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# High-Throughput Development of Amphiphile Self-Assembly Materials: Fast-Tracking Synthesis, Characterization, Formulation, Application, and Understanding

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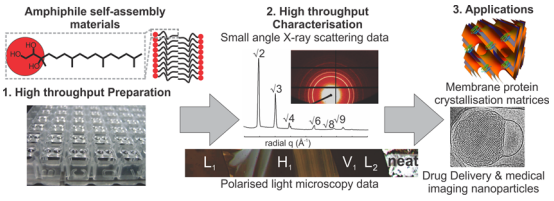
## CONSPECTUS




Amphiphile self-assembly materials, which contain both a hydrophilic and a hydrophobic domain, have great potential in high-throughput and combinatorial approaches to discovery and development. However, the materials chemistry community has not embraced these ideas to anywhere near the extent that the medicinal chemistry community has. While this situation is beginning to change, extracting the full potential of high-throughput approaches in the development of self-assembling materials will require further development in the synthesis, characterization, formulation, and application domains.

One of the key factors that make small molecule amphiphiles prospective building blocks for next generation multifunctional materials is their ability to self-assemble into complex nanostructures through low-energy transformations. Scientists can potentially tune, control, and functionalize these structures, but only after establishing their inherent properties. Because both robotic materials handling and customized rapid characterization equipment are increasingly available, high-throughput solutions are now attainable. These address traditional development bottlenecks associated with self-assembling amphiphile materials, such as their structural characterization and the assessment of end-use functional performance.

A high-throughput methodology can help streamline materials development workflows, in accord with existing high-throughput discovery pipelines such as those used by the pharmaceutical industry in drug discovery. Chemists have identified several areas that are amenable to a high-throughput approach for amphiphile self-assembly materials development. These allow an exploration of not only a large potential chemical, compositional, and structural space, but also material properties, formulation, and application variables. These areas of development include materials synthesis and preparation, formulation, characterization, and screening performance for the desired end application. High-throughput data analysis is crucial at all stages to keep pace with data collection.

In this Account, we describe high-throughput advances in the field of amphiphile self-assembly, focusing on nanostructured lyotropic liquid crystalline materials, which form when amphiphiles are added to a polar solvent. We outline recent progress in the automated preparation of amphiphile molecules and their nanostructured self-assembly systems both in the bulk phase and in dispersed colloidal particulate systems. Once prepared, we can structurally characterize these systems by establishing phase behavior in a high-throughput manner with both laboratory (infrared and light polarization microscopy) and synchrotron facilities (small-angle X-ray scattering).

Additionally, we provide three case studies to demonstrate how chemists can use high-throughput approaches to evaluate the functional performance of amphiphile self-assembly materials. The high-throughput methodology for the set-up and characterization of large matrix in meso membrane protein crystallization trials can illustrate an application of bulk phase self-assembling amphiphiles. For dispersed colloidal systems, two nanomedicine examples highlight advances in high-throughput preparation, characterization, and evaluation: drug delivery and magnetic resonance imaging agents.

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## 1. Introduction

Harnessing the potential of amphiphile self-assembly materials requires control over their chemical, structural, and functional material properties. To establish the optimal parameters for end applications, we must fully characterize these materials on a hierarchy of length scales. Both the production and the characterization of these materials, however, can represent significant bottlenecks en route to their end-use.

Amphiphiles self-assemble in the presence of a polar solvent due to the solvophobic effect, that is, to minimize contact between the solvophobic amphiphile chains and the solvent while maintaining solvation of the solvophilic headgroups.[1,2] The solvent is typically water, although other complex fluids such as ionic liquids and amides are increasingly being explored to increase the potential applications of such materials.[1,3−7] A range of self-assembly morphologies, with various degrees of dimensionality, may be created depending on the molecular geometry,[8] of which the most common nanostructure is the lipid bilayer, ubiquitous in nature as the cell membrane of eukaryotic cells. These self-assembly nanostructures, illustrated in Figure 1, include the 1D bilayer phase (the fluid lamellar phase, $L_\alpha$), the 2D hexagonal phase (H), the 3D bicontinuous cubic phases (Q or V), and the 3D discontinuous micellar cubic and hexagonal phases (I).[9] Typically these phases can exist as type I or type II, which refers to whether the curvature is away from or toward solvent, respectively. Type II phases, such as $H_{II}$, $Q_{II}$, and $I_{II}$ phases (Figure 1), have significant potential applications because they are stable in excess solvent; hence we focus on these.[10−13] The inverse hexagonal ($H_{II}$) phase consists of hexagonally packed solvent tubes surrounded by a monolayer of amphiphiles.[9] The 3D inverse bicontinuous cubic structures ($Q_{II}$), with either double diamond ($Q_{II}^D$), primitive ($Q_{II}^P$), or gyroid ($Q_{II}^G$) geometry, consist of a continuous bilayer, mapped over an infinite periodic minimal surface, separating two nonconnected solvent channels. The inverse discontinuous phases are inverse micelles with solvent cores packed onto a cubic or hexagonal lattice.[14,15]

The dimensions of the amphiphilic and solvent domains vary within each material and are affected by environmental variables such as temperature and pressure or the addition of an additive, for example, a drug. Each material must therefore be tested under multiple conditions, and individual ternary and even higher order phase diagrams must be constructed to fully understand the material properties. Using high-throughput techniques, the optimization of each material for a particular application is possible.

Many self-assembled phases, and in particular the bicontinuous cubic phases, are highly viscous and difficult to handle. Applications of self-assembled materials, particularly *in vivo* applications including drug delivery and biomedical imaging, require the dispersion of the system.[13,16,17] The bulk phase may be simply dispersed to form stable colloidal particles by use of a steric stabilizer. Dispersed lamellar, hexagonal, and cubic phases are known as liposomes, hexosomes, and cubosomes, respectively.

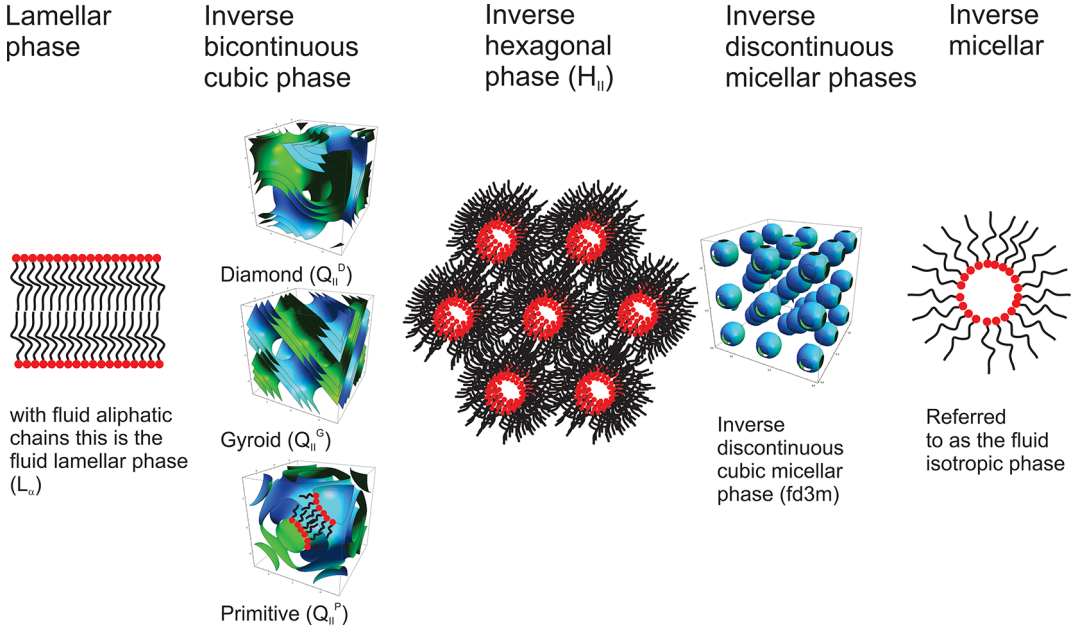


**FIGURE 1.** Range of morphologies adopted by amphiphile self-assembly materials. Phases are ordered from left to right with increasing negative interfacial curvature. Based on a figure from Seddon et al.[9]

Within this Account, we will outline advances in high-throughput methodologies developed to optimize formulation technology.

The ultimate goal in the preparation of novel self-assembly materials is to offer significant improvements relative to current technologies. A prominent example is the burgeoning use of both bulk and dispersed cubic phases in drug delivery technology.[13,18,19] Their amphiphilic nature and partially controllable nanostructure allows for the incorporation of a range of drugs of various polarities and molecular weight.[10] In addition, inverse bicontinuous cubic phase dispersions can possess superior physical and chemical stability, may enhance cellular uptake, and can be made biodegradable. We therefore conclude this Account with an overview of high-throughput strategies, including data analysis, to expedite the performance assessment of these novel materials for specific applications.

## 2. High-Throughput Synthetic Approaches

While the characterization and application aspect of self-assembly materials has taken significant steps toward adopting a high-throughput approach within routine laboratory practice, combinatorial synthesis of such materials has been slow to progress. Indeed, while pharmaceutical and fine chemicals research has embraced combinatorial/high-throughput methodologies for accelerated materials synthesis, synthesis of amphiphile libraries remains in its infancy. This, at least partially, reflects challenges in linking the solvophilic and solvophobic moieties due to limited solubility and often difficult preparation and purification routes.

Akinc et al. have reported the synthesis of a combinatorial library of 1200 lipid-like materials (Figure 2) for the delivery of RNAi therapeutics.[20] The library was synthesized by the combination of nine alkyl-acrylates and eight alkyl-acrylamides with a wide variety of primary amines, the lipids were also quaternized to introduce additional chemical diversity. Within the study, numerous examples were shown to have efficacy *in vitro* and *in vivo* with important structure–performance relationships identified; such as the importance of incorporating amide linkages, chain lengths of 8–12 carbons, and more than 2 alkyl chains. It has recently been shown that these "lipidoid" materials can be incorporated into screening assays to develop an understanding of their siRNA transfection efficacy with the best hits taken to *in vivo* experiments.[21]

Click-chemistry approaches to link hydrophilic headgroups with hydrophobic tails have been tried to create

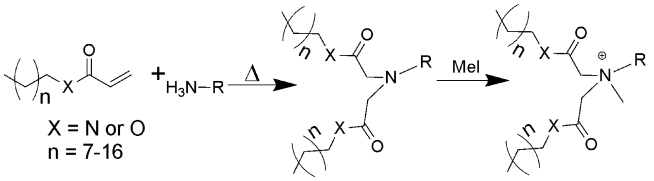


**FIGURE 2.** Synthetic pathway to structural diversity in a library of 1200 amphiphiles. Adapted from Akinc et al.[20]

self-assembling material libraries that can probe a large chemical space.[22]

Dynamic combinatorial chemistry libraries, typically described as combinatorial libraries under thermodynamic control, can be created with self-assembling materials.[23] Libraries that incorporate self-assembling building blocks of amphiphilic materials have been developed by Nguyen and co-workers.[24] Once synthesized, these materials need to be formulated or processed so that their morphology and efficacy can be assessed.

Amphiphile self-assembly materials have also been used as templates in the high-throughput synthesis of inorganic hexagonally ordered gadolinosilicate nanoparticles. This automated synthetic protocol is translatable to the production of other sol–gel derived functional nanomaterials.[25]

## 3. Formulation Techniques

**3.1. Bulk Phase Formation.** Amphiphile mesophases are typically produced manually, a time-consuming process for large numbers of samples required to produce phase diagrams. Imberg and Engstrom[26] have reported high-throughput methods that use automated liquid handling for the preparation of ternary monoolein/solvent/water samples. In addition, a new protocol, also using liquid handling robotics, has recently been developed for high-throughput formation of bulk mesophases.[27,28] Amphiphiles, dissolved in a carrier solvent, can be dispensed in nanoliter volumes in a high-throughput manner. Following original solvent evaporation, mesophase formation occurs spontaneously via automated addition of an appropriate volume of water or another solvent of interest. The process has been shown to accurately and reliably dispense lipid amphiphile including monoolein,[29] monoeicosenoin, and phytanyl monoethanolamide.[30]

**3.2. Dispersion Preparation.** Mesophases, which are stable in excess solvent, can be dispersed in the presence of a steric stabilizer into colloidal dispersions. The ideal colloidal particles have the same internal structure as the parent lyotropic liquid crystalline phase, but have a much larger surface area and exist as low viscosity solutions. These nanoparticulate self-assembled systems are able to

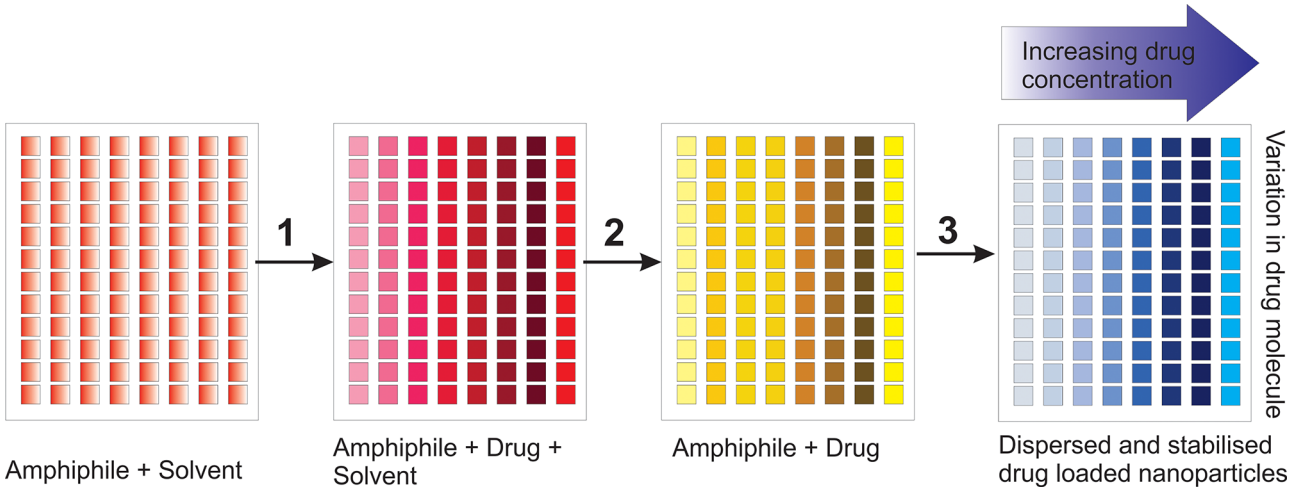


**FIGURE 3.** Schematic depiction of the amphiphile self-assembly material nanoparticle preparation with the Chemspeed SLTII platform. Adapted from Mulet et al.[6]

encapsulate lipophilic compounds, useful for controlled drug delivery,[6] and are also being investigated for the delivery of bioactive compounds in foods.[31] Traditionally, these nanoparticles are made one at a time by mixing the amphiphile and payload, then adding an aqueous stabilizer solution and dispersing through ultrasonication or homogenization. Recently, we have reported the use of a robotic platform for the automated formulation of these nanoparticles.[6] The process, outlined in Figure 3, coupled with high-throughput characterization techniques has proven to be an effective method for screening the incorporation of hydrophobic drug molecules within the dispersed nanoparticles.

## 4. Characterization

**4.1. Methods for High-Throughput Amphiphile–Solvent Phase Mapping.** A range of methodologies is available to determine phase behavior under a variety of external parameters, which can include water content, temperature, and less commonly pressure. Thermal analysis of bulk phases (differential scanning calorimetry (DSC) and thermogravimetric analysis (TGA)) provides information on phase transition temperatures and enthalpies. Cross-polarized light microscopy is often used to scope phase behavior through solvent penetration scans. Small-angle X-ray scattering provides additional information on the underlying nanostructure.

The typical route to identifying and characterizing the phase behavior of a novel amphiphile system or amphiphile formulation comprises multiple steps.

(i) Identification: For a novel binary amphiphile–solvent system, solvent penetration experiments can be used as an initial evaluation of the phase behavior.

(ii) Mapping: Should the system provide interesting and relevant phase behavior, then a more rigorous study of the full phase diagram can be undertaken.

(iii) Characterization: Structural parameters of individual mesophases (e.g., underlying crystallographic cell lattice parameters).

The steps outlined above are usually not performed in a high-throughput fashion; however a handful of examples have emerged in the literature for the fast-tracking of amphiphile phase diagram construction. Laughlin et al.[32] proposed an isothermal swelling method in which water in contact with surfactant in a capillary formed a long-lived concentration gradient. Determination of the compositions along this one-dimensional gradient was achieved using Fourier transform near-infrared microspectrosocpy (FT-NIR). Caffrey has combined a similar lyotropic gradient method with time-resolved small-angle X-ray scattering (SAXS) to construct a phase diagram for monoolein, which however was defined with respect to the absolute position along the capillary rather than in terms of water–amphiphile composition.[33] Moghaddam et al. have used an analogous approach to assess the phase behavior of chelating amphiphiles.[34] This method is generally acceptable for a binary water–surfactant system but is less practical for a ternary or multiple-component system where the order of addition to a formulation may also impact the behavior. In this instance, it is more useful to use high-throughput deposition methods such as those developed by Imberg and Engstrom and Darmanin et al. described in section 3.1.[26,27] Cull and co-workers have used a similar strategy for rapid screening of the clearing and melting points of liquid crystals.[35]

**4.2. High-Throughput Phase Identification Using Light Polarizing Microscopy.** Light-polarizing microscopy (LPM) provides a rapid and convenient measure of the lyotropic phase behavior from subambient temperatures to the solvent boiling point. As solvent penetrates the amphiphile, a concentration gradient is established, and above the Krafft temperature, the neat amphiphile may swell to form lyotropic liquid crystalline phases. These may be identified via their characteristic optical texture using LPM. To differentiate the various isotropic phases (e.g., $Q_{II}$ (viscous) and $L_2$ (fluid)) rapid qualitative rheological observations may be used. Optical textures of surfactant lyotropic phases have been described in detail in the literature, and some are illustrated in Figure 4.[36,37]

**4.2.1. Diffusive Interfacial Transport−Near-Infrared Spectroscopy for Determination of High-Throughput Phase Diagrams.** Traditional methods used to construct phase diagrams not only require large quantities but are also susceptible to long equilibration times required at each temperature. The diffusive interfacial transport−near infrared (DIT-NIR) method described by Laughlin and coworkers[32,36−38] permits a high-throughput methodology for determining temperature−composition phase diagrams, particularly for binary systems.

DIT-NIR is an isothermal method based on the in situ determination of the composition of mesophases formed by swelling of the amphiphile in water. The thin DIT cell and small sample volume (50−100 mg) greatly reduce sample equilibration times and produce long-lived concentration gradients in the horizontal direction. In-situ quantification of water composition at the phase boundaries is achieved by comparison with a calibration curve (Figure 4). The main limitation of the DIT-NIR method is for amphiphiles that undergo anomalous swelling to create myelin textures at the water interface. This technique has been used to determine the binary aqueous phase diagrams of some poly(ethylene oxide) surfactants.[32,37−40]

**4.3. HT SAXS for Structural Determination of Mesophase Structure.** While the DIT-NIR methodology provides extensive phase behavior information, the nature of the isotropic phases cannot be unequivocally determined nor can the size of the unit cell of any of the lyotropic liquid crystalline phases observed. Small-angle X-ray scattering provides information on the structure of the mesophase and the unit cell dimensions. Samples for SAXS analysis are typically contained within quartz capillaries or loaded into a sandwich plate holder sandwiched between X-ray transparent windows of mylar. A custom-designed capillary holder,

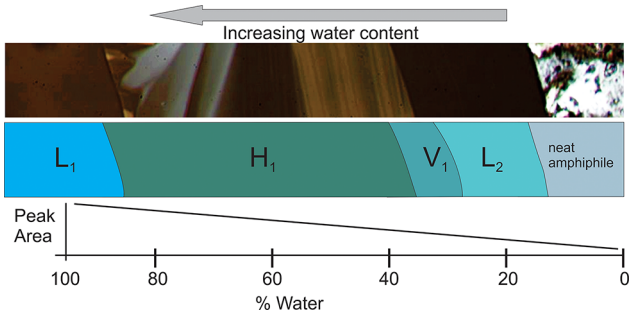


**FIGURE 4.** Validation of the DIT-NIR microspectroscopy method using $C_{12}EO_8$. A penetration scan (non-cross-polarized ×100) showing the progression of phases at 20 °C is shown (top). The boundaries of bands are indicated with assigned phases (middle). Bottom is a representative curve performed at 20 °C using octyldimethylphosphine oxide (peak area is derived from combination band at 5200 $cm^{-1}$).

designed and built at the SAXS beamline of the Australian Synchrotron, allows for medium-throughput analysis of samples contained within 50 capillaries (Figure 5).

Samples contained within 96-well plates may be similarly analyzed in a HT manner. The plate is loaded into a custom-designed plate holder, built at the SAXS beamline of the Australian Synchrotron, and mounted directly onto the beamline (Figure 5).[27] The minimum sample mass that can be characterized is 20 $\mu$g. This is a reduction of 3 orders of magnitude compared with traditional capillary or plate cells (typically 20 mg). Image acquisition is fully automated by using a preloaded set of position variables to raster scan across the experiment plates. A total of 192 data points (96 wells run in duplicate) can be automatically collected in 20 min (temperature control 10−70 °C). Diffuse scatter from the polymer of the plate may be background subtracted. The IDL-based AXcess program, discussed in a review by Seddon et al., allows for medium/high-throughput data analysis of 2D diffraction patterns.[41]

## 5. Applications

The approaches described herein are required to prepare, assess, and optimize the material structural properties for the self-assembling amphiphiles and thus create materials suitable for their end use. Here we present three case studies in which materials libraries are prepared followed by an evaluation of their performance using high-throughput materials characterization.

**5.1. Drug Incorporation or Encapsulation.** High-throughput drug discovery pipelines use automated systems and robotics to screen the activity of thousands of compounds. These employ multiple iterations in order to achieve the best possible balance of a range of parameters, including

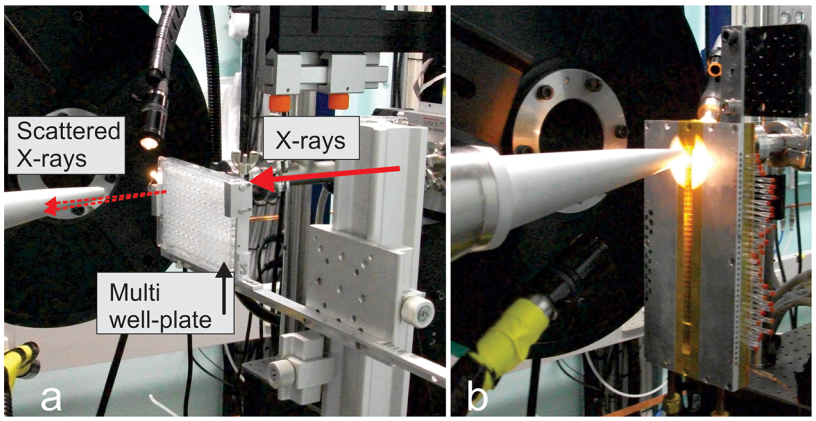


**FIGURE 5.** Sample environments provided by the Australian synchrotron SAXS/WAXS beamline: (a) mount for standard footprint microtiter plates; (b) temperature-controlled multicapillary holder. Temperature control is provided in the range −10 to 90 °C.

efficacy, toxicity, and solubility. The predominant screening protocol is, however, incompatible with compounds of low water solubility. This situation is proving increasingly problematic as many new drug candidates are water insoluble.[42]

To address this problem, Mulet and co-workers developed a high-throughput methodology for the preparation and characterization of drug delivery vehicles; specifically dispersed lyotropic liquid crystalline mesophases.[6] This methodology permits the inclusion of low-solubility drugs in high-throughput drug discovery screens. Along with the efficient loading of the drug, retention of the nanoparticle structure must be verified, because drug incorporation within the nanoparticle matrix can affect both the internal nanostructure and the integrity of the particles.

High-throughput synchrotron SAXS techniques were used to assess the dispersions' structure. In combination, microplate-based spectroscopic assays to assess drug loadings in the particles were employed.[6]

Data obtained on how structure−property relationships influence the phase behavior, particle size, and drug loading levels will expedite understanding of the required characteristics to tailor these colloidal dispersions for individual bioactives. For example, it is possible to closely relate the extent of the effect on phase behavior of the drug delivery vehicle to the octanol/water partition coefficient of each drug molecule. This makes these colloidal dispersions suitable for use in high-throughput screening drug discovery programs. By this approach, significant progress has also been made in discovering and understanding the necessary properties (such as nature of lipophilic group and length of poly(ethylene oxide) chain) to make ideal steric stabilizers for lyotropic liquid crystalline dispersions.[43,44]

**5.2. Contrast Enhancement Agents for Magnetic Resonance Imaging (MRI).** MRI has become a leading diagnostic modality to provide high-resolution 3D information on internal body organs and a variety of diseased tissues. The intrinsically low sensitivity of MRI has been significantly improved with the use of contrast enhancement agents (CEAs). CEAs for MRI are indirectly detected by lowering the longitudinal and transverse relaxation time of the nearby water protons. To date the most commonly used CEAs for clinical MRI are paramagnetic gadolinium or manganese ions, complexed with small chelating molecules that reduce the toxicity inherent with the free ions. Incorporation of Gd-chelates to high molecular weight proteins,[45] dendrimers,[46] or self-assembly materials[47,48] has remarkably improved their activity, specificity, and promise as molecular imaging probes for MRI.

In particular, stable dispersed CEA particulates based on lipid-based self-assembly systems, which benefit from flexibility in design and ease in synthesis of the small amphiphilic unit, have emerged as versatile imaging materials.[34,49,50] Chelation of paramagnetic metal ions within the membranes of ordered nanostructured particulates allows us to potentially combine a high payload with slower tumbling properties, which will increase the generation of contrast. High-throughput techniques can be employed for the formulation and structural characterization of imaging nanoassemblies; however, assessment of the performance of imaging CEAs systems has been rarely investigated. Inhomogeneity of the magnetic field, variation in shimming, and sample throughput have been the main impediments. Liu et al. have recently reported a high-throughput MRI method for simultaneous screenings of multiple chemical exchange saturation transfer (CEST) contrast agents using capillary tubes.[51] They screened a library of 16 samples

and were able to obtain high-quality CEST spectra with an average acquisition time of 2.6 min.

Muir and co-workers evaluated the performance of nitroxide lipid CEA loaded in lyotropic liquid crystalline dispersions by combining high-throughput formulation for dispersions, HT synchrotron SAXS phase characterization, and a novel approach to allow the multiwell plate evaluation of relaxivities for libraries of dispersed particulates at varying concentration and composition of contrast agents in 4.3 T MRI equipment.[52] Using HT approaches provided the means to test a wide compositional space and showed that incorporation of the nitroxide lipid into the dispersions allowed for a greater enhancement of relaxivity when an inverse bicontinuous cubic phase was present compared with the inverse hexagonal phase that appeared at higher nitroxide loadings.

These three approaches of preparation, structural characterization, and efficacy assessment all performed by exploiting high-throughput protocols and techniques has already been applied to the mesoporous gadolinosilicate materials described in section 2, yielding a different class of inorganic MRI contrast agents. This approach yielded not only excellent reproducibility but also a material with $T_1$ relaxation enhancement performance comparable to clinically used moieties.[25]

**5.3. Protein Crystallization.** In meso crystallization uses bicontinuous cubic lipidic phases as matrices for the crystallization of membrane proteins.[53] The fundamental bilayer structure of these mesophases mimics the protein's natural environment within the cell membrane, and the continuous nature of the bilayer and the water networks allow for lateral diffusion of the protein across the plane of the bilayer thus facilitating crystallization. Recent successes using this crystallization method include the dopamine D3 receptor and the adrenergic G-protein coupled receptor.[54]

The highly viscous nature of the cubic phase makes in meso crystallization incompatible with the robotic crystallization systems used for conventional hanging- and sitting-drop experiments. Traditionally, in meso crystallization experiments were set up manually using coupled syringes, a time-consuming and onerous manual handling process.[55] Recently there has been increased focus on automating in meso crystallization to reduce the volume of protein required per sample and increase reproducibility levels between trials. Commercial high-throughput robotics developed specifically for in meso crystallization trials include the Flexus Crystal IMP, Gryphon LCP (Art Robbins/Rigaku), NT8-LCP (Formulatrix), Mosquito LCP (TTP Labtech), and ProCrys Meso (Zinsser-Analytic). However, the requirement to premix the lipid, aqueous phase, and protein solution in a coupling device limits the applicability of such robots for high-throughput techniques. An alternative high-throughput setup, adapted to standard crystallization robotics widely available in crystallization laboratories worldwide, has recently been developed, bypassing the need for a specialized cubic phase surfactant dispensing system.[27] Lipids are deposited using the protocol described in section 2. An appropriate volume of protein solution is added to the dried lipid film to produce a cubic phase with membrane protein incorporated. The crystallization screen, which accelerates crystal growth, is then deposited on top of the cubic phase bolus. The system is fully universal, can be used for all combinations of lipids, proteins, buffers, and precipitants, and has been shown to result in successful crystal growth.[27]

Using this approach, the effect of addition of crystallization screens to lipids was assessed, and due to the large data sets available, the trends observed could be interpreted.[56] Components of the screen had significant impact on the structure of the cubic phase, particularly high molecular weight poly(ethylene oxide) effected a transition from $Q_{II}^{D}$ to $Q_{II}^{G}$. The effect of salts was correlated with their position in the Hofmeister series. Changes in pH and buffer system had a more minor effect on mesophase structure.[56]

## 6. Predictive Tools in the Development of Next Generation Self-Assembly Materials

With the advent of high-throughput techniques and the congruent generation of large data sets, models to predict the molecular self-assembly properties based on experimentally validated data will become necessary. Quantitative structure−property relationship models to assess the physical properties of amphiphiles have been developed. Huibers and co-workers developed models for the prediction of the critical micelle concentration of nonionic and anionic surfactants.[57] A recent review by Hu et al. outlines other modeling techniques that can be used to predict the physical properties such as the hydrophile−lipophile balance of surfactants.[58] Techniques analogous to the self-consistent field theory models used by Drolet and Fredrickson to screen for block copolymer self-assembly could be developed for the prediction of small-molecule amphiphile aggregate nanostructure.[59]

As materials libraries are developed, the analysis of results will have to be expedited through the application of analysis tools such as principal component analysis or live data processing. Modeling systems also need to be developed to predict the outcome of different formulation contents on the self-assembled structure of amphiphilic materials.

## 7. Summary and Conclusions

Large-scale exploration of compositional, structural, and functional features in amphiphile self-assembly materials libraries is growing and blossoming with the recent fertilization from high-throughput techniques enabling rapid preparation, formulation, characterization, and end-use performance evaluation. Future focus will include advanced approaches to design of experiments for materials library creation that is required to take into account complex compositional and material processing parameters. Data processing, manipulation, and visualization (materials informatics) such as multivariate analysis will require optimization as databases are created to allow the materials chemist to exploit the large quantities of information produced.

The application of high-throughput techniques in the development of novel amphiphile self-assembly materials is extremely prospective and will contribute to the development of many novel multifunctional materials.

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BIOGRAPHICAL INFORMATION

**Xavier Mulet** was born in Villeneuve D'Ascq, France, in 1979. After completion of his undergraduate degree at Imperial College London (M.Sci. 2002), he gained a Masters in Research in Biomolecular Sciences (M.Res. 2003). He completed his Ph.D. at the Chemical Biology Centre at Imperial College London in 2007. He is currently performing postdoctoral studies in materials science, exploring the application of self-assembled materials for drug delivery applications.

**Charlotte E. Conn** was born in N. Ireland in 1979. After undergraduate study (Natural Sciences) at the University of Cambridge (B.A., M.Sci., 2002), she earned her Ph.D. in 2007 from Imperial College London for biophysical chemistry research. She joined CSIRO, Australia, in 2006 as a postdoctoral research fellow and is currently a Research Scientist with CSIRO. Her research interests focus on the design and structural characterization of new lipidic materials, and the application of these materials in membrane protein crystallization.

**Celesta Fong** was born in Darwin, Australia, in 1969. She obtained her B.Sc. (Hons) at The University of Sydney (1994) and her Ph.D. at The University of Queensland (1998) in Physical Chemistry. She joined CSIRO as a postdoctoral fellow and is currently a Research Scientist at CSIRO. Her interests include high-throughput characterization of materials properties and amphiphile self-assembly and its applications.

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**Minoo J. Mogaddham** received her B.Sc. in Chemical engineering from Sharif University of Technology in Tehran, Iran. She earned her M.Sc. in chemical engineering from Kyushu University and her Ph.D. in 1989 from Osaka University. She joined CSIRO in 1993 and is currently a Principal Research Scientist with specific research interests in nanostructured lipid-based self-assemblies and their applications for targeted drug and gene delivery and contrast agents for various imaging modalities.

**Calum J. Drummond** was born in Whitehaven, U.K., in 1960. He received a Ph.D. in physical chemistry from The University of Melbourne in 1987. He is currently the CSIRO Group Executive for Manufacturing, Materials and Minerals. Prior to this appointment, he was the recipient of an Australian Research Council Federation Fellowship and Chief of CSIRO Materials Science and Engineering. He has also been Vice President Research at CAP-XX, an Australian company that manufactures electrical double layer capacitors for consumer electronic products. His research interests are in the area of colloid and surface science including applications of amphiphile self-assembly materials.

FOOTNOTES

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The authors declare no competing financial interest.

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