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Large Organized Surface Domains Self-Assembled from Nonpolar Amphiphiles

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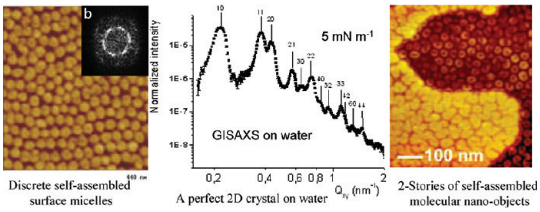
CONSPECTUS

For years, researchers had presumed that Langmuir monolayers of small $C_nF_{2n+1}C_mH_{2m+1}$ (*FnHm*) diblock molecules (such as *F*8*H*16) consisted of continuous, featureless films. Recently we have discovered that they instead form ordered arrays of unusually large (~30–60 nm), discrete self-assembled surface domains or hemimicelles both at the surface of water and on solid substrates.



Discrete self-assembled surface micelles

A perfect 2D crystal on water

2-Stories of self-assembled molecular nano-objects

These surface micelles differ in several essential ways from all previously reported or predicted molecular surface aggregates. They self-assemble spontaneously, even at zero surface pressure, depending solely on a critical surface concentration. They are very large (~100 times the length of the diblock) and involve thousands of molecules (orders of magnitude more than classical micelles). At the same time, the surface micelles are highly monodisperse and self-organize in close-packed hexagonal patterns (two-dimensional crystals). Their size is essentially independent from pressure, and they do not coalesce and are unexpectedly sturdy for soft matter (persisting even beyond surface film collapse). We and other researchers have observed large surface micelles for numerous diblocks, using Langmuir–Blodgett (LB) transfer, spin-coating and dip-coating techniques, or expulsion from mixed monolayers, and on diverse supports, establishing that hemimicelle formation and ordering are intrinsic properties of (perfluoroalkyl)alkanes. Notably, they involve "incomplete" surfactants with limited amphiphilic character, which further illustrates the outstanding capacity for perfluoroalkyl chains to promote self-assembly and interfacial film structuring.

Using X-ray reflectivity, we determined a perfluoroalkyl-chain-up orientation. Theoretical investigations assigned self-assembly and hemimicelle stability to electrostatic dipole–dipole interactions at the interface between *Fn*- and *Hm*-sublayers. Grazing-incidence small-angle X-ray scattering (GISAXS) data collected directly on the surface of water unambiguously demonstrated the presence of surface micelles in monolayers of diblocks prior to LB transfer for atomic force microscopy imaging. We characterized an almost perfect two-dimensional crystal, with 12 assignable diffraction peaks, which established that self-assembly and regular nanopatterning were not caused by transfer or induced by the solid support. These experiments also provide the first direct identification of surface micelles on water, and the first identification of such large-size domains using GISAXS.

Revisiting Langmuir film compression behavior after we realized that it actually was a compression of nanometric *objects* led to further unanticipated observations. These films could be compressed far beyond the documented film "collapse", eventually leading to the buildup of two superimposed, less-organized bilayers of diblocks on top of the initially formed monolayer of hemimicelles. Remarkably, the latter withstood the final, irreversible collapse of the composite films.

"Gemini" tetrablocks, di(*FnHm*), with two *Fn*-chains and two *Hm*-chains, provided two superposed layers of discrete micelles, apparently the first example of thin films made of stacked discrete self-assembled nanoobjects.

Decoration of solid surfaces with domains of predetermined size of these small "nonpolar" molecules is straightforward. Initial examples of applications include deposition of metal dots and catalytic oxidation of CO, and nanopatterning of SiO_2 films.

1. Introduction

The unanticipated finding that Langmuir monolayers of small fluorocarbon/hydrocarbon ($C_nF_{2n+1}C_mH_{2m+1}$, *FnHm*) diblock molecules consist of organized arrays of large discrete self-assembled nanometer-size surface domains (or hemimicelles, Figure 1),[1] rather than of the presumed continuous featureless film, occurred while investigating the stabilizing effects observed upon incorporation of such diblocks in phospholipid-based vesicles[2–4] and emulsions.[5,6]

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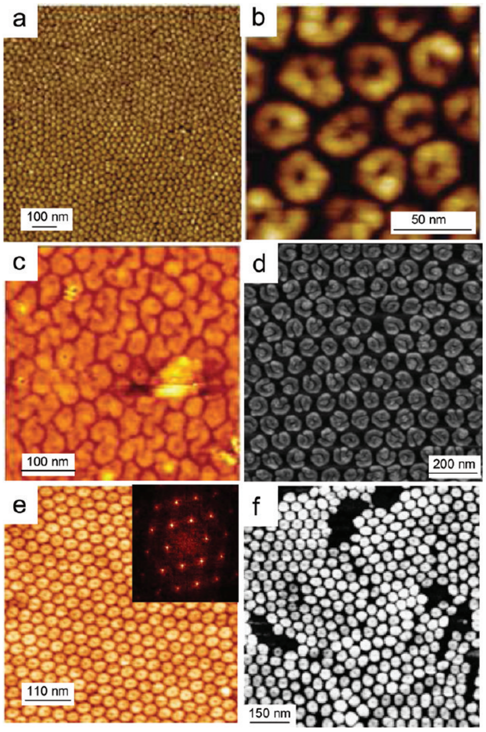


FIGURE 1. AFM images of films of (a) *F*8*H*16 transferred on a silicon wafer at 7 mN m^{-1} (topography);[1] (b) enlargement; (c) *F*8*H*20 transferred at 5 mN m^{-1};[24] (d) *F*14*H*20 spin-coated on mica;[36] (e) *F*8*H*18 spin-coated on a wetted silicon wafer; inset: Fourier transform;[51] (f) scanning-force microscopy of mica exposed to *F*12*H*19 dissolved in supercritical CO_2.[37] (Part (a) reprinted with permission from ref 1. Copyright 2002 Wiley and Sons. Part (f) reprinted with permission from ref 37. Copyright 2006 Royal Society of Chemistry).

A central objective of our team is to explore and exploit the capacity for perfluoroalkyl chains (C_nF_{2n+1}, *F*-chains) to promote self-assembly into molecular systems, as exemplified by the obtaining of stable vesicles from single-chain fluorinated amphiphiles[7,8] and tubules from nonchiral fluorinated components.[9,10] "Fluorous" interactions and halogen bonding provide control over monolayer preparation, liquid crystal properties, DNA immobilization and purification, and so forth.[11−14]

We had found that incorporation of small amounts of appropriate *FnHm* diblocks into phospholipid-based fluorocarbon emulsions increases stability dramatically.[15] Likewise, diblock/phospholipid combinations led to vesicles (liposomes) with improved stability, reduced membrane permeability and fusion kinetics,[3] and greater resistance to enzymatic hydrolysis.[16] Direct involvement of the diblocks in the emulsion's[6] or vesicle's[4] interfacial films was established.

Investigation of Langmuir films as models of the interfacial film of phospholipid/diblock-based emulsions was a logical approach to determining the mechanism of these effects. Separate examination of monolayers of the two film components was part of good laboratory practice.

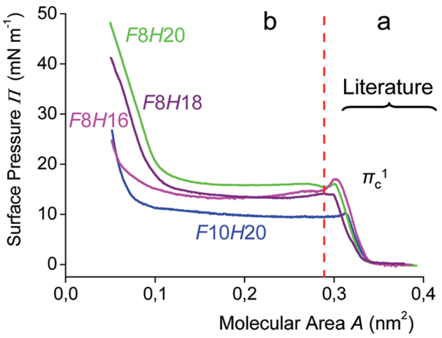


FIGURE 2. Typical Langmuir compression isotherms of *FnHm* diblocks. On the left of the dotted line, the recently uncovered coexistence plateau and second pressure rise.[44]

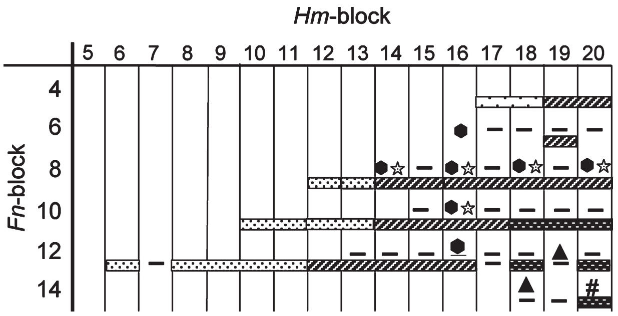
Atomic force microscopy (AFM) was a choice method for film imaging at the nanometer level. Stable Langmuir monolayers of *FnHm* diblocks had been reported and investigated.[17,18] However, formation of surface micelles had not been anticipated and came as a delightful surprise.

AFM examination of monolayers of *F*8*H*16 spread on water as Langmuir films and deposited on silicon wafers using the Langmuir−Blodgett (LB) technique revealed close-packed discrete circular domains (hemimicelles; Figure 1a,b), about 30 nm in diameter and 2.3 nm in height.[1] The hemimicelle population was remarkably monodisperse. Their diameter was essentially independent of transfer pressure (0.5−7 mN m^{-1}). They formed a close-packed hexagonal two-dimensional array even at low transfer pressures (e.g., 1 mN m^{-1}); at 0.5 mN m^{-1} ordering diminished sharply, gaps became wider, and defects more frequent.

The hemimicelles obtained from *F*8*H*16 differ from previously reported or predicted surface aggregates in several important respects: They are much larger (30 nm) and also much larger than the length of the extended diblock (∼3 nm); their aggregation number (∼3000) is higher by 1−2 orders of magnitude; their polydispersity is surprisingly low; their size is essentially independent from pressure; they do not coalesce and are unexpectedly sturdy; the π/A compression isotherms (Figure 2) lack the break and linear segment predicted in case of surface micelle formation. Notably also, they involve "incomplete" surfactants without polar head and limited amphiphilic character.

These findings raised numerous questions: Was formation of surface domains from *F*8*H*16 an isolated observation or an intrinsic property of *FnHm* diblocks? Is their formation really spontaneous? And independent from pressure? Why are they so large? And monodisperse? How do their sizes and morphology relate to block lengths? Is their diameter predictable/controllable? Is their existence reflected/foreseeable

SCHEME 1. Stability Grid for Langmuir Monolayers of *FnHm* Diblocks[a]



[a]Increasing stability is depicted by increasingly darkened patterns. ⬢,[24] #,[36] and ▲[37] indicate observation of surface micelles; ☆ on water;[42,43] —, not investigated.

in Langmuir film compression isotherms? Do self-assembly and ordering occur on water, or during LB transfer for AFM, or are they induced by the solid substrate? What is diblock orientation, *F*-chain-up or *F*-chain-down? Can self-assembly and ordering be explained theoretically? What force drives their formation? What happens when the surface films collapse upon compression? Are the hemimicelles stable enough to provide practical templates (with tunable periodicity?) for elaborating surface nanostructures?

2. Semifluorinated Alkanes: Simple Molecules and Yet...

FnHm diblocks are amphiphilic, one block being fluorophilic and lipophobic, the other lipophilic and fluorophobic, resulting in definite surfactant or cosurfactant activity. They are amphisteric, with cross sections of ~0.30 nm^2 for the *Fn* block versus ~0.20 nm^2 for the *Hm* block, and different block conformations (helical vs planar). They are also amphidynamic, one moiety being stiff, rod-like and prone to crystallization, the other flexible and prone to defects, and experience different types of motions and activation energies. Finally, they carry a strong dipole at the junction between blocks.[19]

Despite the absence of hydrophilic headgroup, *FnHm* diblocks form Langmuir monolayers on water.[17] Numerous pressure π versus molecular area A isotherms were recorded (Scheme 1).[1,18−26] The reported "collapse" pressure π_c (or what was then considered as the collapse pressure) ranged from ~12 to ~22 mN m^{-1}, increasing with diblock length and degree of fluorination. The extrapolated molecular areas remained always close to 0.30 nm^2, slightly larger than the cross-section of *F*-chains, suggesting that packing is essentially governed by segregated *Fn* blocks.

Since the π/A isotherms and GIXD data[18] collected on Langmuir films did not present any feature that foretold the existence of a patterned surface of hemimicelles, it was presumed that diblock monolayers were continuous and featureless.

Formation of small 2D surface micelles had been predicted for surfactant monolayers on water.[27] A specific "surface micelle isotherm" was calculated that exhibits characteristic breaks (clearly visible when the micellar aggregation number reaches ~10, and unmissable when it exceeds 100). The disk-shaped micelles' radii were foretold to be smaller than the length of the extended surfactant molecule. Examination of published isotherms concluded to the existence of surface nanostructures with aggregation numbers in the tens-to-hundreds. However, the surfactants considered had a hydrophilic headgroup, contrary to *FnHm* diblocks, where both moieties tend to avoid contact with water (and with each other), and where the *Fn* blocks provide a strong driving force for self-assembly.

Micelle-like aggregates, have been observed in surfactants layers adsorbed at solid/solution interfaces.[28] Surface patterns are common for copolymers with hydrophilic blocks.[29−31] Gemini surfactants with ammonium head-groups form small-size (4−8 nm) aggregates at solid/liquid interfaces, whose morphology is largely substrate-controlled.[32]

The only previous report of comparably large surface aggregates self-assembled from small molecules in monolayers concerns the highly amphiphilic semifluorinated carboxylic acids *FnHm*COOH ($n = 4-8$; $m = 10-22$), for which ~30 nm large domains were observed by AFM after transfer on glass.[33] However, their formation required high concentrations of cations (K$^+$, Cd^{2+}, La^{3+},[33] or Mg^{2+}[34]) in the subphase. The surface patterns' sharpness and organization increased with the ionic charge, implying a decisive role of these ions in aggregation.

3. An Inherent Behavior for (*F*-Alkyl)alkyl Diblocks

All the Langmuir films of *FnHm* diblocks investigated that were stable enough to withstand transfer on a silicon wafer and AFM imaging were found to exhibit surface micelles and patterned surface films (Scheme 1). Micelle morphologies and dimensions depend on diblock.[24,35] The short *F*6*H*16 and *F*8*H*14 essentially produce circular hemimicelles. Other diblocks also form elongated (worm-like) micelles coexisting with circular ones (e.g., Figure 1c). Morphologic variants, including toroids (doughnuts), pit and tip-centered hemimicelles, coils (nanospirals), ribbons, are also seen (Figure 1).[24,36,37] The mean diameter of the circular *FnHm* hemimicelles is essentially independent from pressure and support. It increases with *Hm*-block length, and notably, depends very little on *F*-chain length, in line with theoretical calculations (section 8).[38]

Our circular hemimicelles typically comprise 2000–6000 molecules. They are much larger than those formed from standard low-molecular-weight surfactants (a few nm) in solution or on solid substrates.[28,32] The spherical micelles of block copolymers formed in solution are always smaller than the molecule's length, while ours are typically 10 times larger.

The area fraction and length of elongated hemimicelles increase regularly (up to 12%) with the length of both blocks and with total diblock length. The AFM images suggest that the circular micelles result from fragmentation, curling and closing of elongated ones. The width of the latter is indeed close to half the diameter of the former. Furthermore, their occurrence and length diminish when surface pressure of transfer π_t increases. The circular/elongated hemimicelle interconversion is reversible.[24] When curling of the segments is incomplete (lower pressures) or not restricted to the interfacial plane (higher pressures), tip-centered or spiral-shaped micelles are formed. For *F*8*H*18, low π_t clearly induces formation of pits, while higher pressures favor curling and tip formation.

Compression causes circular domains to come closer together, causing some deformation from circular to hexagonal, but without merging, and results in more compact arrangement. No coalescence was ever seen, even at pressures near or "beyond" collapse (section 9).

The micelles also resist well, for soft self-assembled organic nano-objects, to the tip of the AFM cantilever, even at small scale/large resolution (Figure 1b) when the frequency of contact is high.

Patterned films of self-assembled domains of *FnHm* diblocks were also observed by other authors,[36,37] using various preparation conditions (e.g., LB, spin-coating, dip-coating in scCO_2 solutions;[37] Figure 1d–f) and supports (hydrophilic silicon, negatively charged mica, hydrophobic graphite, or phospholipid monolayers[39]), confirming that self-assembly is not controlled by transfer procedure or substrate. Only on highly oriented pyrolitic graphite, did the diblocks organize in stripes along the substrate's main crystallographic axis, indicating strong *H*-block/substrate interactions.[37] Exposure to different solvents can also cause morphological modifications.[36]

All the available data establish that spontaneous self-assembly in very large surface micelles, and surface film ordering in nanometric patterns is an intrinsic property of *FnHm* diblocks (Scheme 1).

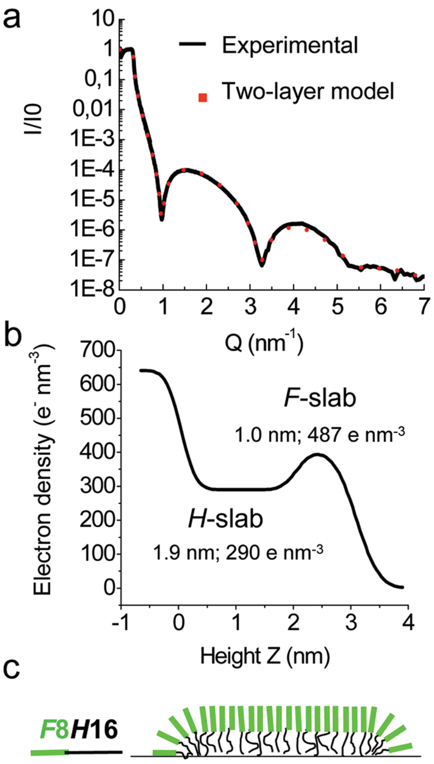


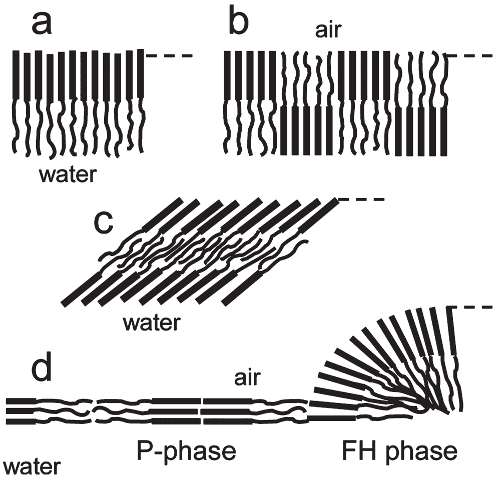
FIGURE 3. (a) X-ray reflectivity curve of a monolayer of *F*8*H*16 transferred onto silicon at 7 $mN\,m^{-1}$; the (almost completely overlaid) dotted curve is the fit with the two-layer model; (b) electron density (*D*) versus height (*Z*), showing a lower-*H*-slab and an upper-*F*-slab; (c) disklike model used in calculations.[1] (Reprinted with permission from ref 1. Copyright 2002 Wiley and Sons).

4. Surface Micelle Structure: *F*-Chains-Up, *H*-Chains-Down

The question of the structure of the surface film and orientation of the *FnHm* molecules in Langmuir monolayers had been controversial even at the time when the monolayers were considered continuous and featureless.

Early structural studies using GIXD of *F*12*H*18 monolayers deposited on water detected a strong diffraction peak that was in agreement with hexagonally close-packed *Fn*-blocks.[18] X-ray reflectivity measured a higher electronic density in the film's upper sublayer, and concluded that it most probably consisted of a dense sublayer of vertically oriented, close-packed *F*12-blocks organized on top of a sublayer of poorly organized *H*18-blocks in contact with water (Scheme 2a). A different structure was proposed for *F*8*H*18 that consisted of a bilayer of antiparallel diblocks, with interleaved *H*18-blocks inside, and *F*8-chains outside (Scheme 2c).[20] This would bring the "super"hydrophobic *Fn*-chains in contact with water, thus creating a considerably higher surface

SCHEME 2. Structures Proposed for *FnHm* Monolayers[a]



[a](a) *F*-chain-up/*H*-chain-down two-slab model in continuous films[18] or hemimicelles;[1,21] (b) alternating anti-parallel nanodomains;[22,40] (c) three-slab continuous bilayer hypothesis;[20] (d) two-phase model: upright hemimicelle FH-phase[1] embedded in a liquid-condensed P-phase of diblocks laying parallel to the surface.[38]

tension than when *Hm*-chains are on water, and would involve sublayers thinner than the actual resolution of the X-ray reflectivity method used (~1 nm). Still a further structure was suggested by molecular dynamics simulations[40] and at low pressures[22] that had mixed diblock orientations (Scheme 2b).[20]

The diblock orientation within the surface domains was established by X-ray specular reflectivity on LB films of *F*8*H*16 (~97% circular micelles).[1,35] The electron density distribution data were in excellent agreement with a two-layer model (Figure 3) with a 1.0 nm thick upper-layer having an electron density of 487 e nm^{-3} (a fluorinated layer) and a 1.93 nm thick lower-layer with an electron density of 290 e nm^{-3} (a hydrogenated layer). The total film thickness was 2.93 nm, comparable to the length of the *F*8*H*16 molecule (3.39 nm, as calculated from ref 41). This diblock orientation confirms the earlier X-ray studies on *F*12*H*18[18] and is in line with more recent data on *F*14*H*20.[36] It is also supported by our theoretical investigation of diblock self-assembly.[38]

5. Predicting Hemimicelle Size

The height of the surface micelles (2.93 nm) is slightly shorter than the fully extended length of a *F*8*H*16 molecule (3.32 nm), likely reflecting the liquidlike state of the *Hm*-chains.

The proportion of electrons found by the reflectivity experiment in the upper sublayer is only 46%, while it should be 61% for a continuous flat sublayer with all *Fn*-blocks parallel. Such packing would result in a lack of density in the *H*-sublayer. This lack of density can indeed be relieved by formation of discrete domains with edges bend toward the surface.

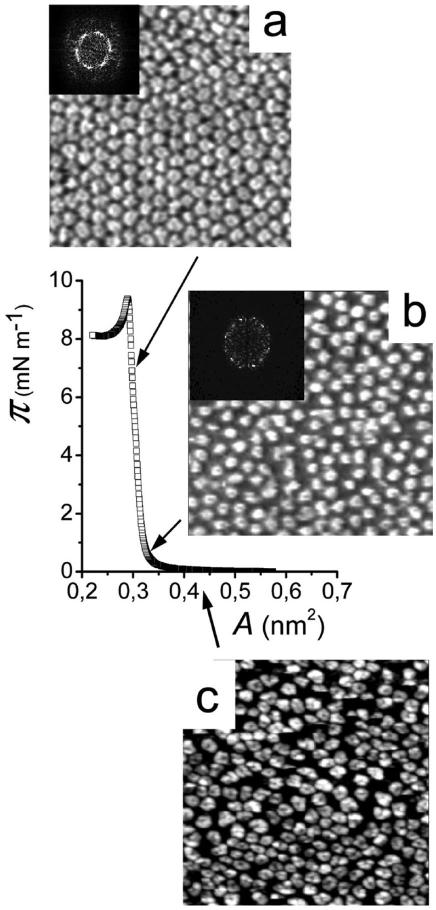


FIGURE 4. Compression isotherm and AFM images of hemimicelles self-assembled from *F*8*H*16 and transferred at (a) 7, (b) 0.5, and (c) ≈0 mN m^{-1} pressure.[25] (Reprinted with permission from ref 25. Copyright 2007 Royal Society of Chemistry).

We proposed a disk-like shape for the circular micelles on the basis of electron density calculations.[24] Indeed, the interfacial area between *F*- and *H*-sublayers should be equal to the product of the cross-section (0.28 nm^2) of the *FnHm* molecule by its aggregation number. The micelle's size is then solely controlled by the density mismatch between *F*- and *H*-blocks, and depends primarily on *m*. The model allows reasonably accurate prediction of the micelle's diameter for any given diblock.

Other models consider the mismatch between the blocks' cross sections.[36] However, all the models assume fully extended *H*-blocks, which is likely not the case. The density mismatch could indeed also be mitigated without resorting to micelle formation by tilting of *Hm*-chains or by conformation defects.[38]

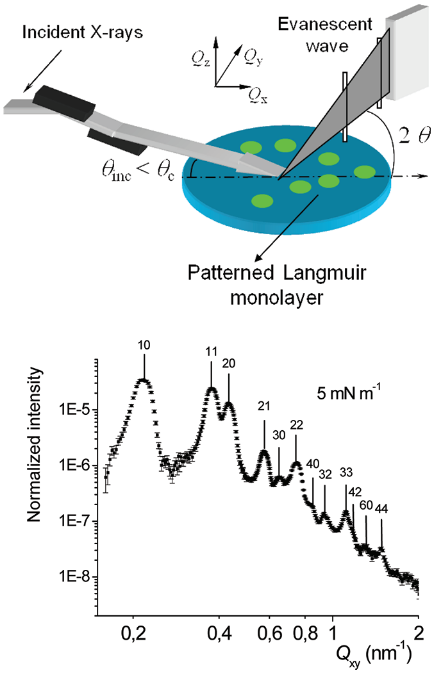


FIGURE 5. GISAXS spectrum recorded directly on water on a monolayer of *F8H*16. Note the exceptional number of reflections.[42]

6. Surface Micelle Formation at Zero Surface Pressure

Understanding hemimicelles formation within Langmuir monolayers required information about their possible occurrence, size and morphology at zero or very low surface pressures. Information about isolated micelles could not be obtained directly on water since they are too small for Brewster angle (BAM) and other optical microscopy techniques and not sufficiently organized for diffraction techniques. AFM after transfer on a solid surface was deemed a reasonable alternative.

No surface aggregates were seen for *F8Hm* ($m = 14-20$) at very large molecular areas (0.20 to 0.60 nm^2). In contrast, well-formed isolated disklike micelles were observed by AFM for *F8H*14 and *F8H*16 (Figure 4) for $A = 0.49$ and 0.41 nm^2, respectively. At such large *A* values, the surface pressure experienced by the molecules is essentially null. The micelles were not regularly organized. Again, compression did not affect their size. No surface aggregates were seen at $\pi_t = 0$ for the longer *Hm* diblocks *F8H*18 and *F8H*20, but micelles were found for all the diblocks investigated when transferred at $\pi_t = 0.5$ mN m^{-1}.

The absence of surface aggregates at very large *A* means that a critical surface concentration is required for diblock self-assembly. We thus established that micelle formation is not promoted by surface pressure, and did not result from nucleation induced by evaporation of the spreading solvent, but depends solely on the surface area available, and hence, on a critical surface concentration. These experimental results are in line with the theory for hemimicelle formation developed in section 8.

7. *FnHm* Hemimicelles Self-Assemble and Organize Directly on Water

When we first identified hemimicelles for *F8H*16, it was on Langmuir films transferred onto silicon wafers using the LB procedure.[1] This immediately raised the critical question of whether micelle formation occurred on water or was induced by transfer or involved the solid support. This question was resolved by a grazing-incidence small-angle X-ray scattering (GISAXS) study of *F8H*16 monolayers performed directly on the surface of water in the Langmuir trough using the European Synchrotron Facility (ESRF) in Grenoble.

GISAXS provided unambiguous direct evidence for a highly organized hexagonal network of circular domains on the surface of water.[42] The domains were seen as soon as GISAXS measurements started (~15 min after diblock deposition) and their size did not change throughout the observation period (up to 6 h). The domains were ~33 nm in diameter, in line with those observed by AFM after transfer.[1,24] Measurements at surface pressures ranging from 0.5 to 7 mN m^{-1} confirmed that hemimicelle size was essentially independent of pressure and that hexagonal ordering persisted at pressures as low as 0.5 mN m^{-1}.[42]

The diffraction spectrum at 5 mN m^{-1} (Figure 5) exhibits 12 assignable peaks (which is exceptional for soft matter) that could be fitted by Lorentzian curves. Peak indexation is consistent with a 2D-pattern of circular structures of 33.5 nm in diameter, close-packed in a regular hexagonal lattice. Long-range ordering was greater than that after LB transfer, providing a unique example of almost perfect two-dimensionnal crystal self-assembled from small molecules at the surface of a liquid.[42]

These data demonstrate unambiguously that hemimicelles of *F8H*16 exist in Langmuir monolayers spread on water prior to LB transfer and that diblock self-assembly and nanoscale surface patterning are not caused by transfer and not induced by the support. No micelles were detected by GISAXS on water at zero surface pressure, likely because they would not be sufficiently organized to diffract X-rays.

To our knowledge, this is the first time that surface micelles are identified directly on water; previous evidence for such micelles had always been obtained on solid substrates.[28] Further studies performed directly on water for the *F*8*Hm* series ($m = 14-20$), combining BAM, GISAXS and GIXD, confirm these findings.[43]

8. Theory: A Two-Phase Formation Process

A theoretical investigation using statistical physics confirmed that *FnHm* should form stable, large, and narrowly dispersed circular surface micelles that should organize in essentially crystalline hexagonal arrays at the water/air interface. It describes the micelle formation process and highlights the essential role of dipole–dipole interactions.[38] Interestingly, it also emphasized that the experimentally observed, thermodynamically more favorable upright micellar phase (or FH-phase) should coexist with an ordered interstitial phase (the P-phase) in which the diblocks lie parallel to the surface.

The proposed two-phase liquid–liquid model involves a high-density phase, consisting of disklike hemimicelles whose molecules are perpendicular to the interface, coexisting with a lower density matrix of diblock molecules lying on the surface of water within the film.[38] The stability and large size of the micelles, much larger than the molecule's length, called for long-range electrostatic interactions. These interactions were determined to involve the permanent dipole moments carried by the micelles at the interface between their *Fn*- and *Hm*-sublayers. This dipole moment is reflected by a measurable surface potential of ~0.9 V (*F*8*H*18).[22] Electrostatic repulsion between micelles prevents them from growing or fusing and is the cause for polydispersity lowering as surface pressure increases.

Reinterpretation of published X-ray reflectivity data that indicated a nearly uniform electron density at $A > 45$ nm^2 for *F*8*H*18,[22] suggested for the P-phase a structure in which the *Fn*- and *Hm*-blocks of the *FnHm* molecules parallel to the surface form alternating stripes, with each stripe being a bilayer of oppositely oriented similar blocks (Scheme 2d). A first-order transition between P- and FH-phases is supported experimentally by the change in surface electric potential measured for *F*8*H*18.[22]

The sequence along which hemimicelles of *FnHm* diblocks were anticipated to develop at zero pressure is the following: initially, the molecules would be more or less randomly disseminated on the surface. Spontaneous self-assembly would produce small islands of P-phase surrounded by a very dilute surface gas phase. As the islands grow, the energetically more favorable FH-phase would nucleate in these P-phase islands, turning them into upright FH-islands standing out of a continuous P-matrix. The FH-phase islands would grow further, likely through fusion (coalescence) until electrostatic repulsion would suppress fusion and limit growth. As *A* decreases further, the surface gas phase eventually disappears. The reason why the break that was predicted to occur in the π/A isotherms when surface micelles are present[27] is not seen may be that it occurs at such high surface areas that it cannot be detected.

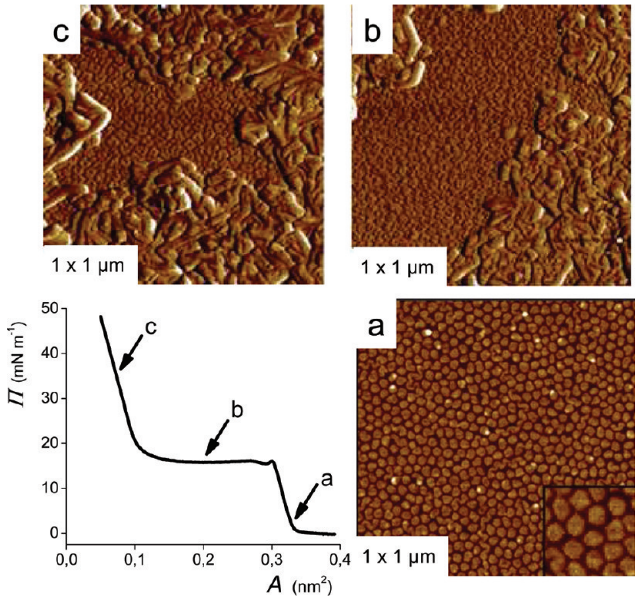


FIGURE 6. Diblocks beyond collapse.[44] Phase AFM images of *F*8*H*20 films transferred on silicon at (a) 3 mN m^{-1}; (b) 16 mN m^{-1} (0.20 nm^2); (c) 35 mN m^{-1}.

Compression increases surface pressure. A pressure threshold is reached for the interaction-driven suppression of micelle polydispersity (e.g., ≈0.5 mN m^{-1} for *F*8*H*16). Data from the AFM and GISAXS experiments[1,24,42] allowed calculation of the parameters that determine the compression isotherms. Transition from disordered (liquid) polydisperse micelles to an ordered (crystalline) hexagonal array of monodisperse micelles occurs for *F*8*H*16 at roughly 0.5 mN m^{-1} ($A \approx 0.33$ nm^2).

9. Surface Micelles Survive Film Collapse: Exploring the 2D/3D Transition

Langmuir film compression behavior was revisited after we realized that it actually concerns the compression of nanometric *objects*, and also because the observation that surface micelles withstand compression without coalescence raised the question of what happens to them when Langmuir films of *FnHm* diblocks collapse. This led to the unanticipated observations that compression could be pursued far beyond the documented film "collapse" and that the hemimicelles

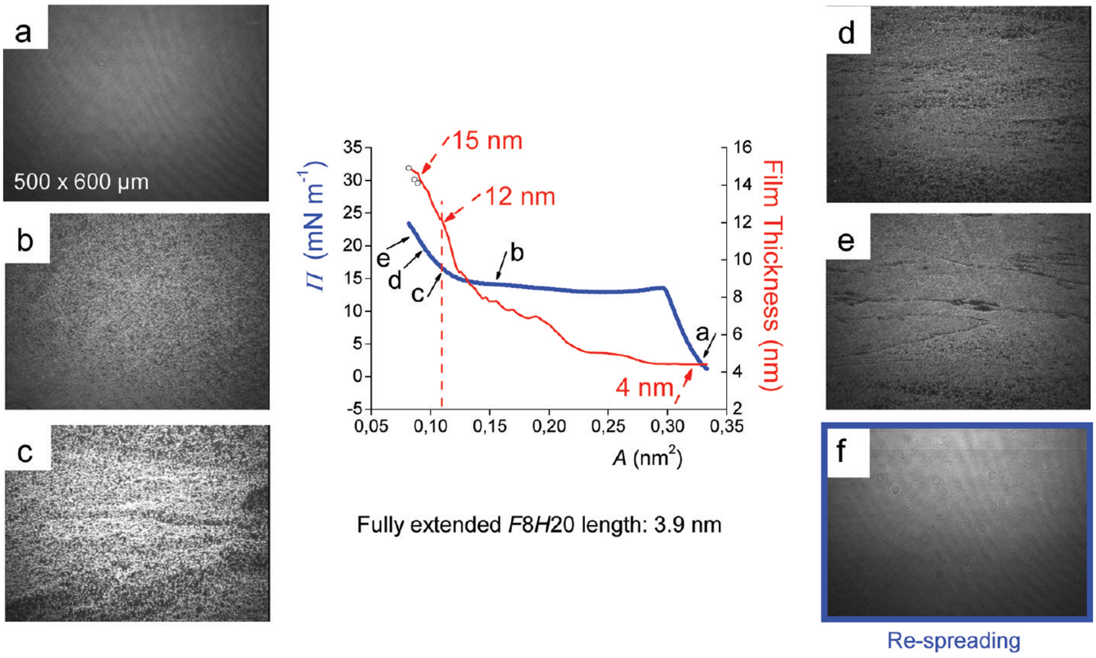


FIGURE 7. Diblocks before and beyond "collapse": BAM of films of *F*8*H*20 on water. (a) Homogenous, compact monolayer; (b, c) development of a higher phase in the 3rd dimension; (d, e) disruption of the upper phase; (f) re-expansion of the film. Blue, compression isotherm; red, film height variation.[44]

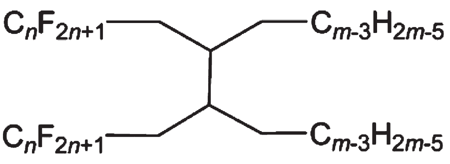
coexist (in part reversibly) with multilayered structures over a large pressure range.[44]

We recorded π/A isotherms of various diblock films at pressures near and *beyond* the published "collapse" pressures (from here on designated as π_c^1) and found an unexpected, wide horizontal plateau, followed by a second pressure rise (Figure 2b). Thus, Langmuir films of *F*8*H*16, *F*8*H*18, *F*8*H*20, and *F*10*H*16 could be compressed far beyond π_c^1 at $\sim$0.30 nm^2. For *A* between 0.30 and 0.10 nm^2, a partially reversible transition occurs between the monolayer of hemimicelles and a multilayer on the plateau. When $A < 0.10$ nm^2, π increases again, reaching $\sim$48 mN m^{-1} before the film eventually collapses irreversibly.

BAM and AFM monitoring of *F*8*H*20 films on the plateau established that the initial monolayer of hemimicelles is progressively covered by one and eventually two superimposed bilayers of diblocks (Figures 6 and 7).[44] Further compression leads to further increase in film thickness and, eventually, to film disruption.

The films formed beyond π_c^1 are composite, comprising a bottom layer of close-packed hemimicelles, toped, in the case of *F*8*H*20, by one, and eventually a second, less-organized bilayer(s) of diblocks. Compression of films of the more rigid *F*10*H*16 diblock, resulted in formation of crystalline-like dendritic influorescences. Remarkably, in both cases, the lower hexagonal array of surface micelles is consistently seen, even when the film eventually disrupts, meaning that the monolayer of hemimicelles resists both pressure rises, confirming outstanding sturdiness. It is also noteworthy that the final (irreversible) collapse of the composite films occurs at pressures comparable to those found for regular surfactants bearing polar head groups.

SCHEME 3. Molecular Structure of Gemini Fluorocarbon/Hydrocarbon Tetrablocks



n = 8, 10 ; *m* = 14-20

10. Tetrablocks: Stacked Layers of Self-Assembled Nano-Objects

A further question (motivated by potential applications) was whether one could further improve the stability of one-molecule-thin arrays of surface micelles. Grafting a polar head did not seem promising since even the small carboxylic headgroup of *FnHm*COOH, in spite of organization via positively charged ions in the subphase,[33] appears to provide less-ordered films than the neutral "head-less" *FnHm* diblocks. One logical approach was to covalently link two or

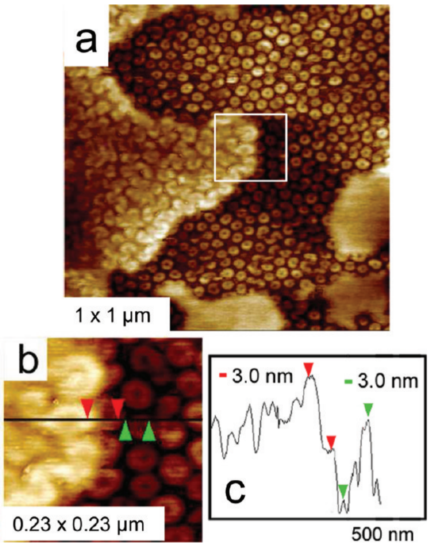


FIGURE 8. (a) AFM image of films of di(*F*8*H*20) spin-coated onto mica; (b) magnification (0.23 × 0.23 μm^2) of the framed area, highlighting the two stories of micelles; (c) height profiles taken between the red or green marks.[45]

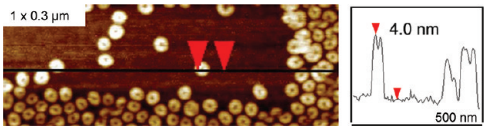


FIGURE 9. AFM image (1 × 0.3 μm^2) of tetrablock di(*F*8*H*20) spin-coated onto mica. Gentle scratching with the cantilever tip separated intact individual micelles; height profile between the red marks.

more diblocks and thus benefit from expected entropic effects. We therefore synthesized gemini fluorocarbon/hydrocarbon tetrablock amphiphiles (di(*FnHm*), Scheme 3).[45]

AFM and BAM investigations of films of di(*F*8*H*20) spin-coated on silicon or mica established that the tetrablock self-assembles into stratified nanopatterned surface films that display, at high pressures, two levels of structuration (Figure 8).[45] The π/A isotherms show, like for diblocks, two surface pressure increases separated by a large plateau. At large molecular areas ($A > \sim 0.60$ nm^2) and during the first pressure increase, the tetrablocks form a carpet of densely packed, essentially circular hemimicelles (~40 nm large, ~4 nm high), very similar to those of diblocks. Gentle scratching of the film with the tip of the cantilever successfully separated individual micelles of di(*F*8*H*20) (Figure 9), allowing determination of micelle height (~4.0 nm). This had not been possible with diblocks, indicating increased stability/resistance of the micelles of tetrablocks. Upon further compression, this lower carpet, contrary to diblocks, is progressively surmounted by a *second layer of discrete domains*, also ~4.0 nm in height, most of which circular, also ~40 nm in diameter, some of which worm-like, again

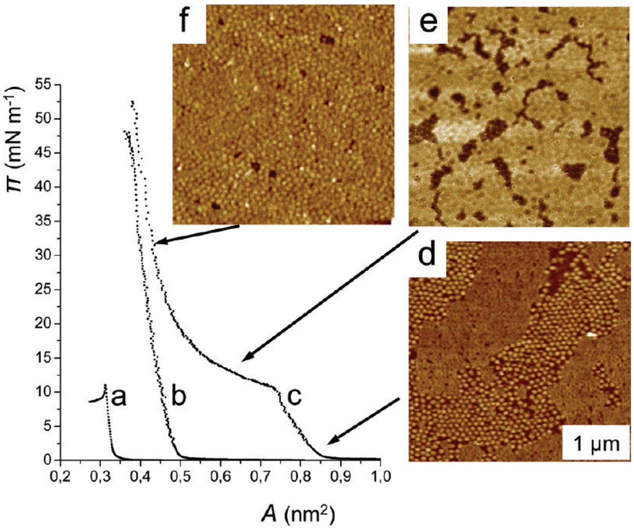


FIGURE 10. Lateral and vertical phase separation of *F*8*H*16 hemimicelles within and on top of a monolayer of DPPE. π/A isotherms for (a) *F*8*H*16, (b) DPPE, and (c) the *F*8*H*16/DPPE (1.3:1) molar ratio corresponding to the threshold at which *F*8*H*16 forms a continuous monolayer of hemimicelles on top of a continuous monolayer of DPPC. AFM: In (d) domains of circular *F*8*H*16 micelles coexist with laterally phase-separated DPPE domains; (e) shows higher regions of vertically phase-separated hemimicelles; in (f) the hemimicelles cover totally the DPPE monolayer; the film is indistinguishable from that of pure *F*8*H*16.[39]

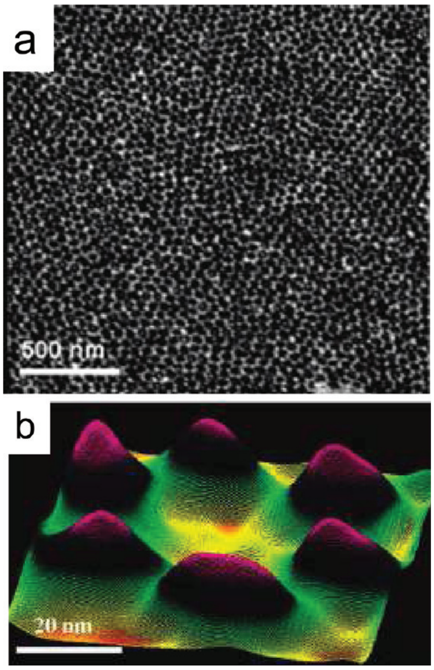


FIGURE 11. (a) AFM image (1.75 × 1.75 μm^2) of a hexagonal network of gold nanoparticles deposited on a Langmuir–Blodgett network of hemimicelles of *F*8*H*20; (b) detail.[48]

comparable to those found for *FnHm* diblocks (Figure 8). Eventually ($A < \sim 0.30$ nm^2), surface pressure increases again, reaching an irreversible collapse at $\pi_c{}^2 \geq 50$ mN m^{-1} (again remarkably high for amphiphiles devoid of polar head).

The self-assembly behavior of the di(*FnHm*) tetrablocks is thus substantially different from that of the *FnHm* diblocks and provides the first example of thin films made of stacked self-assembled molecular nano-objects.

11. Vertical Phase Separation in Mixed Films of Diblocks with Phospholipids

Mixing *FnHm* diblocks with other amphiphiles (e.g., phospholipids for fluorocarbon emulsion stabilization[6]) does not prevent surface micelle formation. In addition to lateral segregation of the diblocks from nonfluorinated components within monolayers, we observed a reversible *vertical* phase segregation phenomenon within Langmuir films.[21,46]

Investigation of monolayers of *F8H*16/dipalmitoylphosphatidylethanolamine (DPPE) mixtures after transfer on silicon wafers demonstrated coexistence of separate regions of densely packed circular *F8H*16 hemimicelles with regions of DPPE monolayer. Further compression led to vertical separation of the two components (Figure 10).[21] The *FnHm* micelles formed on the lipophilic substrate constituted by the DPPE-only monolayer are essentially identical to those obtained from *F8H*16 alone, further demonstrating that hemimicelle formation is independent of substrate.[39]

12. Perspectives and Applications

The possibility of decorating solid surfaces with regular arrays of stable highly hydrophobic nanometric surface domains of predetermined size using simple small "nonpolar" *FnHm* diblock molecules may provide a new approach to organic 2D templates of tunable periodicity for controlled elaboration of arrays of nanoparticles. The development of nanoelectronics and "smart" materials relies on suitably sized functional building blocks. Nanoparticles, which fill the ten-to-hundred nanometer gap between supramolecules, dendrimers and bio(macro)molecules, and patterns obtained by the most advanced lithographic procedures, offer a route to a variety of electronic and sensor components. Control of nanoparticle organization on surfaces is pivotal in the development of such architectures because it governs their collective properties.[47]

Examples of applications in materials science have already been reported. Thus, self-assembly of *FnHm* diblocks allowed patterning of square-centimeter-large surfaces with metal nanoparticles arranged in a high-density hexagonal network (Figure 11).[48] Catalyzed oxidation of CO into CO_2 could be achieved at low temperature. Hemimicelles of perfluorinated acids have served as templates for producing patterned thin films of SiO_2.[34]

Surfaces nanopatterned with highly hydrophobic, low adhesion material could influence cell behavior (e.g., allow cell adhesion control) and play a role in lung surfactant replacement preparations.[49,50]

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BIOGRAPHICAL INFORMATION

Marie Pierre Krafft was born in 1960 in Oran (Algeria). She obtained her Ph.D. and Habilitation from the University of Nice and did postdoctoral work in Japan and California. Presently a Research Director at the Institut Charles Sadron (CNRS) and University of Strasbourg, she focuses on the synthesis and uses of highly fluorinated components for the engineering of functional self-assembled systems. She investigates multicompartmented micro- and nanoscale objects, including surface films, vesicles, tubules, emulsions, and microbubbles, with applications in biomedical (lung surfactant, tissue oxygenation, cell adhesion control, diagnosis) and materials (control of nanoparticle organization on flat or spherical nanopatterned surfaces for multiscale devices) sciences.

FOOTNOTES

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REFERENCES

1 Maaloum, M.; Muller, P.; Krafft, M. P. Monodisperse surface micelles of nonpolar amphiphiles in Langmuir monolayers. *Angew. Chem., Int. Ed.* **2002**, *41*, 4331–4334.

2 Riess, J. G.; Krafft, M. P. Advanced fluorocarbon-based systems for oxygen and drug delivery, and diagnosis. *Artif. Cells, Blood Substitutes, Immobilization Biotechnol.* **1997**, *25*, 43–52.

3 Ferro, Y.; Krafft, M. P. Incorporation of semi-fluorinated alkanes in the bilayer of small unilamellar vesicles of phosphatidylserine. *Biochim. Biophys. Acta* **2002**, *1581*, 11–20.

4 Schmutz, M.; Michels, B.; Marie, P.; Krafft, M. P. Fluorinated vesicles made from combinations of phospholipids and semi-fluorinated alkanes. *Langmuir* **2003**, *19*, 4889–4894.

5 Krafft, M. P.; Riess, J. G. Highly fluorinated amphiphiles and colloidal systems, and their applications in the biomedical field. *Biochimie* **1998**, *80*, 489–514.

6 Marie Bertilla, S.; Thomas, J.-L.; Marie, P.; Krafft, M. P. Co-surfactant effect of a semifluorinated alkane at a fluorocarbon/water interface. *Langmuir* **2004**, *20*, 3920–3924.

7 Krafft, M. P.; Giulieri, F.; Riess, J. G. Can single-chain perfluoroalkylated amphiphiles alone form vesicles and other organized supramolecular systems? *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 741–743.

8 Krafft, M. P.; Giulieri, F.; Riess, J. G. Supramolecular assemblies from single-chain perfluoroalkylated phosphorylated amphiphiles. *Colloids Surf., A* **1994**, *84*, 113–119.

9 Giulieri, F.; Krafft, M. P.; Riess, J. G. Stable flexible fibers and rigid tubules made from single-chain perfluoroalkylated amphiphiles. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1514–1515.

10 Giulieri, F.; Krafft, M. P. Tubular microstructures made from non-chiral single-chain fluorinated amphiphiles. *J. Colloid Interface Sci.* **2003**, *258*, 335–344.

11 Bruce, D. W. Calamitics, cubics, and columnars-liquid-crystalline complexes of silver. *Acc. Chem. Res.* **2000**, *33*, 831–840.

12 Berger, R.; Resnati, G.; Metrangolo, P.; Weber, E.; Hulliger, J. Organic fluorine compounds: a great opportunity for enhanced materials properties. *Chem. Soc. Rev.* **2011**, *40*, 3496–3508.

13 Beller, C.; Bannwarth, W. Noncovalent attachment of nucleotides by fluorous-fluorous interactions: Application to a simple purification principle for synthetic DNA fragments. *Helv. Chem. Acta* **2005**, *88*, 171–179.

14 Motreff, A.; Raffy, G.; Guerzo, A. D.; Belin, C.; Dussauze, M.; Rodriguez, V.; Vincent, J.-M. Chemisorption of fluorous copper(II)-carboxylate complexes on SiO_2 surfaces: versatile binding layers applied to the preparation of porphyrin monolayers. *Chem. Commun.* **2010**, *46*, 2617–2619.

15 Riess, J. G.; Cornélus, C.; Follana, R.; Krafft, M. P.; Mahé, A.-M.; Postel, M.; Zarif, L. Novel fluorocarbon-based injectable oxygen-carrying formulations with long-term room-temperature storage stability. *Adv. Exp. Med. Biol.* **1994**, *345*, 227–234.

16 Riess, J. G. Fluorinated vesicles. *J. Drug Targeting* **1994**, *2*, 455–468.

17 Gaines, G. L. Surface activity of semifluorinated alkanes $F(CF_2)_m(CH_2)_nH$. *Langmuir* **1991**, *7*, 3054–3056.

18 Huang, Z.; Acero, A. A.; Lei, N.; Rice, S. A.; Zhang, Z.; Schlossman, M. L. Structural studies of semifluorinated hydrocarbon monolayers at the air/water interface. *J. Chem. Soc., Faraday Trans.* **1996**, *92*, 545–552.

19 Krafft, M. P.; Riess, J. G. Chemistry, physical chemistry and uses of molecular fluorocarbon-hydrocarbon diblocks, triblocks and related compounds-Unique apolar components for self-assembled colloid and interface engineering. *Chem. Rev.* **2009**, *109*, 1714–1792.

20 El Abed, A.; Pouzet, E.; Fauré, M.-C.; Sanière, M.; Abillon, O. Air-water interface-induced smectic bilayer. *Phys. Rev. E* **2000**, *62*, R5895–5898.

21 Krafft, M. P.; Giulieri, F.; Fontaine, P.; Goldmann, M. Reversible stepwise formation of mono- and bilayers of a fluorocarbon/hydrocarbon diblock on top of a phospholipid Langmuir monolayer. A case of vertical phase-separation. *Langmuir* **2001**, *17*, 6577–6584.

22 El Abed, A.; Fauré, M.-C.; Pouzet, E.; Abillon, O. Experimental evidence for an original two-dimensional phase structure. *Phys. Rev. E* **2002**, *65*, 051603-1–4.

23 Krafft, M. P.; Goldmann, M. Monolayers made from fluorinated amphiphiles. *Curr. Opin. Colloid Interface Sci.* **2003**, *8*, 243–250.

24 Zhang, G.-F.; Marie, P.; Maaloum, M.; Muller, P.; Benoit, N.; Krafft, M. P. Occurence, shape and dimensions of large surface hemimicelles made of semifluorinated alkanes. *J. Am. Chem. Soc.* **2005**, *127*, 10412–10419.

25 Gonzàlez-Pérez, A.; Contal, C.; Krafft, M. P. Experimental evidence for a surface concentration-dependent mechanism of formation of hemimicelles in Langmuir monolayers of semi-fluorinated alkanes. *Soft Matter* **2007**, *3*, 191–193.

26 Broniatowski, M.; Romeu, N. V.; Dynarowicz-Latka, P. Study of the collapse mechanism of selected fluorinated surfactants. *J. Colloid Interface Sci.* **2008**, *325*, 464–471.

27 Israelachvili, J. Self-assembly in two dimensions: Surface micelles and domain formation in monolayers. *Langmuir* **1994**, *10*, 3774–3781.

28 Warr, G. G. Surfactant adsorbed layer structure at solid/solution interfaces: impact and implications of AFM imaging studies. *Curr. Opin. Colloid Interface Sci.* **2000**, *5*, 88–94.

29 Cox, J. K.; Eisenberg, A.; Lennox, R. B. Patterned surfaces via self-assembly. *Curr. Opin. Colloid Interface Sci.* **1999**, *4*, 52–59.

30 Goren, M.; Lennox, R. B. Nanoscale polypyrrole patterns using block copolymer surface micelles as templates. *Nano Lett.* **2001**, *1*, 735–738.

31 Meli, M.-V.; Lennox, R. B. Preparation of nanoscale Au islands in patterned arrays. *Langmuir* **2003**, *19*, 9097–9100.

32 Manne, S.; Schäffer, T. E.; Huo, Q.; Hansma, P. K.; Morse, D. E.; Stucky, G. D.; Aksay, I. A. Gemini surfactants at solid-liquid interfaces: control of interfacial aggregate geometry. *Langmuir* **1997**, *13*, 6382–6387.

33 Kato, T.; Kameyama, M.; Ehara, M.; Limura, K. Monodisperse two-dimensional nanometer size clusters of partially fluorinated long-chain acids. *Langmuir* **1998**, *14*, 1786–1798.

34 Kataoka, S.; Takeuchi, Y.; Endo, A. Nanometer-sized domains in Langmuir-Blodgett films for patterning SiO_2. *Langmuir* **2010**, *26*, 6161–6163.

35 Zhang, G.; Maaloum, M.; Muller, P.; Benoit, N.; Krafft, M. P. Surface micelles of semifluorinated alkanes in Langmuir-Blodgett monolayers. *Phys. Chem. Chem. Phys.* **2004**, *6*, 1566–1569.

36 Mourran, A.; Tartsch, B.; Gallyamov, M. O.; Magonov, S.; Lambreva, D.; Ostrovskii, B. I.; Dolbnya, I. P.; de Jeu, W. H.; Moeller, M. Self-assembly of the perfluoroalkyl-alkane F14H20 in ultrathin films. *Langmuir* **2005**, *21*, 2308–2316.

37 Gallyamov, M. O.; Mourran, A.; Tartsch, B.; Vinokur, R. A.; Nikitin, L. N.; Khokhlov, A. R.; Schaumburg, K.; Möller, M. Self-assembly of (perfluoroalkyl)alkanes on a substrate surface from solutions in supercritical carbon dioxide. *Phys. Chem. Chem. Phys.* **2006**, *8*, 2642–2649.

38 Semenov, A. N.; Gonzàlez-Pérez, A.; Krafft, M. P.; Legrand, J.-F. Theory of surface micelles of semifluorinated alkanes. *Langmuir* **2006**, *22*, 8703–8717.

39 Maaloum, M.; Muller, P.; Krafft, M. P. Lateral and vertical nanophase separation in Langmuir-Blodgett films of phospholipids and semifluorinated alkanes. *Langmuir* **2004**, *20*, 2261–2264.

40 Kim, N.; Shin, S. Formation of ordered structure in Langmuir monolayers of semifluorinated hydrocarbons: Molecular dynamics simulations. *J. Chem. Phys.* **1999**, *110*, 10239–10242.

41 Tournilhac, F. G.; Bassoul, P.; Cortès, R. Structure of the smectic B phase formed by linear and branched perfluoroalkyl-alkanes. *Mol. Cryst. Liq. Cryst.* **2001**, *362*, 45–65.

42 Fontaine, P.; Goldmann, M.; Muller, P.; Fauré, M.-C.; Konovalov, O.; Krafft, M. P. Direct evidence for highly organized networks of circular surface micelles of surfactant at the air/water interface. *J. Am. Chem. Soc.* **2005**, *127*, 512–513.

43 Bardin, L.; Faure, M.-C.; Limagne, D.; Chevallard, C.; Konovalov, O.; Filipe, E. J. M.; Waton, G.; Krafft, M. P.; Goldmann, M.; Fontaine, P. Long range nanometer scale organization of semi-fluorinated alkanes at the air/water interface. *Langmuir* **2011**, *27*, 13497–13505.

44 de Gracia Lux, C.; Gallani, J.-L.; Waton, G.; Krafft, M. P. Compression of self-assembled nano-objects - 2D/3D transitions in films of (perfluoroalkyl)alkanes. *Chem. Eur. J.* **2010**, *16*, 7188–7198.

45 de Gracia Lux, C.; Krafft, M. P. Non-polar gemini amphiphiles self-assemble into stacked layers of nano-objects. *Chem. Eur. J.* **2010**, *16*, 11539–11542.

46 Wang, S.; Lunn, R.; Krafft, M. P.; Leblanc, R. M. One and a half layers? Mixed Langmuir monolayer of 10,12-pentacosadiynoic acid and a semifluorinated tetracosane. *Langmuir* **2000**, *16*, 2882–2886.

47 Pileni, M.-P. Inorganic nanocrystals self ordered in 2D superlattices: How versatile are the physical and chemical properties? *Phys. Chem. Chem. Phys.* **2010**, *12*, 11821–11835.

48 Charrault, E.; He, M.; Muller, P.; Maaloum, M.; Petit, C.; Petit, P. A facile route to homogeneous high density networks of metal nanoparticles. *Langmuir* **2009**, *25*, 11285–11288.

49 Gerber, F.; Vandamme, T. F.; Krafft, M. P. Impact of perfluorooctylethane on the formation of a semi-crystalline liquid condensed phase in a phospholipid monolayer and of perfluorooctyl bromide on the adsorption of albumin on such a monolayer. *C. R. Acad. Sci. (Chimie)* **2009**, *12*, 180–187.

50 Sanchez Dominguez, M.; Krafft, M. P.; Maillard, E.; Sigrist, S.; Belcourt, A. *ChemBioChem* **2006**, *7*, 160–1163.

51 Bardin, L.; Fauré, M.-C.; Filipe, E.; Fontaine, P.; Goldmann, M. Highly organized crystalline monolayer of a semi-fluorinated alkane on a solid substrate obtained by spin-coating. *Thin Solid Films* **2010**, *519*, 414–416.