Synthesis of inorganic materials with complex form

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Recent developments in inorganic materials chemistry suggest that concepts such as morphogenesis, replication, self-organization and metamorphosis could be useful for devising new synthetic strategies. Inorganic materials with complex form can be chemically synthesized by pattern replication of self-organized organic assemblies, such as micelles, vesicles and foams.

THE patterning of synthetic inorganic materials, exemplified by the complex, ordered pore networks of zeolites and other crystalline microporous materials, has traditionally been restricted to the nanometre scale (less than 1.5 nm). In these solids, the patterning of the pore architecture is achieved through the spatially controlled assembly of inorganic building blocks, facilitated by cationic or neutral organic molecules. In general, the templating function of the organic additive is to fill space, direct structure and balance charge[1]. Recently, the imposition of patterns (pore networks) at a scale larger than the molecular has been achieved by using surfactant aggregates as templates that undergo cooperative self-assembly with inorganic species to form mesoporous materials with channel diameters of 1.5–10 nm (refs 2, 3). Structural patterning in inorganic materials synthesis at this scale still falls a long way short of the organic template-directed processes that result in the complexity of form and structure in biological minerals such as bone, shells and teeth.

Many biominerals are organized from the nanoscale to the macroscopic scale (a loose definition used here is: nanoscopic, <1.5 nm; mesoscopic, 1.5–100 nm; microscopic, 0.1–100 μm; and macroscopic >100 μm) to give hierarchical materials that are sculpted with complex form—spirals, spheroids and skeletons, for example—with apparent disregard for the rigid geometric symmetry of their inorganic constituents. Mackay[4] has recently described the 'flexicrystallography', structure and symmetry properties of about 50 periodic minimal-energy surfaces, and how they allow one to transcend the boundary of traditional crystallography and the 230 classical space groups, to encompass periodic curved surfaces found in soft structures such as liquid-crystal mesophases and biological assemblies. This concept may provide a unifying connection between pattern formation in biomineralization and the sculpting of inorganic materials with complex form by synthetic organic templates.

The motivation for chemically constructing materials with meso- and microscopic form centres around the importance of shape and texture in determining properties such as flow and transport behaviour, catalytic activity, separation efficiency, adhesion, and storage and release kinetics in 'smart' colloids. Synthesizing inorganic materials with complex patterns could therefore be relevant to the design of new types of catalyst supports, membranes for the separation of large polymers, colloids and cells, biomedical implants with macroporosity, drug carriers, and vectors for delivery and release of viruses and DNA in transfection procedures. Acoustic behaviour, and heat- and mass-transport properties could be influenced by surface patterning or the fabrication of hollow and cellular structures.

To realize the perceived benefits of complex form in synthetic inorganic materials, it will be necessary to control the chemistry responsible for the 'synthesis with construction' of inorganic and organic components on a series of length scales[5]. In this regard, biomineralization has much to offer in providing ideas and inspirations that can be developed in the synthesis of biomimetic materials[6–11]. Here we focus on synthetic approaches related to biomineralization, illustrating how preorganized or self-organizing vesicles can expand the scale of inorganic materials patterning. An important aspect of biomineralization is that self-assembled organic templates are transformed by materials replication into organized inorganic structures. We show how this strategy can act as a guideline for synthesizing inorganic materials with complex form. The use of nonlinear diffusion-based processes[12]—typical of snowflakes and electrochemical deposits—or processing methods involving microlithography or physical moulding[13,14] is excluded from our discussion because our objective is to identify potential chemical strategies for the 'one-pot' synthesis of patterned inorganic materials. Our aim is not to provide a comprehensive review of a new field of materials chemistry, but to stimulate further development by offering an agenda for the future.

Pattern formation in biomineralization

Although the complex form of biological minerals was of great interest to the nineteenth-century morphologists[15], and later to D'Arcy Thompson[16], the genetic basis for the diversity and evolution of biomineral patterns remains unknown. From a materials

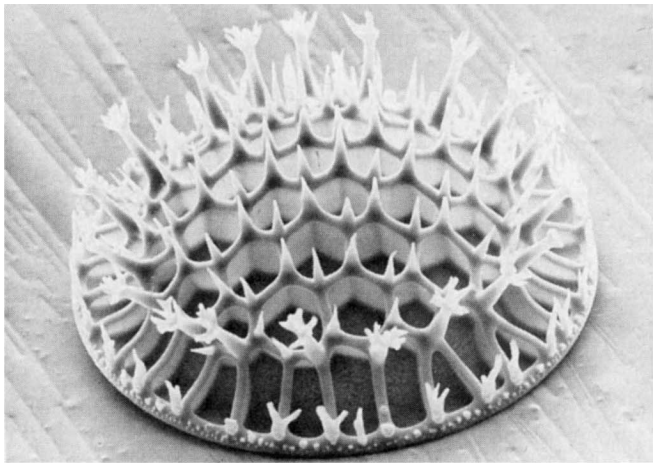


FIG. 1 Single valve of an unidentified diatom found in a deep-sea core of an Eocene marine deposit[49]. (Picture courtesy of *Phil. Trans.*)

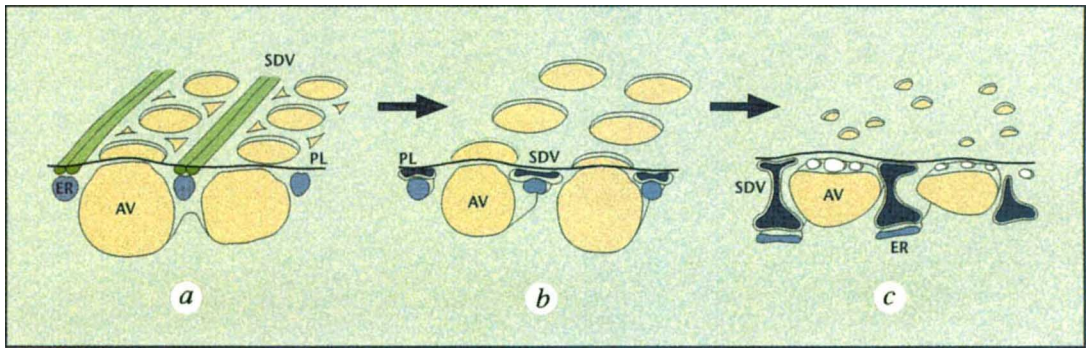


FIG. 2 Illustration of the important stages in the formation of the siliceous diatom exoskeleton. *a*, Silica deposition vesicles (SDV) are preorganized with microtubules around the boundary spaces of large areolar vesicles (AV) attached to the plasmalemma (PL). *b*, The SDVs are mineralized with amorphous silica (dark blue) to give a patterned porous wall. *c*, The mineralized wall is thickened by extension of each SDV in association with the endoplasmic reticulum (ER). Detachment and retraction of the areolar vesicles from the plasmalemma results in infiltration with new SDVs and further mineralization of the pore spaces. Adapted from ref. 18.

perspective, the delicate filigree microskeletons of diatoms and radiolarians, or the spirals and cones of foraminiferal shells (Fig. 1), conflict with a commonplace view of inorganic minerals as rigid, inert, immutable materials of limited form and fabric. The complexity of these biomineral forms cannot be accounted for simply on the basis of inorganic processes of crystallization. Instead, they are patterned by assemblages of vesicles and other bilayer structures that are arranged and rearranged by cellular processes.

For example, the perforated silica shells of diatoms and many radiolarians are derived from close-packed arrays of large (areolar) vesicles that are secreted and attached to the membrane wall (plasmalemma) of the cell before mineralization (Fig. 2)[17,18]. The areolar vesicles are not mineralized but their arrangement into a thin polygonal foam provides a patterned template extending to the meso- and microscale. In the diatom *Coscinodiscus*, a thin tubular membrane system is secreted from the Golgi apparatus and assembled along with microtubules in the gaps between the areolar vesicles[18]. Silica deposition is then confined tangentially within these tubular vesicles such that an open geometric mesh of mesopores is replicated (Fig. 2). Although this architecture often represents the final microskeletal form in radiolarians, diatoms often continue to process the areolar spaces with a delicate nanoporous pattern of silica. This is achieved by detachment and withdrawal of the areolar vesicles from the plasmalemma, and infiltration of the new interface with cytoplasm containing silica deposition vesicles and small unmineralized Golgi vesicles (Fig. 2). Together these vesicles self-assemble to produce a species-specific pattern of nanopores across the surface of the diatom shell.

An important determinant of the complexity of pattern and form expressed by biominerals is scale[16]. Different length scales bring into operation different biological processes. For relatively small-scale structures, such as the curved silica rods of choanoflagellates, vesicles can be shaped before mineralization by attachment to the cytoplasmic membrane using two stress filaments[19]. In contrast, large architectures (coccoliths[20], for example) are usually constructed by patterning of the vesicles during biomineralization. Changes in shape arise as the mineral develops, and it is possible that the evolving pattern of morphogenesis results from a synergism between crystallographic and biological forces[4]. For multicellular organisms, the positioning and movement of cohorts of cells can generate patterns on a micro- and macroscopic length scale[16]. For example, the triradiate symmetry of spicules formed in calcareous sponges is initiated from a cluster of three sclerocytes[21]. Continuous assemblages in the form of foams and rafts of closely packed cells facilitate the assembly of the labyrinthine skeleton of the crystalline shell (test) of echinoderms[22]. The spatial positioning of epithelial cells in shell mantle[23], osteoblasts and osteoclasts in bone matrix[24], and ameloblasts in enamel[25], is time-dependent, such that new patterns can evolve as mineralization proceeds.

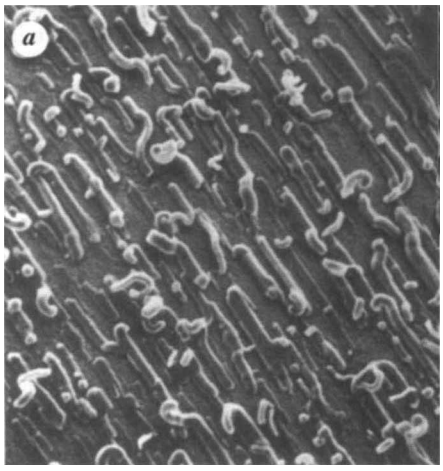
Inorganic morphosynthesis

Can an understanding of pattern formation in biomineralization be integrated within a synthetic approach to inorganic materials with complex form? Certainly the use of vesicles to expand the scale of materials patterning seems a plausible biomimetic strategy. Some important connections stand out. First, the biomineralized forms are generated by materials replication of patterned organic aggregates or supramolecular assemblies. Second, if the vesicles remain fixed in shape throughout mineralization, then the inorganic pattern is 'transcribed' from the self-assembled organic architecture. Alternatively, both mineral and associated vesicles develop synergistically, and new morphological patterns are added by coassembly of the inorganic and organic components. Third, continuous structures can be patterned around close-packed vesicle foams if the mineralization environment is restricted to the interstitial spaces and boundary edges.

The aim is to integrate these features into biomimetic strategies by using appropriate organic patterning agents to orchestrate the

TABLE 1 Pattern replication in inorganic morphosynthesis

Process	Pathway	Examples
Transcriptive synthesis	Self-assembly → Transcription → Replication	Tubular/lamellar/mesoporous silica, thin films, CdS arrays
Synergistic synthesis	Coadaptation → Coassembly → Replication	Mesoporous silica, metal oxides
Metamorphic reconstruction	Coasembly → Replication → Reconstruction	Microskeletal calcium phosphate, silica
Microphase separation	Coassembly → Evolution → Replication	Mesolamellar aluminophosphate, cellular calcium carbonate
Systems synthesis	Molecular assembly → Supramolecular assembly → Microphase assembly → System assembly	



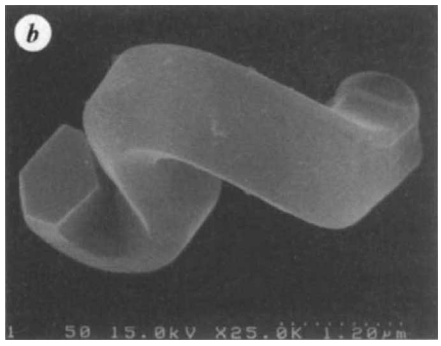


FIG. 3 *a*, As-synthesized mesoporous thin film grown on mica showing the initial nucleation of separate small oriented crystal ribbons with a preferred alignment[41]. (Field of view; width 49 μm, depth 51 μm.) *b*, Particle of mesoporous silica formed by bulk synthesis showing complex morphology[43]. Dotted scale bar, 1.20 μm.

positioning, interconnection and stabilization of inorganic building blocks at the nano-, meso-, micro- and macroscopic level. We make the empirical assumption that the dimensionality of the patterning agent is commensurate with the length scale on which order and form are to be established. We highlight four mechanisms of inorganic morphosynthesis (Table 1). (1) Transcriptive synthesis involves stable, preorganized, self-assembled organic architectures serving as chemical and structural templates for patterned materials deposition. (2) Synergistic synthesis involves essentially one-step coassembly and pattern replication of inorganic precursors and associated organic molecules and aggregates, such as surfactants, micelles and microemulsions. (3) Metamorphic reconstruction involves coassembly and replication followed by *in situ* changes in the organization of the reaction field, so that new materials patterns develop. (4) In microphase separation, inorganic materials with microscopic and macroscopic patterning are formed as replicas of self-organized metastable structures, such as foams and vesicles.

Transcriptive synthesis. Implicit in this strategy is that the pattern and form of an inorganic material correspond closely with that of a preformed, self-assembled organic architecture. The template is preorganized and relatively stable, with chemical and morphological information 'written' into the surface structure (Table 1). Interfacial nucleation and crystal growth result in direct materials replication of the preformed organic shape. Several studies have investigated the use of compressed Langmuir monolayers[26,27] and functionalized self-assembling monolayers[28,29] as preorganized templates for the oriented nucleation of two-dimensional arrays of inorganic crystals and thin films. In many cases, the electrostatic, stereochemical and geometric properties of the surfactant headgroups are transcribed within the first layer of the inorganic nucleus by molecular recognition at the interface between monolayer and solution. This approach has been extended to more complex forms by using preformed, self-assembled bilayer templates that remain intact during and after inorganic mineralization. Such structures contain functionalized headgroups to facilitate site-directed nucleation as well as patterned architectures for materials replication. For example, certain biolipids have been used as preorganized fibrous templates for the production of hollow silica tubes[30], cylinders coated with iron oxide[31], and helical strings of gold crystals[32]. Recently, lamellar silicas have been synthesized within the interlayer regions of multilamellar vesicle spheres[33]. A similar approach has been used to produce coaxial cylinders of mesostructured aluminophosphates organized within the interlayers of multilamellar rod-shaped surfactant micelles[34].

Although the forms of these materials are reproducible, they are relatively simple, being based on spatially discrete organic architectures such as individual monolayer sheets, vesicle spheres, lipid tubes and surfactant rods. More complex inorganic patterns require templates preorganized within extended phases, such as polymerized bicontinuous microemulsions, liquid crystals, polypeptide and polysaccharide networks, and organogels. For instance, liquid crystals of non-ionic surfactants have recently been used as direct templates for the synthesis of mesoporous silica[35] and cadmium sulphide superlattices[36]. However, a common problem with this approach is that penetration of the inorganic precursors into the preformed organic materials is low, resulting in low mineral volume fractions and poor infiltration of the voids within the continuous framework, although this difficulty could be alleviated by incorporating artificial ion channels and auxiliary organics into the matrix.

Synergistic synthesis. We consider synergistic synthesis to imply that the development of mineralized patterns is based on cooperative interactions between inorganic and organic constituents present in the reaction media. A general feature of this process is the coadaptation of independent self-assembled systems with the formation of new organizational states replicated by materials deposition (Table 1). At the nanoscale, inorganic building blocks can be assembled around single organic molecules (silicate anions around quaternary ammonium cations in zeolite synthesis, for example[37]). The association and ordering of the two components depends on the degree of chemical and structure complementarity at the inorganic–organic interface. The mechanism of zeolite formation has been proposed to involve the assembly of silicate and aluminate building blocks on curved, periodic minimal-energy surfaces having zeolite-like topologies[38]. Such surfaces have their

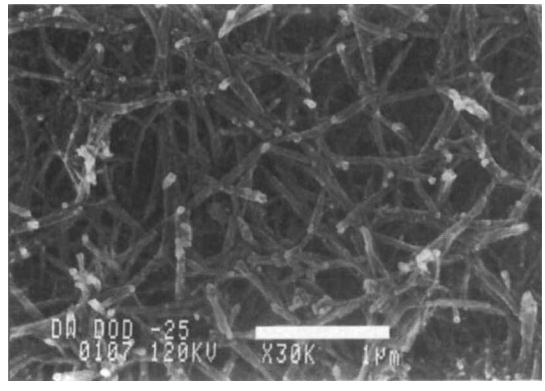


FIG. 4 Microskeletal framework of calcium phosphate formed by precipitation in bicontinuous microemulsions[46]. Scale bar, 1 μm.

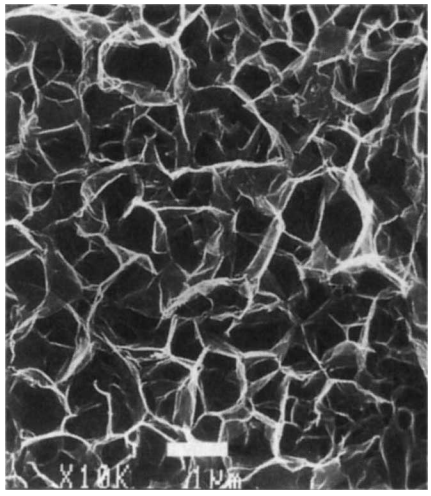


FIG. 5 SEM image of a thin cellular membrane of calcium carbonate formed by patterned mineralization of a biliquid oil/water foam[47]. (Micrograph courtesy of D. Walsh, Univ. Bath.) Scale bar, 1 μm.

origin in density fluctuations of transient local order delineated by the organic template in a synthesis mixture.

These patterning processes can be extended to the mesoscale by using supramolecular aggregates of surfactant molecules[2,39]. For example, the synthesis of mesoporous and mesolamellar silicas is initiated by ion binding and exchange of soluble silicate species at the cationic headgroups of quaternary ammonium surfactant molecules in weakly associated micellar and lamellar mesostructures, respectively[40]. These cooperative interactions result in a change in the spatial charge density and steric requirements at the headgroup–silicate interface. The extent of coadaptation is very sensitive to the stoichiometry and relative chemical potentials of the reactants, that is, to the balance of thermodynamic and kinetic driving forces within the system. Thus a high supersaturation of silicate species induces phase separation through inorganic precipitation of amorphous silica, whereas low silicate concentrations give rise to soluble products. At intermediate concentrations, the interfacial energetics dominate so that lamellar, hexagonal or cubic arrays of the inorganic and organic constituents are coassembled either by *de novo* nucleation from ion pairs in solution, or by rearrangement and aggregation of coadapted micelles. At this stage, the assembled architecture is essentially a liquid-crystalline inorganic salt of the cationic surfactant, but can be further processed by ageing or increasing the temperature to induce the *in situ* condensation of the silicate species assembled within the organized biphasic array.

Two factors dominate the replication of the supramolecular assembly: the ability of oxyanions to undergo condensation by facile hydrolysis, and the flexibility in the bond angle of covalently linked Si–O–Si units. This 'plasticity' provides remarkable structural connectivity and stability, such that the 1-nm-thick curved walls enclosing the 3–5-nm cages remain intact after calcination of the organic template around 500 °C; the structural integrity is maintained until 1,100 °C. The resulting mesoporous silica is a kind of 'crystalline glass' with ordered mesopores whose inorganic walls are amorphous—an observation that highlights the hierarchical nature of these materials.

Recent studies indicate that continuous and oriented mesoporous, silica thin films can be synthesized on mica substrates[41], presumably by the interaction of surfactant molecules with the mica surface which facilitates the organization and assembly of silica-surfactant micelles. This has been confirmed by atomic force microscopy studies of the surfactants adsorbed from aqueous solution onto mica, which reveal the presence of cylindrical aggregates rather than planar bilayers[42]. The silica mesophase nucleates and grows into regular patterns of thin ribbons that are preferentially oriented within the plane of the mica substrate (Fig. 3*a*). Thus the synergistic assembly of the silica–surfactant biphase is coupled with a transcriptive process involving direct templating at the mica surface. Similar interactions could be operating in the conventional synthesis of mesoporous silica in bulk solution. For example, particles of the biphasic material often exhibit a curved 'worm-like' morphology (Fig. 3*b*) that seems to be related to the topography of reaction spaces delineated by the higher-order organization of silica-surfactant vesicles in the synthesis gels[43].

Metamorphic reconstruction. It is possible that the synergistic synthesis of coassembled inorganic materials can be coupled ineractively with the surrounding reaction medium. In principle, the nucleation and initial growth of an inorganic material within an organized multicomponent system, such as a water/surfactant/oil microemulsion or surfactant/water liquid crystal, can induce changes in the local structure and phase behaviour, such that new morphological patterns develop from existing architectures (Table 1). These changes might be relatively small and confined to localized reconstruction of the initial motif; for example, expansion of pore size (from 3 to 7 nm) in siliceous mesoporous materials by mild hydrothermal treatment of the surfactant biphasic products[44]. Under alkaline conditions, part of the internal silica wall material is redistributed from regions of high to low curvature. The driving force for reorganization corresponds to a reduction in surface free energy, and occurs without loss of the imbibed surfactant template.

Alternatively, large changes in the scale and form of patterns replicated during mineralization could generate materials with complex architectures that do not resemble the initial organization of the associated reaction medium. For example, the mineralization reactions within the nanoscopic, interconnecting water channels of bicontinuous microemulsions produce microscopic, mesh-like architectures of silica[45] or calcium phosphate[46]. The first stage in the formation of microskeletal calcium phosphate involves the coassembly of inorganic precursors (Ca^{2+}, HPO_4^{2-}, OH^-) and cationic surfactant molecules (didodecyldimethyl ammonium bromide (DDAB)) within an optically clear microemulsion made from the appropriate mixture of supersaturated aqueous solution, surfactant and tetradecane. Nucleation of hydroxyapatite ($Ca_{10}(OH)_2(PO_4)_6$) at the surface of the DDAB headgroups, and subsequent growth of the crystals within the nanoscale water conduits for a few hours, results in filamentous networks of inorganic crystals with dimensions consistent with the microemulsion structure. But if samples are extracted after several days, an intact reticulated framework of micrometre-sized needle-like crystals, clearly incommensurate with the dimensions of the associated reaction media, is obtained (Fig. 4). The results suggest that the microskeletal inorganic form 'evolves' by localized disruption and reordering of the microemulsion due to incipient crystallization. Thus assembly of the inorganic framework seems to depend on the ability of the self-organized reaction

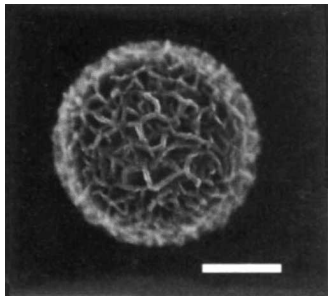


FIG. 6 Image of an intact 1-μm-diameter hollow shell of mesoporous aragonite[47].

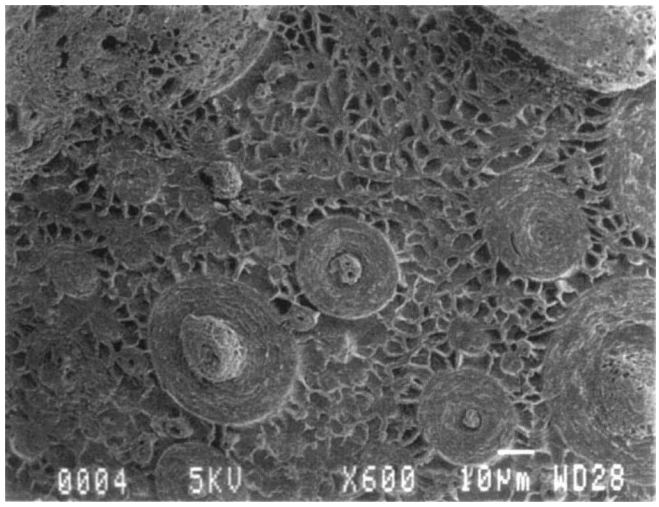


FIG. 7 Image showing complex surface patterns formed by mesolamellar aluminophosphate vesicles during hydrothermal synthesis. Scale bar, 10 µm.

environment to undergo restructuring or 'metamorphosis' during inorganic crystallization. Implicit in this transformability is that the surfactant headgroups initially act as the boundaries of nanoscale containers and templates but then become growth directors as crystallization proceeds.

In general, we consider that there could be metamorphic transformations running through various stages of hierarchical inorganic materials synthesis. Inorganic–organic composite materials are particularly susceptible because inefficient space-filling and mismatching in interfacial structure and charge could readily lead to metastability and *in situ* changes in form. Thus, patterns might become obscured by sequential deposition and subsequently hidden in the structural evolution of these materials.

Microphase separation. Extending the scale of inorganic morphosynthesis beyond the mesoscopic level necessitates the use of commensurate organic patterning agents. To this end, it seems feasible that the induction of localized microphase separation in multicomponent reaction systems—foams, vesicles and microemulsions—could be used to generate boundary surfaces and imprints for the sculpting of complex form in inorganic materials (Table 1). An important aspect of this strategy is that the formation of the microphase architectures must be synchronized with the onset of inorganic deposition, so that the self-organized patterns are replicated before disintegration.

One possibility is to use biliquid foams as patterned assemblies for synthesizing inorganic materials with honeycomb or mesh morphologies. For example, solvent extraction of oil and surfactant from a supersaturated microemulsion film results in a thin cellular film of porous calcium carbonate (aragonite) (Fig. 5)[47]. The microscopic mesh pattern is generated by demixing, which results in the evolution of close-packed oil droplets surrounded by a thin continuous layer of supersaturated aqueous calcium bicarbonate solution. This soapy foam is rapidly mineralized by loss of carbon dioxide to give an inorganic replica of the microphase-separated reaction media. Superficially, the system is analogous to the packing of areolar vesicles in the biomineralization of diatoms (see above)[18]. When uniform micrometre-sized polystyrene beads are coated in a thin film of the supersaturated microemulsion and washed with hot solvent, spherical shells of perforated calcium carbonate are formed. Dissolution and heat treatment of the polymer beads after mineralization results in intact hollow microspheres of the patterned inorganic material[47] (Fig. 6).

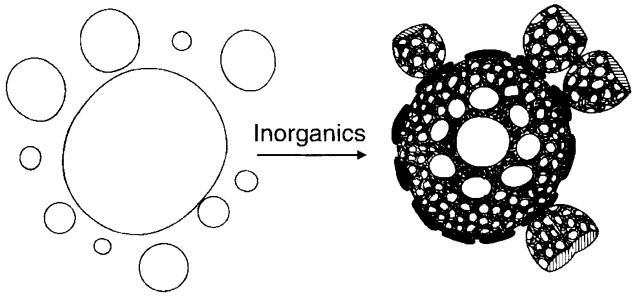


FIG. 8 Illustration of vesicle-templating of a hierarchical inorganic material. Mesolamellar aluminophosphate vesicles undergo fusion, fission, reshaping and collapse to form synthetic patterns with complex form[48].

In principle, it should be possible to induce a series of localized phase separations on different length scales so that hierarchical patterns can be replicated. Recent studies involving the formation of a mesolamellar aluminophosphate by heat treatment of hydrated aluminium hydroxyoxide with a decylammonium dihydrogenphosphate lamellar precursor in tetraethylene glycol (TEG) have shown that a wide range of microscopic pores and surface patterns can be imprinted on unusual macroscopic morphologies such as solid spheroids and hollow shells (Fig. 7)[48]. Some of these patterns display a striking resemblance to the biomineralized forms of diatoms and radiolaria, although we emphasize that mechanistically they are generated by different pathways. The macroscopic features, such as the bowl-shaped depressions and their associated mesh patterns, appear to be formed by the adhesion of mesolamellar aluminophosphate vesicles onto the surface of large spheres of the growing materials. An important aspect of this patterning process is that these higher-order vesicular aggregates can undergo microscopic phase separation together with fusion, fission, reshaping and collapse (Fig. 8). Replacement of TEG with ethylene glycol does not produce materials with complex forms, suggesting that the fine-scale architecture might arise from TEG-rich surface domains formed by phase separation within the vesicle bilayers[48]. Overall, these observations illustrate how surfactants can be used to template a mesolamellar structure which in turn is self-patterned on longer length scales by multicomponent vesicles to produce a hierarchical organic–inorganic composite with complex morphology.

Future prospects

The development of inorganic morphosynthesis suggests that the seemingly disparate fields of biological assembly and inorganic materials chemistry can be conceptually linked. Where such connections have been made, for example in the chemical study of biomineralization and biomimetic materials chemistry[5–11], the level of integration has been formulated primarily from the viewpoint of the physical sciences. Perhaps it is time to take a 'biological view' of inorganic materials chemistry? For example, in this Article, biological concepts such as morphogenesis, replication, self-organization, transcription, synergism and metamorphosis have been used as constructs for thinking about novel ways of synthesizing inorganic materials exhibiting complex form across a range of length scales. Of course, a change of idiom is only significant if it leads to the design of new experiments and scientific objectives.

The use of hierarchical design concepts in inorganic morphosynthesis could lead to integrated systems with enhanced or highly adjustable mechanical properties, engineered biomaterials, bioactive ceramic–matrix composites, environmentally responsive systems, organized catalyst supports and more efficient membranes for liquid and gas separations, and water purification. In addition, understanding pattern replication across different length scales provides an opportunity to fabricate functional gradients in inorganic materials. We suggest that, in the longer

term, the fabrication of bone and advanced materials will be described by the same paradigm of 'system-based synthesis' (Table 1). The constructional rules are likely to be different at different length scales, depending on the emerging properties and underlying patterns. Although the synthesis of such materials is far from being realized, the approaches highlighted in this Article suggest that a new conceptual framework may soon become available. □

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