable aqueous pK_as (4.71 and 10.81) providing pH and temperature sensitivity leading to diverse phase behaviour through continual control over hydrophilicity.

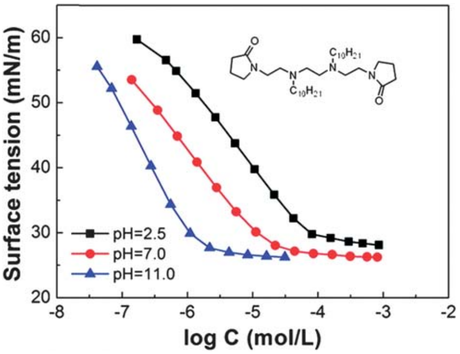

Fig. 1 Variation of the surface tension *versus* logarithm concentration of Di-C_{10}P at different pH at 25 °C. Inset shows structure of Di-C_{10}P. Reprinted with permission from *Langmuir*, 2012, **28**, 7174–7181. Copyright (2012) American Chemical Society.[7]

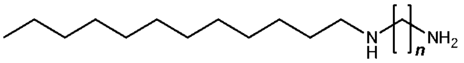

Fig. 2 Molecular structure of *N*-dodecyl-1,3-diaminopropane (C12NC*n*N).

Table 1 cmc and γ_{cmc} of Di-C_nP measured by surface tension in the absence of salt at different pH at 25 °C (ref. 7)

Surfactant	pH ± 0.2	cmc/(M)	γ/(mN m^{-1})
Di-C_6P	2.5	3.91×10^{-3}	32.2
	7.0	1.09×10^{-3}	31.3
	11.0	3.82×10^{-5}	29.6
Di-C_8P	2.5	4.66×10^{-4}	30.5
	7.0	2.42×10^{-4}	28.6
	11.0	1.50×10^{-5}	27.8
Di-C_{10}P	2.5	1.06×10^{-4}	30.1
	7.0	5.01×10^{-5}	27.5
	11.0	4.01×10^{-6}	27.0
Di-C_{12}P	2.5	2.22×10^{-5}	28.6
	7.0	1.19×10^{-5}	26.5
	11.0	—	—

Wormlike micelles are long and highly flexible, which entangle to form transient networks with remarkable viscoelastic properties.[10–12] These properties have gained considerable attention in applications ranging from cosmetics to drag reduction agents owing to their superior properties, including mildness to the skin and eyes, foaming and solubility. Therefore the possibility of controlling viscoelastic fluids using pH is of huge interest.[12] Li *et al.* demonstrated that C12NC3N readily evolves from spherical micelles (pH 1.98) to rod-like micelles (pH 8.00) into wormlike micelles (pH 9.01), which then transform into perforated vesicles (pH 9.97) and fully closed vesicles (ΔT) (Fig. 3).[8] This is important as even small changes in pH and temperature can give rise to dramatic changes in system properties such as viscosity, solubilisation and stability.

For many applications, pH-responsive surfactants are not used exclusively but are often added to surfactant mixtures. However, it should be realized that at an appropriate pH a solution of pH-sensitive surfactant behaves by itself like a binary surfactant mixture of the protonated and deprotonated forms, where relative compositions of the monomers and the micelles are controlled primarily by the solution pH.[13] For example, for the surfactant dodecyldimethylamine oxide in 0.1 M NaCl at pH 3, around 1% of the monomeric surfactant molecules are deprotonated, while 10% of the micellized surfactant molecules are deprotonated.[14] Blankschtein and Goldsipe[13] have developed a predictive molecular-thermodynamic theory to model micellization in mixtures containing pH-responsive and conventional surfactants, with inputs including molecular characteristics of the surfactants and solution conditions such as pH, and concomitantly highlighted the much more complex interplay between hydrogen bonding and electrostatics in such surfactant mixtures.

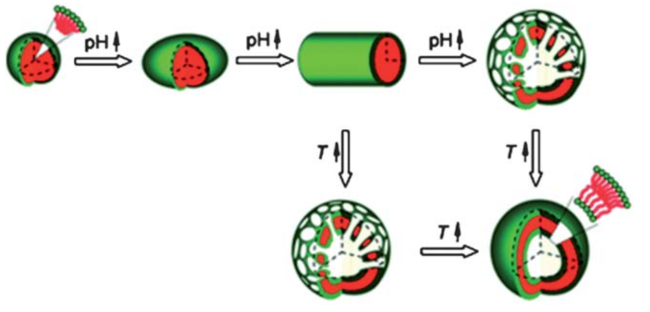

Fig. 3 pH and temperature-induced micelle-to-vesicle transition (not to scale). Reprinted with permission from *ChemPhysChem*, 2010, **11**, 3074–3077.[8]

In 2008 Rannard *et al.*[15] demonstrated that by selecting a pH-responsive core-forming monomer and a hydrophilic macromonomer, pH-responsive branched amphiphilic copolymers (polymeric surfactants) could be formed. These may be considered analogous to cross-linked micelles.[16,17] One such copolymer is that of methacrylic acid (MA) and poly(ethyleneglycol)methacrylate (PEGMA) which can stabilize oil-in-water droplets with high morphological control and uniformity and allows for disassembly using a pH-trigger. In basic conditions there is steric and electrostatic stabilization but in acidic conditions there are multiple hydrogen bonds causing aggregation (Fig. 4).[18] Polymer stoichiometry and architecture leads to further control of emulsion kinetics and hierarchical assembly.[19,20]

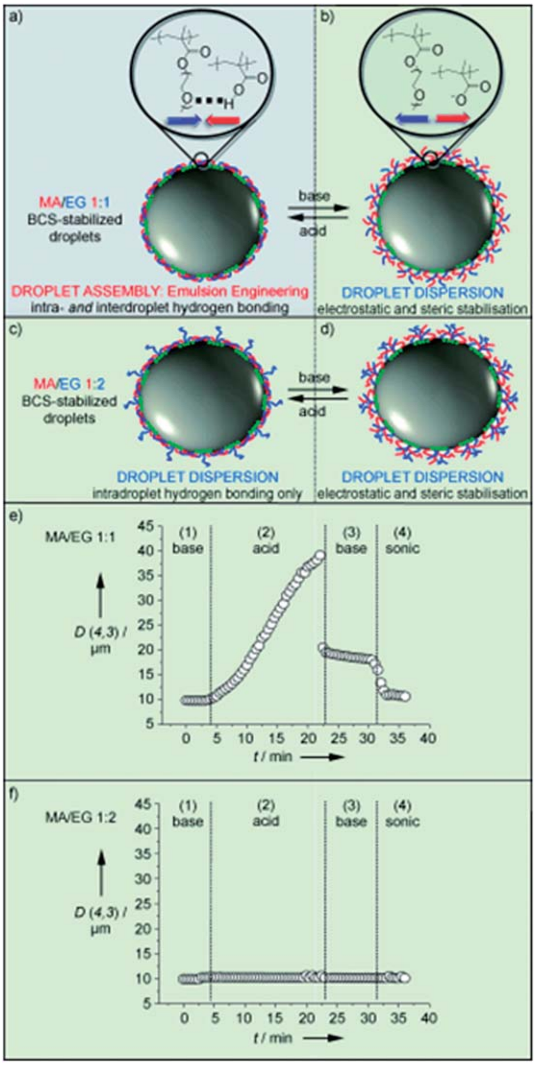

Fig. 4 Effect of branched copolymer surfactant composition on interdroplet interactions. (a) intra- and interdroplet hydrogen bonding occurs at low pH for MA/EG 1 : 1 droplets, which causes interdroplet attraction and assembly; (c) excess steric stabilization from MA/EG 1 : 2 droplets prevents interdroplet hydrogen bonding, interdroplet repulsion predominates at low pH; (b and d) steric and electrostatic stabilization occurs at basic pH, thus interdroplet repulsion predominates in both cases. Average droplet diameters, *D*(4,3), of (e) MA/EG 1 : 1 and (f) MA/EG 1 : 2 droplets under various conditions: (1) pH 9, (2) reducing the pH value of the solution to 2, (3) increasing the pH value of the solution to 11, and (4) gentle sonication at pH 11. Reprinted with permission from *Angew. Chem., Int. Ed.*, 2009, **48**, 2131–2134.[18]

Gene delivery has become one of the most important areas of nanomedicine, where pH-responsive surfactants have a role to play in intracell transfer.[21] A variety of pH-sensitive (–NH–containing) gemini surfactants have been used to control DNA–nanoparticle structure and zeta potential, and therefore membrane fusion and transfection rates (release of entrapped DNA).[22–25] This occurs as certain structures and mesophases lead to greater membrane fusion. For example the pH-dependent transition from lamellar to inverse hexagonal phase for the DNA–carbohydrate gemini surfactants leads to increased gene delivery.[26]

CO_2-responsive surfactants

A variation of pH control is offered by CO_2-responsive surfactants. Exposing long-chain alkyl amidine compounds to an atmosphere of carbon dioxide can transform them into charged surfactants (Fig. 5): bubbling nitrogen, argon or air through the amidinium bicarbonate solutions at 65 °C reverses the reaction, releasing carbon dioxide. The reversibility and repeatability were confirmed by monitoring the conductivity of a solution of **1a** in wet dimethyl sulfoxide (DMSO) while CO_2 and then argon were bubbled through the solution over three cycles (Fig. 6). Conductivity rose when CO_2 was bubbled through and dropped again upon argon addition.[27] These surfactants also have the capacity to stabilize alkane/water emulsions as well as styrene-in-water emulsions (for the purpose of microsuspension polymerization)[27] functioning as switchable demulsifiers.

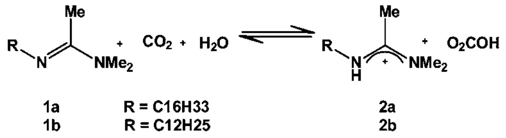

Fig. 5 *N*′-Alkyl-*N*,*N*-dimethylacetamidine (**1a** and **b**) converted into *N*′-hexadecyl-*N*,*N*-dimethylacetamidinium bicarbonate (**2a** and **b**) by CO_2.[27]

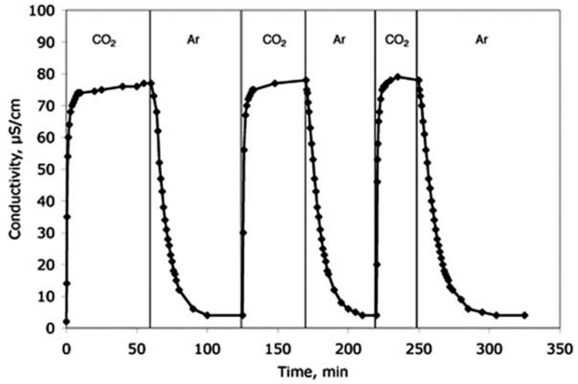

Fig. 6 The conductivity of a DMSO solution of **1a** at 23 °C as a function of time during three cycles of treatment with CO_2 followed by argon. Reprinted with permission from *Science*, 2006, **313**, 958–960.[27]

N_2/CO_2 triggered switchable surfactants have also allowed a new and simple method to control latex stability and the potential to achieve reversible coagulation and redispersion.[28–30] This is significant as for many industrial applications the only way to destabilize or force coagulation of latex particles is through the addition of salts or large excesses of acid or base. This results in washing processes followed by the removal of organic additives, generating substantial amounts of waste water.[28]

Recently, Zhang *et al.* demonstrated that a CO_2-responsive dispersant, *N*,*N*-dimethyl-*N*′-(pyren-1-ylmethyl) acetimidamidinium ($PyAH^+$), which bears both a pyrene moiety and an amidinium cation, could functionalize single-walled carbon nanotubes (SWNTs), and promote dispersion in water.[31] Gas triggered interconversions between the amidinium cation and amidine, through bubbling of CO_2 or Ar, then led to the reversibly controlled solubility of SWNTs.

Yuan and co-workers produced amphiphilic amidine-containing diblock copolymers which respond to CO_2.[32] This was tested by measuring electrical conductivity as a function of CO_2 exposure time. Over 20 minutes the conductivity rose dramatically from 3.4 to 26.9 μS cm^{-1} accompanied by a decrease of the pH value from approximately 6.94 to 5.68, implying that a number of protonated species formed in the copolymer chains.[32] On treatment with Ar conductivity was restored. The polymeric surfactants aggregated in water to form vesicles, which, after treatment with CO_2 for 20 minutes, increase in internal volume by ~800% with wall thickness halving, compared to the counterpart without gas stimulus. This process is completely reversible after passing through Ar producing vesicles that behave "*as if a bubble is breathing*".[32] It is interesting to include here new reports of cytomimetic chemistry involving "breathing" vesicles, whereby changes in morphology occur concomitantly with changes in fluorescence. This is achieved by including dimethylaminoazobenzene groups into the polymer chain. However, in this case pH is controlled not by CO_2 but by the addition of HCl or NaOH.

Redox-responsive surfactants

In 1980 Baumgartner and Fuhrhop reported the first amphiphiles containing redox-active terminal groups.[33] These compounds were based on pyridinium ions and were fairly insoluble in water. However, after sonication vesicles with a diameter up to 600 Å were formed which could solubilize hydrophobic dyes. This lead the authors to hypothesize whether "*electrons and protons could be transferred from the aqueous phase via the redox-active surface into the hydrophobic interior of the membrane*".

It has been more than 25 years since Saji *et al.* reported the first low-molecular weight surfactants with a ferrocene-based redox moiety for which the cmc and micellization behaviour changed with the stimulus of electron transfer. Through spectroscopic studies they observed that micelles could be broken up into monomers by oxidation and re-formed by reduction.[34,35] This approach was then extended beyond single-chain cationic ferrocene-based surfactants.[36–40] In the late 90's it was demonstrated that redox-active surfactants containing ferrocene could reversibly and dramatically control the surface tension of solutions (Fig. 7),[41] whereby oxidation of the ferrocene group at concentrations below 10 mM led to an increase in surface tension with a maximum change of 23 mN m^{-1} (from 49 mN m^{-1} to 72 mN m^{-1}). This increase is due to both a reduction in the hydrophobic driving force for adsorption and a change in electrostatics. Changes in oxidation state can also lead to changes in the microstructure of aggregates.[42–44] This has been taken advantage of by mixing a ferrocenyl-based surfactant with sodium salicylate.[45] Abe *et al.* used this concept to control worm-like micelle deformation electrochemically with a fourfold decrease in viscoelasticity.

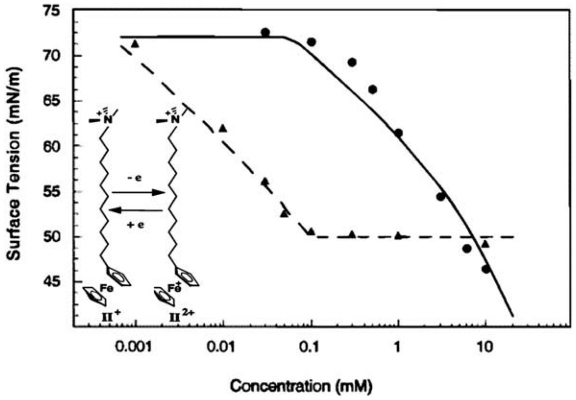

Fig. 7 Equilibrium surface tensions of aqueous solutions (0.1 M Li_2SO_4, pH 2, 25 °C) of ferrocenyl surfactants: experimental measurements for II^+ (triangles) and II^{2+} (circles). Inset: Molecular structures of the ferrocenyl surfactants. Adapted with permission from *Langmuir*, 1999, **15**, 722–730. Copyright (1999) American Chemical Society.[41]

A clear and comprehensive review of redox-active surfactants detailing work up to 2009 has recently been published by Liu and Abbott detailing with electrochemical control of self-assembly, interfacial properties, and interactions with DNA (lipoplexes) and so the reader is directed here for further information.[40] However, it is important to at least mention here some new trends.

A new class of redox-responsive surfactants has recently been developed. In 2008 Cronin *et al.* produced surfactants with polyoxometalate (POM) head groups.[46] A polyoxometalate is usually an anion, that consists of transition metal oxyanions linked together by shared oxygen atoms to form clusters. The headgroups were based on Mn-Anderson clusters[46] and functionalized with two alkyl chains forming vesicles in MeCN–water mixtures. In 2010 Wu *et al.* showed these vesicles could be made sensitive to photo-irradiation by adding azobenzene groups.[47]

Later that year catalytically active POM-surfactants were published[48] and finally, in 2012 new Ru-based POM-surfactants demonstrated reversible redox-responsivity, observed through changes in hydrodynamic radius. Importantly, electrochemical activity converted the Ru-metal centre between magnetic high-spin d^5 configuration and low-spin d^6, however magnetic sensitivity was not explored.

Future progress appears to be focussed primarily on extending the work done on redox-responsive surfactants to amphiphilic polymers, incorporating inorganic building blocks for the synthesis of smart materials.[49–51]

Photo-responsive surfactants

Surfactants incorporating suitable chromophores, either in the headgroup or the hydrophobic chain, have been investigated in terms of photoinduced isomerization. Appropriate photo-active groups include azobenzenes, stilbenes and spiropyrans and may be classified in two ways: one is thermally stable and converted using light of different wavelengths, and the other forms a metastable state on illumination and therefore responds only if light is continuously supplied. Azobenzene surfactants undergo *cis–trans* isomerism depending on the incident wavelength. Thermodynamically stable, planar *trans* isomers are generally transformed into bent, less-hydrophobic *cis*-form by irradiation at around $\lambda = 360$ nm and converted back at around $\lambda = 460$ nm. A change in hydrophobicity is attributed to an increase in dipole moment associated with the bent conformation.[52] Complete conversion is not generally possible due to an overlap of isomeric absorption spectra. Instead the systems reach a photostationary state with the mixture comprising both *cis* and *trans* isomers.[53]

The first mention of photo-responsive surfactants was by Shinkai *et al.* in 1982, who demonstrated that surfactants with azobenzene headgroups underwent photoinduced isomerism affecting aggregation.[54] There have been some very nice reviews in this area,[40,55] and the aim of this section is to introduce the most significant more recent advances.

Monteux *et al.* recently studied the adsorption dynamics at the air–water interface of a photo-responsive surfactant (azo-TAB) with an azobenzene moiety in its hydrophobic tail, observing that changes in conformation cause a decrease in surface tension (γ).[56] They also found that the *cis* isomer adsorbs 10 times faster than the *trans* isomer but the *cis* conformation also desorbs 300 times faster, leading to a non-stimulated mono-layer packed almost exclusively with *trans* isomer. The group then investigated irradiation at the interface, "pumping out" the newly photoconverted *cis*-isomer, which rapidly decreases the surface excess and increase γ driving Marangoni flow (Fig. 8). This results in a stationary vertical gradient of concentration below the surface. This work is interesting as it limits dynamic surface tension stimulating faster equilibration and allows for tuning of surface tension, γ.

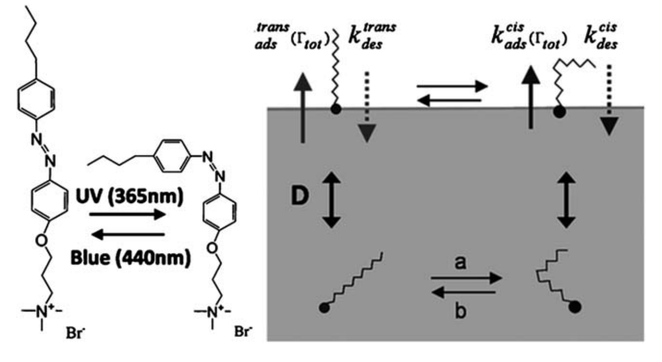

Fig. 8 (left) Photo-conversion from the *trans* to the *cis* isomer of azoTAB. Under UV light ($\lambda = 365$ nm) the solution contains 16% of *trans* isomers as compared with 66% of *trans* isomer under monochromatic blue light ($\lambda = 436$ nm); (right) overview of the fluxes in solution. Surfactants are photo-converted with kinetic constants *a* and *b*. *Trans* and *cis* conformations are characterized by adsorption constants, k_{ads} and k_{des}, and the bulk diffusion coefficient, *D*, to the interface.[56]

For many years, and primarily with an eye on biomedical applications, there has been a large drive towards encapsulating a payload in a nanoassembly and controlling its release photochemically.[57] The use of light stimuli is attractive as it can be applied with high spatial and temporal precision through modification of a broad range of parameters (wavelength, intensity, duration, *etc.*). Matyjaszewski and co-workers reported a spiropyran-containing polymethacrylate-based block co-polymer that undergoes reversible light-triggered isomerization accompanied by a transformation between an amphiphilic and a double-hydrophilic block copolymer.[58] Here, UV-light converts spiropyran into hydrophilic merocyanine and visible light converts it back to the hydrophobic spiro form. Hydrophobic dye could be encapsulated into the spiropyran and completely released after irradiation with 365 nm light for 60 min, as confirmed by AFM. Partial reloading of the dye was possible with reconstitution of the micelles after irradiation with 620 nm light for 240 min (confirmed by AFM fluorescence).

Spiropyran-modified surfactants terminated with permanently charged quaternary ammonium headgroups were first investigated around 15 years ago.[59] Since then much work has been carried out on control of micellar morphology,[59] wettability[60] and the preparation of Langmuir–Blodgett films.[61–63] In 2010, the first report of the self-assembly of spiropyran-modified surfactants (SP-Me-6, Fig. 9) on colloidal and flat silica was published.[64] Importantly, this work was carried out in an aqueous medium and investigated *in situ* morphological changes in the adsorbed layer, induced by photoisomerization.

Adsorption isotherm data indicated that the more hydrophobic SP form gives a greater adsorbed amount when compared with the zwitterionic MC form. While AFM measurements (Fig. 10) demonstrated that the MC form forms disk-like surface aggregates in the adsorption plateau region on a flat silica plate whereas the SP form gives larger surface aggregates as a result of its greater hydrophobic/associative

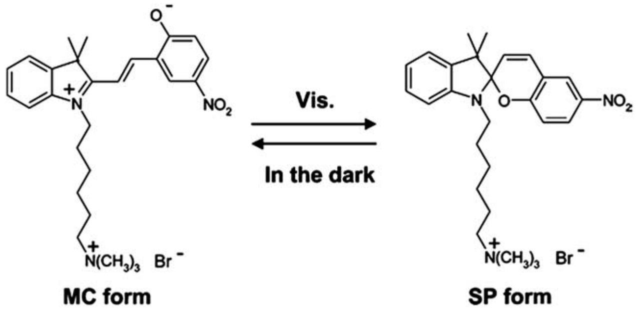

Fig. 9 Chemical structures of SP-Me-6 for both isomers. The MC form (left) is spontaneously formed in aqueous solution, and visible light irradiation results in photoisomerization to the SP form (right). The original MC form reappears when the isomerized SP solution is stored in the dark.

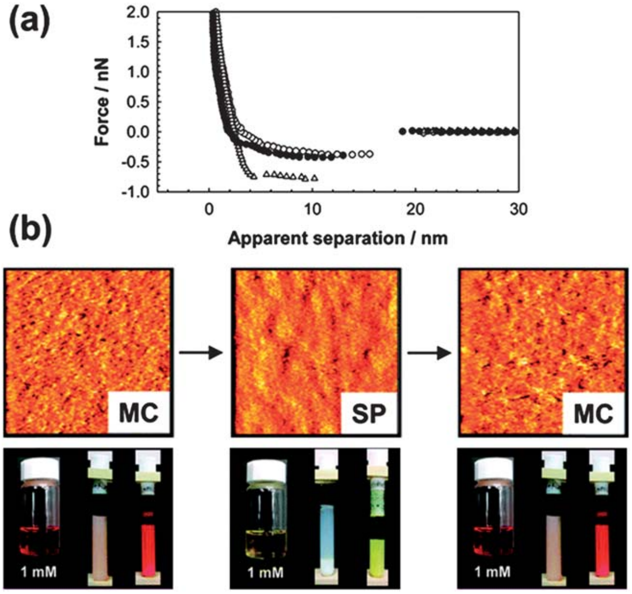

Fig. 10 (a) Force–distance data and (b) the corresponding soft-contact 300 nm AFM deflection images obtained for the MC–SP–MC isomerization cycle. Adsorption was performed in the dark (MC, ○) at an SP-Me-6 concentration of 0.1 mM in the presence of 10 mM NaBr. Then, the system was stored under visible light ($\lambda > 420$ nm) irradiation for 30 min (SP, △) and equilibrated in the dark again for 60 min (MC, ●); (below) silica suspensions with the adsorption of SP-Me-6. The surfactant solutions adjusted to 1 mmol dm^{-3} (without silica particles) in vials are shown on the left side for each isomerization form. Reprinted with permission from *Langmuir*, 1999, **15**, 722–730. Copyright (1999) American Chemical Society.[64]

character. This difference in the hydrophobic nature between the two isomers induces reversible changes in the dispersion stability of silica suspensions as well as in the surface force, in response to the photoisomerization. Taking the *in situ* and *ex situ* colour changes into consideration (Fig. 10, below), the group suggested it was probable that the photoisomerization occurs reversibly even after surfactant adsorption on silica, and concluded that it is possible to fabricate photoresponsive smart surface coatings in aqueous media as a result of the spontaneous adsorption of SP-Me-6.[64]

Another approach to applying photo-surfactants is to consider host–guest modulation. One of the most interesting and most recent examples of this is to use the photoisomerization of azobenzene to control the host–guest interaction of an azobenzene-surfactant and cyclodextrin (CD) and tune molecular amphiphilicity.[65,66] The azobenzene-surfactant studied (AzoC10) by Zhang *et al.* formed vesicle-like aggregates in aqueous solution.[67] Binding α-CD to the azobenzene enhanced water solubility and disrupted the vesicles. However, upon photoirradiation with UV-light α-CD cannot bind with the azobenzene any more and slides over the alkyl chain. This resulted in the reformation of vesicles, whose size is smaller than those in the α-CD-free system (Fig. 11). This process could be reversed by applying visible light and recovering azobenzene into its *trans* form. By carefully choosing the CD concentration fine tunability of vesicle morphology or cmcs may be achieved.[68] The same idea was later employed by the same group to fabricate self-assembled monolayers which could control wettability of a gold substrate.[69]

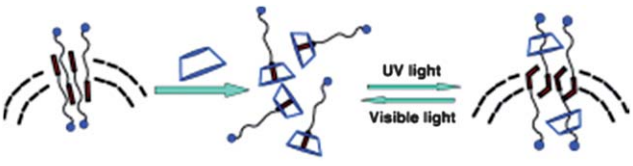

Fig. 11 Illustration of the photocontrolled reversible assembly and disassembly of AzoC10; red bar: azobenzene moiety, blue spot: pyridinium group. Reprinted with permission from *Angew. Chem., Int. Ed.*, 2007, **46**, 2823–2826.

Magneto-responsive surfactants

Surfactants containing metal ions have been frequently reported.[70–72] However, their intrinsic magnetic properties had always been overlooked. Recently, Eastoe *et al.* demonstrated the first ionic liquid surfactants containing magneto-active metal complex ions such as 1-methyl-3-decylimidazolium tetrachloroferrate (C_{10}mimFe).[73] These magneto-responsive cationic surfactants are interesting as they are molecular liquids, rather than typical magnetic fluids (ferrofluids) which comprise magnetic colloidal particles ($\geq$10 nm) dispersed in a carrier fluid. Most surprisingly these surfactants retain a magnetic response even in dilute aqueous solution. At the air–water interface, in the absence of an applied field, the magneto-responsive surfactants are more effective than their magnetically inert analogues, showing greater surface tension (γ) reduction of water for the same concentration. Interestingly, placing a magnet (0.4 T) in close proximity to aqueous solutions of the paramagnetic magneto-responsive surfactants reduces γ even further, demonstrating bifunctionality (Fig. 12 and 13). Since then f-block metals have been introduced as magnetic counterions to increase magnetic susceptibility and provide greater responsivity.[74,75]

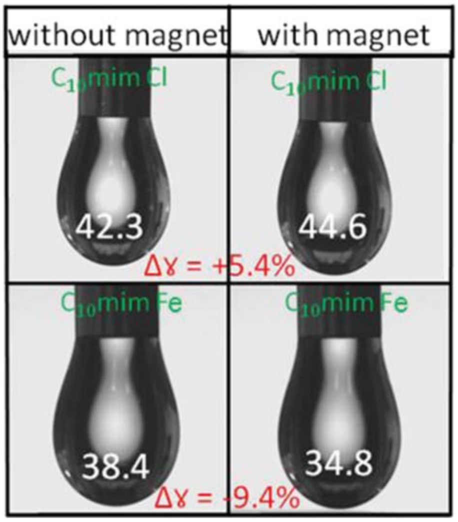

Fig. 12 Pendant drop profiles of magneto-responsive C_{10}mimFe and the inert analogue C_{10}mimCl with and without a magnet.[75]

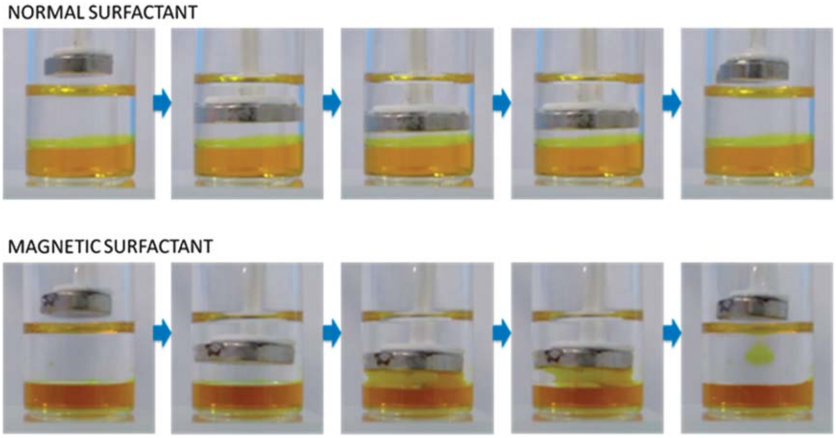

Fig. 13 Effect of magnetic field through dodecane on 20 wt% aqueous surfactant solutions. Above inert C_{10}mimCl, below magnetically active C_{10}mimFe. The C_{10}mimCl solution was dyed with trace methyl orange (to aid the eye).[75]

Using these magneto-responsive surfactants, magneto-responsive emulsions (MREs) have become accessible, which previously had only been realized with Pickering emulsions stabilized by magnetic nanoparticles.[76] Oil-in-water MREs were made from brine and lubrication oil suggesting applications from environmental cleanup to nanomedicine. Concerning targeted drug delivery, MREs could also be manipulated against an effective "flow" of solvent with relatively small magnetic fields,[77] emulating nanoparticle capture *in vivo*.

Magnetic microemulsions from magneto-responsive anionic surfactants (Aerosol-OT based) were then produced exhibiting monodomain magnetic behaviour (superparamagnetism) intermediate between magnetic nanoparticles and molecular magnets.[78] Importantly, due to partitioning of surfactant molecules at the water–oil interface only surface anisotropy is observed. These new systems allow for *in situ* tunability through composition and the solubilization of hydrophobic additives.

Finally, using magneto-responsive surfactants DNA chains and other biomolecules and their movement in solvent can be controlled simply by surfactant binding and the switching "on" and "off" of a magnetic field.[73] Such control is essential for biotechnological applications such as transfection and the regulation of gene suppression.[79–81] UV-vis spectroscopy was employed to reveal a small reduction in the intensity of the characteristic absorbance maximum at 260 nm on mixing very low concentrations of DTAG (50 μM) and DNA (150 μM) in the absence of a magnetic field, but importantly there was no evidence of aggregation over 96 hours (Fig. 14A). Significantly, applying a small magnetic field (0.44 T, gradient ~36 mT mm^{-2}) to stable aqueous solutions of DNA–surfactant complexes resulted in a notable reduction in the 260 nm peak intensity (Fig. 14B), which equated to a decrease in DNA concentration of 48% over four days. This was accompanied by a concomitant elevation of the baseline, which was indicative of aggregation due to the increased concentration of the complexes adjacent to the magnet surfaces.

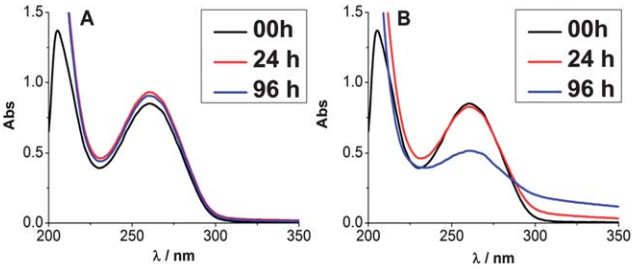

Fig. 14 UV-vis spectra of the stable DNA–DTAG complexes in (A) the absence of a magnetic field and (B) in the presence of an applied magnetic field. $t = 0$ (black solid line), $t = 24$ h (dashed line) and $t = 96$ h (dotted line). Reprinted with permission from *Adv. Mater.*, 2012, **24**, 6244–6247.[74]

Enzyme-responsive surfactants

Despite there being many systems that rely on enzymes to stimulate formation, destruction or morphological change in an assembly[82–86] until very recently these changes had always been irreversible. Gianneschi *et al.* prepared spherical micelles from polymer-peptide block copolymer amphiphiles containing substrates for protein kinase A (PKA), protein phosphatase-1 (PP1), and matrix metalloproteinases 2 and 9.[87] When subjected to phosphorylation by PKA for 24 h at 30 °C phosphate groups are introduced into the shell of the micellar aggregates and the hydrodynamic radius increases 50-fold. The reason for the radius increase is unclear but is postulated to be due to dipole-induced-dipole interparticle interactions. Importantly, subsequent dephosphorylation by PP1 resulted in the reversion of the micelle to its original size, which was repeated over three cycles.

Cleavable surfactants and dynamic combinatorial chemistry

The field of cleavable surfactants began in the late sixties when Distler patented a vinyl sulfonate that was surface-active under acidic conditions but not under basic.[88] Cleavable surfactants contain a weak bond that has deliberately been built in between the headgroup and the tail and breaks down in a controlled way. There are many possible linkages including different types of

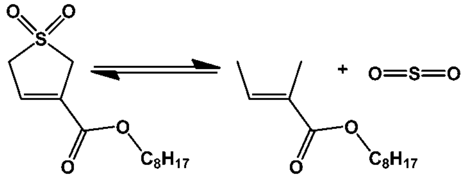

Fig. 15 Reversible decomposition of 2,5-dihydro-3-thiophenecarboxylic acid-1,1-dioxide octyl ester.

esters, amides, acetals, ketals and azo groups (amongst others) and cleavage may be triggered through responses to pH,[89] ozone,[90] light,[91] and heat decomposition.[92] For a comprehensive background, the 2007 review by Holmberg and Tehrani-Bagha[93] is highly recommended.

Surfactants based on furan–maleimide adducts have been prepared[92] by the Diels–Alder reaction and spontaneously decompose at moderate temperature (>60 °C) as a result of a retro Diels–Alder reaction taking place, with the degradation products exhibiting no surface activity. The authors noted that "*the measurements of surface tension were taken after the samples had cooled and are convincing evidence that the dissociation accompanying the retro DA is irreversible in micelles*." However, no further investigation has been carried out into the reversibility of this system.

In a similar manner, surfactant compounds such as 2,5-dihydro-3-thiophenecarboxylic acid-1,1-dioxide octyl ester may provide an alternative approach. It decomposes to form one molecule of butadiene derivative and one molecule of sulfur dioxide (Fig. 15). Sulfur dioxide is a stable gas and can be used to re-form the surfactant providing a two-way switch. Again, no details on the feasibility of using such systems exist and provide an interesting direction for the future study of responsive surfactants.

An alternative approach recently presented and already used to construct supramolecular architectures may provide a solution. The techniques is called dynamic combinatorial chemistry (DCC)[94–96] and allows for the self-assembly of micellar aggregates by reversible displacement of the equilibrium between nonamphiphilic building blocks and their amphiphilic counterparts.[97] Van Esch demonstrated that by combining an apolar primary-amine functionalized chain extender and a polar aldehyde-functionalized headgroup fragment, amphiphiles could be formed *in situ* through the formation of covalent imine bonds (Fig. 16). Equilibrium was then altered through responses to temperature and pH.

Fig. 16 Dynamic formation of imine amphiphiles. Reprinted with permission from *J. Am. Chem. Soc.*, 2009, **131**, 11274–11275. Copyright (2009) American Chemical Society.[97]

The authors claimed that the dynamic nature of the system and the use of nonamphiphilic materials could provide an easy method to producing a variety of complex aggregates after simple mixing using a library approach. Van Esch and co-workers have since demonstrated responsive vesicles[98] and gels using DCC.[99]

Conclusions

Spatial and temporal control over interfacial and bulk solution properties can be achieved using surfactants responsive to a variety of triggers, including pH,[7] light,[55] magnetic field,[75] CO_2,[27] redox[100] and enzymes.[87] This review explains how responsive surfactants can be used reversibly, cleanly, and importantly without changes in composition or thermodynamic conditions (potentially affording low energy impact). This exciting field has economic and environmental implications for reducing surfactant usage, waste and process remediation costs.

It is anticipated that responsive surfactants will impact on advanced applications. Fine control over wettability and interfacial tensions may find niches in nanotechnology or transport processes; making/breaking emulsions and control over vesicle stability may lead to novel controlled-release systems, for example in targeted drug delivery. Also highlighted are new directions in synthetic methodology,[101] developments in new and multi-responsive surfactants and simplified chemical routes for accessing more commercially viable systems.

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