7

Self-assembling nanostructured molecular materials and devices

7.1 INTRODUCTION

Soft materials are ubiquitous in everyday life, in soaps, paints, plastics and many other products. Their properties rely on the self-assembly of amphiphiles, colloids and polymers into a variety of mesophases, with nanoscale order of the constituent molecules. Nature also exploits self-organization of soft materials in many ways, to produce cell membranes, biopolymer fibres and viruses, to name just three. Mankind has recently begun to be able to design materials at the nanoscale, whether through atom-by-atom or molecule-by-molecule methods (top-down) or through self-organization (bottom-up). The latter endeavour encompasses much of soft nanotechnology, which is the focus of this chapter, as well as Chapters 6, 8 and 9. Strategies that take inspiration from nature are being followed, but alternative ab initio rational design methods which may one day improve on evolved structures (which often contain redundant elements) are also being pursued.

Self-organization of soft materials can be exploited to create a panoply of nanostructures for diverse applications. The richness of structures results from the weak ordering due to non-covalent interactions, and the consequent importance of thermal energy which enables phase transitions with differing degrees of order. The power of self-organization may be harnessed most usefully in a number of applications, including the preparation of nanoparticles, the templating of nanostructures, nanomotor design, the exploitation of biomineralization and the development of functionalized delivery vectors (for drugs, most importantly).

The intricate structures that can be formed by complex self-organizing molecules are truly amazing – for example helical and ferroelectric structures from non-chiral and

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non-polar molecules, biomimetic structures, artificial motors and muscles and protein or DNA recognition systems. The field of bionanotechnology is the subject of Chapter 9.

In the next few decades, the creation of a wealth of new materials and devices using soft nanotechnology will be witnessed. The impact of this on the quality of life of people everywhere will be immense. All this from a new materials chemistry, taking elements from colloid and polymer physical chemistry, sprinkling in a good dose of synthetic chemistry and biochemistry and sitting back to watch the explosion of novel research.

In this chapter the principles of self-assembly underpinning nanoscale structure formation in soft materials are elucidated. Examples of applications for nanoscale self-assembly are provided. In such a broad subject there are inevitably omissions. There is only a brief discussion of some aspects of bionanotechnology, since this chapter mainly emphasizes synthetic nanomaterials. Supramolecular chemistry is also not considered, although it is a powerful tool for the programmed self-organization of molecules and has been proposed as a means to create nanomachines (see the famous book by Drexler cited in the bibliography).

This chapter is organized as follows. Section 7.2 introduces the molecular components of self-organizing structures. Section 7.3 outlines the principles of self-assembly. Section 7.4 considers self-assembly routes to the preparation of nanoparticles as well as applications in nanotechnology; nano-objects are also briefly discussed. Section 7.5 summarizes templating methods for the fabrication of inorganic nanostructures. Section 7.6 covers nanotechnology applications of liquid crystal phases, both lyotropic and thermotropic. Section 7.7 contains a summary and outlook.

7.2 BUILDING BLOCKS

Self-assembling soft materials can be divided into synthetic and biological types. The chemistry of the constituent molecules or supramolecular aggregates are considered here, along with an introductory summary of the structures formed by these systems, which include polymers, colloids, liquid crystals, proteins, DNA and other biopolymers.

7.2.1 Synthetic

Polymers are long-chain molecules, usually organic. Biopolymers are considered separately in Section 7.2.2 and in Chapter 9. A wide variety of synthetic polymers can now be made by an extensive range of polymerization methods. Although conventional polymers spontaneously self-assemble into nanostructures, for example crystalline lamellae in crystalline polymers, the focus in this chapter will be on the engineered self-assembly of polymers into designed structures. A prime example is the microphase separation of block copolymers into a rich variety of nanostructures (Sections 7.6.2 and 7.6.3).

Surfactants are surface-active agents. Surfactant molecules are said to be amphiphilic; this means they contain both a hydrophilic (water-liking) tail group and a hydrophobic (water-hating) head group. The combination of these components leads to their preferential segregation to surfaces, where they can be active, such as in detergents.

Synthetic surfactants may have ionic head groups (as in cationic or anionic surfactants) or they may be non-ionic. The tail group is often a hydrophobic alkyl chain.

Lipids are biological amphiphiles. Many types of lipid such as phospholipids (containing a phosphate-based head group) have more than one hydrophobic tail. Amphiphiles aggregate into nanostructures in water to minimize the contact of the hydrophobic groups with H_2O molecules. A common nanostructure is a micelle, which can be spherical or cylindrical. These structures form with a hydrophobic core and a hydrophilic corona in order to avoid contact of the hydrophobic part of the molecule with water. Vesicles can also form; these are hollow spherical structures in which the shell is formed by layers of surfactant molecules. The lamellar phase comprises flat layers of amphiphilic molecules. Inverse micellar structures can be formed in 'oil' (i.e., an organic liquid) as the hydrophilic groups tend to segregate from the medium.

Colloids may be defined as microscopically heterogeneous systems where one component has dimensions in the range 1 nm to 1 μm, which at the lower end enters the nanoscale domain. This covers many types of material, including aerosols, foams and emulsions. This chapter mainly considers colloidal sols, which are dispersions of solid particles (often spherical latex beads) in a liquid.

Liquid crystals are materials with molecular order intermediate between that of a liquid and that of a crystal. Thermotropic liquid crystal phases are formed by organic molecules in the absence of solvent on heating from a low-temperature crystal phase. Lyotropic liquid crystal phases are formed by amphiphiles in solution, as discussed in Section 7.3.2. Molecules forming liquid crystal phases are termed mesogens. Thermotropic mesogens must be anisotropic. They may have a rod-like (calamitic) or disc-like (discotic) structure. Thermotropic liquid crystal phases are characterized by long-range molecular orientational order and in the case of smectic (layered) and columnar phases by various types of long-range translational order. There are many types of smectic and columnar phases; details can be found in *Introduction to Soft Matter* (Hamley) or *Introduction to Liquid Crystals: Chemistry and Physics* (Collings and Hird), both of which are cited in the bibliography for this chapter. The positional order of molecules in a nematic phase is short-range, as in a liquid, although there is long-range orientational order, characterized by the director (a unit vector along the direction of average orientation).

7.2.2 Biological

Structural proteins are commonly fibrous proteins such as keratin, collagen and elastin. Skin, bone, hair and silk all depend on such proteins for their structural properties.

Silk is produced by insects and arachnids to make structures such as webs, cocoons and nests. Silk from silkworm cocoons (of the moth *Bombyx mori*) has been used by mankind to make fabrics, because it has excellent mechanical properties, particularly its high tensile modulus. Spider silks also have outstanding strength, stiffness and toughness that, weight for weight, are unrivalled by synthetic fibres. The structures (several types have been recorded) all consist of silk based on antiparallel β-sheets of the fibrous protein fibroin. A β-sheet is a so-called secondary structure of a protein, formed by intermolecular hydrogen bonding between peptide chains (Section 7.3.1). Long stretches

of the polypeptide chain consist of sequences (Gly-Ser-Gly-Ala-Gly-Ala), where the symbols indicate different amino acods. The Gly chains extend from one surface of the β-sheets and the Ser and Ala from the other, forming an alternating layered structure. The orientation of the chains along the β-sheet underpins the tensile strength of silk, while the weak forces between sheets ensure that silk fibres are flexible. Silk fibres have a complex hierarchical structure, in which a fibroin core is surrounded by a skin of the protein sericin. Within the core, termed *bave*, there are crystalline regions containing layered β-sheets and amorphous regions that may contain isolated β-sheets.

Collagen is the major component of connective tissues, found in all multicellular animals. The molecule has a triple-helix structure. In vivo, collagen is organized into covalently cross-linked fibrils. Denatured collagen is better known as gelatine. Denaturation refers to the destabilization of the secondary structure due to unfolding of the protein, commonly brought about by heating or by chemical means. Keratins are a group of fibrous proteins that form hair, wool, nails, horn and feathers. There are two major types of keratin: α-keratins in mammals and β-keratins in birds and reptiles. As the name suggests, the structure of α-keratins is based on the α-helix (actually a coil of α-helices). β-keratin proteins form a β-sheet in their native state. In the natural material, keratins are arranged into fibrillar structures. The α-helix is the other common secondary structure formed by intramolecular hydrogen bonding of peptide chains. Further details on protein secondary structures can be found in the texts listed in the bibliography.

Globular proteins are found in a range of substances, including enzymes, transporter proteins and receptor proteins. They may contain α helix and/or β-sheet secondary structures. Many common arrangements of these secondary structures occur in unrelated globular proteins and are termed motifs or domains; an example is the $\beta\alpha\beta$ motif. A recent model represents these structures in a 'periodic table' parameterized according to the number of layered structures (formed by packed α-helices or β-sheets) and the shape of the motif (flat, curled or barrel). The twist of β-sheets leads to a staggered arrangement for the secondary structures in the outer layers. These sheets can also curl, and a combination of curl and stagger can produce *barrels* (hydrogen-bonded cylinders). This periodic table provides a good match for over 90% of known single-domain structures. It has also been shown that, in many aspects of their physical chemistry, globular proteins behave like charged colloidal particles.

The double-helix structure of DNA is famous. Less well known is the formation of lyotropic liquid crystal phases by DNA fragments in solution. Short fragments behave like rods, and so the formation of liquid crystal phases is possible. On increasing the concentration (above 160 mg/ml for 50 nm DNA in physiological salt solutions), cholesteric and hexagonal columnar phases may be observed. Cholesteric phases are better known as chiral nematic phases, because this indicates that they are anisotropic fluids in which the local orientation follows a helix (the helical ordering refers to the director, not the individual molecules). Cholesteric phases (originally observed in a cholesterol derivative) are characterized by bright interference colours, as the pitch of the helix is usually close to the wavelength of light. At temperatures just below those at which the cholesteric phase exists, a 'blue phase' is sometimes observed. This phase is named for the colour arising from the double-twist cylinders that result from the packing of helices. These cylinders pack into various cubic structures, as discussed for example in the texts cited in the bibliography.

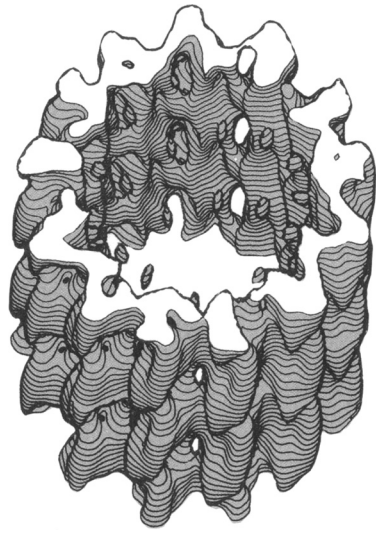

Figure 7.1 The 1.8 nm resolution X-ray structure of a microtubule. Reproduced from D. Voet and J. G. Voet, *Biochemistry*, Wiley, 1995, with permission

Microtubules are of interest in nanotechnology for a number of reasons. They are tubular structures formed from the protein tubulin (Figure 7.1), and could be used as nanochannels for the transport of liquid, or as 'struts' to support nanostructures. However, probably the main interest stems from the fact that they are a key component of one of the main motility systems of cells found in eukaryotes (the other being muscle). Eukaryotes are the cells of living organisms, except bacteria, and they contain a nucleus. The motion of cilia, which are the hair-like strands that undulate to sweep fluid across the surface of organs such as the respiratory tract, depends on the sliding of subfibres formed from microtubule arrays past one another. The whip-like structures responsible for motion in many types of cell called flagella (e.g., sperm cell tails) also move in this way. In contrast to the linear waving motion of cilia and eukaryote flagella, bacterial motion is impelled by rotation of flagella via a propeller-type structure that spans the bacterial membrane. As in muscles and cilia, the motion is driven by an ATPase (ATP is the molecule adenosine triphosphate) that acts as a transducer, converting the energy from ATP to ADP hydrolysis into mechanical energy (ADP is adenosine diphosphate). The detailed structure of the bacterial flagellum is complex, and further information can be found in a good biochemistry text. It remains to be seen whether nanomotors like those used in cilia or bacterial flagella will be incorporated directly into nanomachines or will inspire designs for artificial motors.

Viruses consist of nucleic acid molecules (RNA or DNA) encased in a protein coating. Virus capsids (protein shells) can be near spherical or rod-like (helical). Spherical viruses all have an icosahedral structure (a polyhedron with 20 triangular faces). Many common viruses, including rhinovirus (responsible for the common cold) and herpes simplex virus (Figure 7.2(a)) have this structure. The first virus to be discovered, tobacco mosaic virus, has a helical structure (Figure 7.2(b) and (c)), leading to a rod-shaped particle $\sim$300 nm long and 18 nm in diameter.

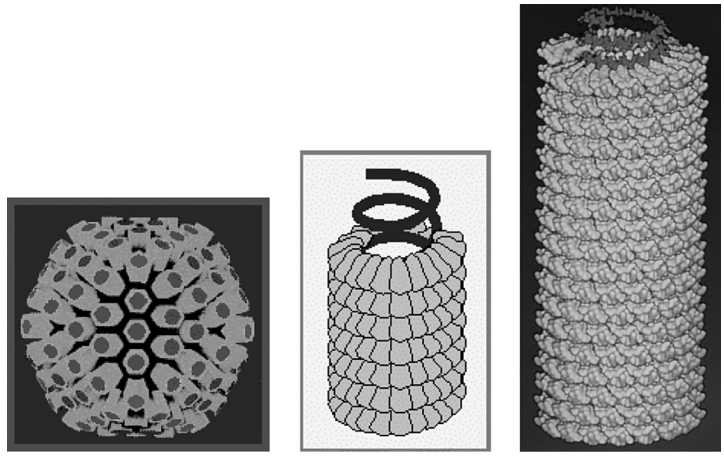

Figure 7.2 Models of (a) icosahedral structure of herpes simplex virus protein shell, (b, c) helical tobacco mosaic virus. Parts (a) and (b) reproduced from www.uct.ac.za/depts/mmi/stannard/ virarch.html; copyright L. M. Stannard. Part (c) reproduced from www.molbio.vanderbilt.edu/ fiber/ images.html. First published in K. Namba, D. L. D. Caspar and G. Stubbs, *Biophys. J.* **53**, 469 (1988)

7.3 PRINCIPLES OF SELF-ASSEMBLY

The term 'self-assembly' is used with a variety of meanings in different scientific contexts. For example, in Chapters 1 and 3, 'self-assembly' was used to describe the growth of semiconductor quantum dots using a particular MBE growth mode. In that context, 'self-assembly' referred to the spontaneous formation of the quantum dots as a consequence of the growth conditions (strain fields), without any need to define explicitly the dot size or shape. In the context of molecular materials, the term self-assembly is used to describe the reversible and co-operative assembly of predefined components into an ordered superstructure. Two categories of such self-assembly have been identified. Static self-assembly involves systems at equilibrium that do not dissipate energy. The formation of a structure may require energy, but once formed it is stable. In dynamic self-assembly, on the other hand, the formation of structures or patterns occurs when the system dissipates energy. Examples are patterns formed by reaction and diffusion processes in oscillating chemical reactions. The focus of this chapter is on materials that form static self-assembled structures, although a brief summary of possible routes to the fabrication of nanomotors involving dynamic self-assembly are outlined.

Self-assembly in soft materials relies on the fact that the fluctuations in the position and orientation of molecules or particles due to Brownian motion have energies comparable to thermal energy. Thermal energy has a dramatic influence on soft materials at the nanoscale as weak non-covalent bonds are broken and sometimes reformed. This enables the system to reach thermodynamic equilibrium, which is often a non-uniform state. Because of the relatively weak interactions between molecules, transitions between different structures can readily be driven by changes in conditions, such as temperature or pH. These external triggers that induce phase transitions could lead to a host of

responsive materials, or coupled with an appropriate source of energy to nanomechanical systems. There is a diversity of phase transitions between different structures in soft materials, and examples are considered in subsequent sections.

7.3.1 Non-covalent interactions

For self-assembly to be possible in soft materials, it is evident that the forces between molecules must be much weaker than the covalent bonds that hold molecules together. Weak intermolecular interactions responsible for molecular ordering in soft materials include hydrogen bonds, coordination bonds in ligands and complexes, ionic interactions, dipolar interactions, van der Waals forces and hydrophobic interactions. These are now summarized.

The hydrophobic effect arises when a non-polar solute is inserted into water. The hydrophobic effect can be distinguished from hydrophobic interactions, which result from the association of two non-polar moieties in water. The hydrophobic effect is conventionally ascribed to the ordering of water molecules around an unassociated hydrophobic molecule. This leads to a reduction in entropy. This entropy loss can be offset when association of hydrophobic molecules into micelles occurs, because this leads to an increase in entropy as the 'structured water' is broken up. An enthalpy penalty for demixing of water and solute should also be outweighed by the entropy increase in order for the Gibbs free energy change for micellization to be negative. The structured water model is based on orientational ordering of water molecules around the inserted solute molecule. An alternative model proposes that the high free energy cost of inserting a non-polar solute into water is due to the difficulty of finding a cavity due to the small size of water molecules. However, it has been argued that the hydrophobic effect is more subtle, depending on *solute* size and shape as well.

Hydrogen bonding is particularly important in biological systems, where many protein structures in water are held together by hydrogen bonds. Of course, the existence of life as we know it depends on hydrogen bonds, which stabilize H_2O in the liquid form. In proteins, intramolecular hydrogen bonds between N—H groups and C=O groups that are four amino acid units apart underpin the formation of the α-helix structure. On the other hand, hydrogen bonds between neighbouring peptide chains lead to β-sheet formation. Similarly, collagen fibres contain triple-helical proteins held together by hydrogen bonding. The folding pattern of proteins is also based on internal hydrogen bonding The smaller the number of hydrogen bonds in the folded protein, the higher its free energy and the lower its stability. The reason that nature has evolved means to exploit hydrogen bonds in this way is due to the strength of the bond. Hydrogen bonds are weaker than covalent bonds (about 20 kJ mol^{-1} for hydrogen bonds compared to about 500 kJ mol^{-1} for covalent bonds), so superstructures can self-assemble without the need for chemical reactions to occur, yet the bonds are strong enough to hold the structures together once formed, since the energy is still larger than thermal energy (2.4 kJ mol^{-1}).

Molecular recognition between artificial receptors and their guests can be combined with self-organization to program the self-assembly of nanostructures. Many types of non-covalent interaction can be exploited in supramolecular chemistry, including hydrogen bonding, donor–acceptor binding and metal coordination complexation. A diversity of methods have been employed to create receptors for ionic and molecular

guests. Another important example is the use of cyclodextrins as hosts for the delivery of drugs or pesticides.

Stabilizing colloidal dispersions against aggregation (known as coagulation when irreversible, flocculation when reversible) is important in everyday things such as foods or personal care products. Often the system is an oil-in-water dispersion that can be stabilized by adding interfacially active components such as amphiphiles or proteins. These segregate to the oil–water interface and stabilize emulsions by reducing interfacial tension, and the enhanced rigidity and elasticity of the membrane that forms also help to prevent coalescence. Colloidal sols found in paints and pastes also need to be stabilized for long shelf life; this can be achieved in several ways. First, for charged colloidal particles in an electrolyte medium, the balance between the repulsive electrostatic and attractive van der Waals contribution to the total potential energy can be adjusted, so that a barrier to aggregation is created. The phenomenon of charge stabilization can be analysed using the Derjaguin–Landau–Verwey–Overbeek (DLVO) theory, which is described in many colloid science textbooks. A second method to prevent aggregation is steric stabilization. Here long-chain molecules are attached to colloidal particles, creating a repulsive force as chains interpenetrate when the particles approach one another. The attached molecule may be chemisorbed (e.g., a long-chain fatty acid) or more commonly an adsorbed polymer. In contrast to charge stabilization, steric stabilization works in non-aqueous media and over a wide range of particle concentrations. The choice and concentration of polymer are critical in steric stabilization, since at low concentration, polymer chains can attach themselves to two (or more) particles, leading to so-called bridging flocculation. On the other hand, at higher polymer concentrations, if the polymer is non-adsorbing then it can lead to depletion flocculation, the mechanism for which was first recognized by Asakura and Oosawa. The polymers cannot penetrate the particles and are excluded from a depletion zone around them. When the particles are close together, the depletion zones overlap and the dispersal of polymers into the bulk solution is favoured entropically. An osmotic pressure of solvent from the gap between particles leads to an effective attraction between them, and hence flocculation. When the colloidal particle concentration is such that, on average, they are further apart than a polymer coil radius, and the polymer concentration is high, then depletion stabilization is possible. Forcing the particles together would require the 'demixing' of polymer from bulk solution. This increases the free energy so that the effective interaction between particles is repulsive.

7.3.2 Intermolecular packing

At high concentration, the packing of block copolymer or low molar mass amphiphilic molecules in solution leads to the formation of lyotropic liquid crystal phases, such as cubic-packed spherical micelles, hexagonal-packed cylindrical micelles, lamellae or bicontinuous cubic phases (Figure 7.3). The phase formed depends on the curvature of the surfactant–water interface. One approach to understanding lyotropic phase behaviour computes the free energy associated with curved interfaces. The curvature is analysed using differential geometry, neglecting details of molecular organization. In the second main model, the interfacial curvature is described by a molecular packing parameter. These two approaches will be described in turn.

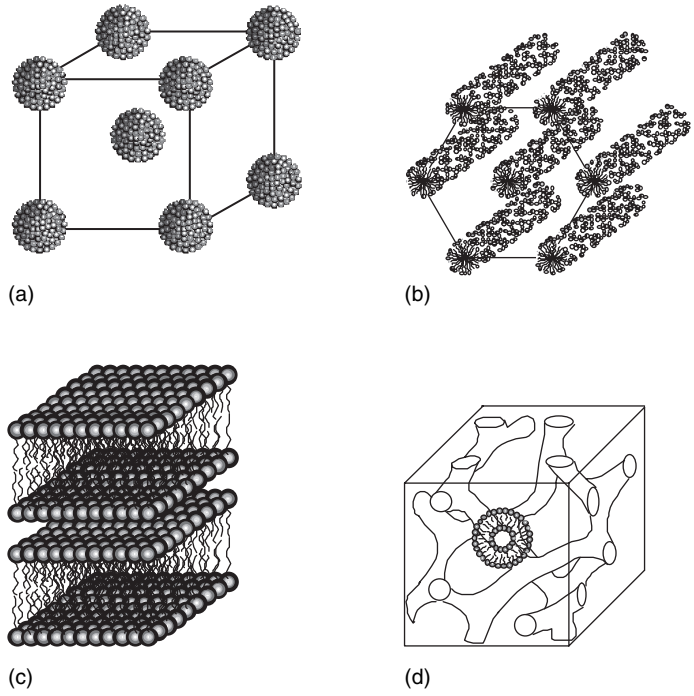

Figure 7.3 Lyotropic liquid crystal structures: (a) cubic-packed spherical micelles, (b) hexagonal-packed cylindrical micelles, (c) lamellar phase, (d) bicontinuous cubic structure. Here the amphiphilic molecules (not shown everywhere for clarity) form a bilayer film separating two continuous labyrinths of water. Reproduced from I. W. Hamley, *Introduction to Soft Matter*, Wiley, 2000, with permission

In the model for interfacial curvature of a continuous surfactant film, we use results from the differential geometry of surfaces. A surface can be described by two fundamental types of curvature at each point P in it: mean curvature and Gaussian curvature. Both can be defined in terms of the principal curvatures $c_1 = 1/R_1$ and $c_2 = 1/R_2$, where R_1 and R_2 are the radii of curvature. The mean curvature is $H = (c_1 + c_2)/2$, and the Gaussian curvature is defined as $K = c_1 c_2$.

Radii of curvature for a portion of a so-called saddle surface (a portion of a surfactant film in a bicontinuous cubic structure) are shown in Figure 7.4, although they can equally well be defined for other types of surface such as convex or concave surfaces found in micellar phases. To define the signs of the radii of curvature, the normal direction to the surface at a given point P must be specified. This is conventionally defined as positive if the surface points outwards at point P. In Figure 7.4 c_1 is negative and c_2 is positive. The mean and Gaussian curvatures of various surfactant aggregates are listed in Table 7.1.

It should be noted that end effects in elongated micelles due to capping by surfactant molecules that lead to an ellipsoidal or spherocylindrical (cylinder capped by hemispheres) structure are neglected. This will, however, change both mean and Gaussian curvatures to an extent that depends on the relative surface area of cap and tubular

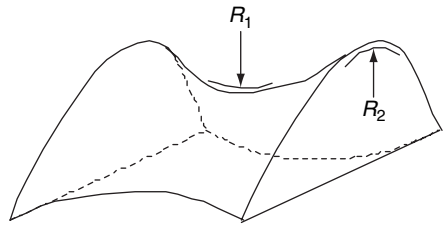

Figure 7.4 Principal radii of curvature of a saddle surface

Table 7.1 Mean and Gaussian interfacial curvature for common aggregate shapes. Here $R = R_1 = R_2$ denotes a radius of curvature

	Mean curvature $H=(c_1+c_2)/2$	**Gaussian curvature** $K=c_1c_2$
Spherical micelles of vesicle (outer layer)	$1/R$	$1/R^2$
Cylindrical micelles	$1/2R$	0
Bicontinuous cubic phases	0 to $1/2R$	$-1/R^2$ to 0
Lamellae (planar bilayers)	0	0
Inverse bicontinuous cubic phases	$-1/2R$ to 0	$-1/R^2$ to 0
Inverse cylindrical micelles	$-1/2R$	0
Inverse spherical micelles or inner layer of vesicle	$-1/R$	$1/R^2$

parts. The elastic free energy density associated with curvature of a surface contains, for small deformations, the sum of contributions from mean and Gaussian curvatures. The interfacial curvature model is thus useful because it defines the elastic moduli κ and $\overline{\kappa}$ for mean and Gaussian curvature, respectively. These can be measured (e.g., by light scattering) and characterize the flexibility of surfactant films. Uncharged surfactant films typically have elastic energies $F_{el} \leq k_B T$; i.e., they are quite flexible.

An alternative approach to describing lyotropic mesophases in concentrated solution is based on the packing of molecules. The effective area of the head group, a, with respect to the length of the hydrophobic tail for a given molecular volume controls the interfacial curvature. The effective area of the head group (an effective molecular cross-sectional area) is governed by a balance between the hydrophobic force between surfactant tails which drives the association of molecules (hence reduces a) and the tendency of the head groups to maximize their contact with water (and thus increase a). The balance between these opposing forces leads to the optimal area per head group, a, for which the interaction energy is minimum.

Simple geometrical arguments can be used to define a packing parameter, the magnitude of which controls the preferred aggregate shape. For a spherical micelle, it can be shown that the following condition holds: $V/la \leq 1/3$, where V is the volume of a molecule and l is the length of an extended hydrophobic chain (which can easily be calculated). The term $N_s = V/la$ is called the surfactant packing parameter, or critical packing parameter. The surfactant parameter can be used to estimate the effective headgroup area, a, or vice versa. The surfactant parameter is concentration dependent, reflecting changes primarily in a (but to a lesser extent in V) on varying the amount of solvent.

Just as spherical micelles can be considered to be built from the packing of cones, corresponding to effective molecular volumes, other aggregate shapes can be considered to result from packing of truncated cones or cylinders.

The surfactant packing model and the interfacial curvature description are related. A decrease in the surfactant packing parameter corresponds to an increase in mean curvature. The packing parameter approach has also been used to account for the packing stabilities of more complex structures, such as the bicontinuous cubic phases. Here the packing unit is a wedge, which is an approximation to an element of a surface with saddle-type curvature (Figure 7.4). Then it is possible to allow for differences in Gaussian curvature between different structures, as well as mean curvature.

7.3.3 Biological self-assembly

Understanding the folding of proteins is one of the outstanding challenges of science, let alone biophysics and biochemistry. Although much progress has been made in modelling protein folding, there is no consensus on the best method. Most methods consider a protein folding energy landscape. The problem is that this is a rough surface, with many local minima, and it can often be hard to model the guiding forces that stabilize the native structure and cause the free energy to adopt a 'funnel' landscape. Many minimalist models are based on computer simulations of particles on a lattice, and they are always based on coarse-grained approaches. Fully atomistic models seem some way off. Some structural insights on protein conformational dynamics have emerged from steered molecular dynamic simulations in which Monte Carlo moves are used as well as molecular dynamics trajectories.

DNA will be an important component of many structures and devices in nanobiotechnology. DNA computing is an application currently attracting considerable attention. In one approach, single DNA strands are attached to a silicon chip. Computational operations can then be performed in which certain DNA strands couple to added DNA molecules. Multi-step computational problems can also be solved. Here the DNA strands encode all possible values of the variables. Complementary DNA strands are then added, and attach themselves to any strand that represents a solution to one step of the computation. Single strands remaining are removed. This process is repeated sequentially for each step, and the DNA that is left is read out, via polymerase chain reaction (PCR) amplification, to provide the solution, represented in binary form, where a given binary number corresponds to an eight-nucleotide sequence. The DNA-directed assembly of proteins, using oligonucleotides capped with the molecule streptavidin, is another exciting realm of applications. The method can be used to fabricate laterally patterned arrays of many types of macromolecules with the biotin organic group as an end group, since a strong complex is formed between this and streptavidin.

The charged nature of DNA has been exploited to bind metal ions that aggregate into nanoparticles of silver, for example; they are then used as seeds for further deposition of silver to produce nanowires. Positively charged C_{60} fullerene derivatives have also been condensed onto DNA. Similarly, CdS nanoparticles have been templated on the charged DNA backbone. Arrays of DNA-functionalized CdS have been assembled, layer by layer, on a gold electrode using a set of two populations of DNA-capped CdS

nanoparticles and a soluble DNA analyte. The two oligonucleotides bound to CdS nanoparticles are complementary to the ends of the target DNA. The construction of nanoscale geometric objects and frameworks using three- and four-arm synthetic DNA molecules has also been reported. The use of nanoparticle-tagged DNA solutions in gene sequence detection is discussed in Section 7.4.2.

Modified or artificial cells could find applications in bionanotechnology as nanoscale delivery agents or nanoreactors. A membrane in a cell wall fulfils a number of functions. It acts as a barrier to prevent the contents of a cell from dispersing and also to exclude external agents such as viruses. The membrane, however, does not have a purely passive role. It also enables the transport of ions and chemicals such as proteins, sugars and nucleic acids into and out of the cell via the membrane proteins. Membranes are important not only as the external cell wall, but also within the cell of eukaryotes, where they subdivide the cell into compartments with different functions.

A cell membrane is illustrated in Figure 7.5. It is built from a bilayer of lipids, usually phospholipids, associated with which are membrane proteins and organic macromolecular sugar molecules called polysaccharides. The lipid bilayer is the structural foundation, and the proteins and polysaccharides provide chemical functionality. Proteins are associated with cell membranes in a variety of ways. Integral proteins are very tightly bound within the membrane. Some proteins are associated with a specific surface within the bilayer, such as the hydrophobic surface between hydrocarbon tails. Those spanning the membrane are known as transmembrane proteins. These are obviously important in transporting ions or molecules across the cell membrane. Integral proteins are amphiphilic; the two ends extending into the aqueous medium contain hydrophilic groups whereas the region within the bilayer is predominantly hydrophobic. Integral proteins are believed to form an α-helix in the transmembrane domain (Figure 7.5), due to hydrogen bonding in the polypeptide backbone. This reduces the exposure of polar $-OH$ and $-NH_2$ groups to the apolar environment of the bilayer. Because of the non-polar nature of the interior of lipid bilayers, they are impermeable to most ionic and

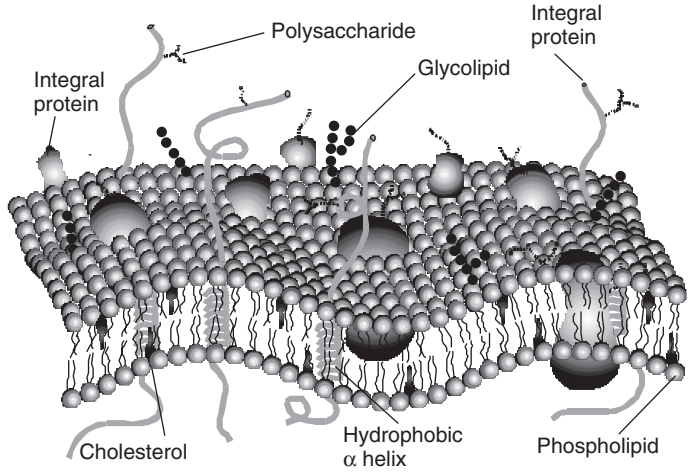

Figure 7.5 Schematic of a cell membrane. Adapted from D. Voet and J. G. Voet, *Biochemistry*, Wiley, 1995

polar molecules and indeed this is the basis of the barrier activity of lipid membranes. Integral proteins are bound in the lipid bilayer, and often act as channels for the transport of ions and molecules. These channels have to be highly selective to prevent undesirable material entering the cell and so are opened and closed as necessary. Membrane transport is also carried out by proteins that are not integral to the membrane. Transport proteins are then required to move ions, amino acids, sugars and nucleotides across the cell wall. They can either ferry these species across or form channels to transport them. An example of the latter is bee venom which contains the channel-forming protein melletin. In contrast to integral proteins, peripheral proteins are not bound within the membrane but are associated to it either by hydrogen bonding or electrostatic interactions. Peripheral proteins often bind to the integral proteins.

Vesicles formed by lipids (termed liposomes) represent model systems for the cell membrane. The incorporation of channel-forming proteins (porins) into lipid bilayers has been studied for many years, and synthetic structural and functional mimics have been devised. It is straightforward to form vesicles from the lipid bilayers. Block copolymers form vesicles that can be polymerized, which has obvious advantages in encapsulation applications. The incorporation of channel-forming proteins into planar polymerized triblock copolymer membranes has been reported. This further extends the delivery and nanoreactor capabilities of the biomimetic structures. Recently, pH-swellable porous core–shell latexes have been developed. These are analogous to the pH-controlled pore opening of the protein shell of cowpea chlorotic mosaic virus. By appropriate surface functionalization, the recognition properties of bilayers can be enhanced, as required for many drug delivery applications. A model recognition system is the biotin–streptavidin complex, for which the free energy of binding is comparable to that of a covalent bond.

7.3.4 Nanomotors

A key element of any nanomachine is a nanomotor. A variety of approaches are being followed in the manufacture of nanomotors. The crudest is to make miniature versions of motors from the macroscopic world, however the ability to scale such structures downwards is limited by energy dissipation due to friction. Alternative strategies include attempts to mimic motors in biological systems, and the simpler 'motors' driven by chemical potential or concentration gradients, such as oscillating gels. Here we briefly discuss nanomotors based on soft matter.

Considering first biological motors as models for artifical motors, we can define two classes. In the first, proteins such as kinesin, dynein and myosin behave as linear slides. Among rotory motors, well-studied systems include the ATP synthesis complex, and bacterial flagellar motors, which are described in detail in Section 9.2.2.

Artificial motors exploit out-of-equilibrium chemical phenomena, such as a concentration gradient, as in ATP synthesis. Using this knowledge, it is possible to design simpler systems than those operating in nature. A minimal system can be constructed based on osmotic pumping using lipid vesicles in a gradient of solute concentration. The lipid bilayers act as osmotic membranes, allowing the passage of water molecules but not of solute molecules. Thus, when placed in a high osmotic pressure environment, the vesicles shrink and in a uniform solution do not move.

However, in a solute concentration gradient, a directional motion is imposed. Unidirectional motion can also be imparted to liquids confined in capillaries by a temperature gradient. An interesting concept to drive fluid motion in microcapillaries uses optical trapping of colloid particles, which can be manipulated to create pumps and valves. Although the scale of the particles is of order micrometres, it would be exciting if this could be extended to the nanoscale using smaller particles and shorter wavelength radiation. Other systems rely on the Marangoni effect. Due to dynamic surface tension fluctuations, surface-active molecules flow into higher surface tension regions (or away from low surface tension regions), to restore the original surface tension. This is the origin of the motion of camphor 'boats' that move freely on the surface of water. The origin of this motion was explained by Lord Rayleigh over a century ago, but the system has been revisited recently as a simple analogue of artifical motors.

A particularly attractive artifical motor system relies on oscillating chemical reactions to drive volume changes in polymer gels. The Belousov–Zhabotinsky (BZ) reaction was used to create an oscillating redox potential. This was then coupled to the most familiar polymer gel system exhibiting a volume phase transition, poly(*N*-isopropylacrylamide), or PNIPAM, in water. The PNIPAM was modified by covalent attachment of ruthenium tris(2,2′-bypyridine) units, which act as catalysts for the BZ reaction. Thus the oscillations in the BZ reaction were translated into periodic swelling and deswelling of the gel due to changes in the charge on the ruthenium complex.

7.4 SELF-ASSEMBLY METHODS TO PREPARE AND PATTERN NANOPARTICLES

7.4.1 Nanoparticles from micellar and vesicular polymerization

The fabrication of nanoparticles of controlled size, shape and functionality is a key challenge in nanotechnology. There are several established routes to nanoparticle preparation. Roughly spherical nanoparticles can be prepared by very fine milling (Section 5.3.5); this route is used to prepare iron oxide nanoparticles in ferrofluid dispersions or zinc oxide nanoparticles for use in sunscreens. So-called colloidal methods produce nanoparticles with much more uniform size and shape distribution than milling. Metal and metal oxide nanoparticles have been prepared using micellar nanoreactors where, for example, salts are selectively sequestered in the micellar core then reduced or oxidized. Such nanoparticles can be used in catalysis, separation media, biopolymer tagging and light-emitting semiconductor (CdS) quantum dots.

Recent work has shown that metal nanoparticles can be patterned at the surface using the self-organization of block copolymers. Two main routes have been exploited: nanoparticle formation within micelles in solution which may subsequently be deposited on a solid substrate, and direct patterning at the surface using selective wetting. Figure 7.6 shows examples of nanoparticle direct patterning by selective wetting at the surface of a diblock copolymer.

Nanocapsules; i.e., shell particles with a hollow interior, can be prepared by a number of routes, including the cross-linking of the shell of block copolymer vesicles.

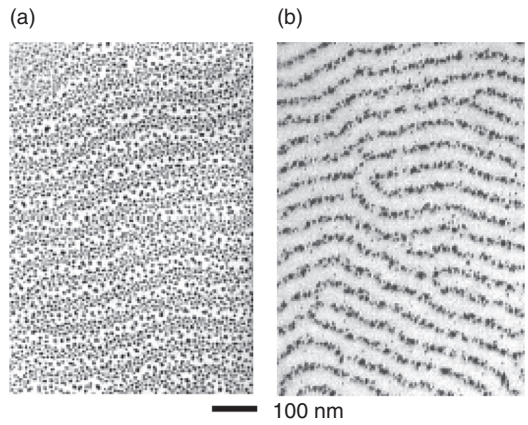

Figure 7.6 Examples of nanoparticle and nanowire arrays templated by a stripe pattern formed at the surface of a polystyrene–poly(methyl methacrylate) diblock copolymer by vapour deposition of gold. The gold selectively wets polystyrene domains. Reproduced from W. A. Lopes and H. M. Jaeger, *Nature* **414**, 735 (2001)

An alternative approach has recently been developed, using polyelectrolyte multilayers assembled around a colloidal core that is subsequently dissolved. Biological particles, such as apoferritin and cowpea chlorotic mosaic virus, with hollow fillable interiors are described in Sections 7.4.6 and 7.3.3, respectively.

7.4.2 Functionalized nanoparticles

Functionalized nanoparticles will find numerous applications, for example in catalysis and as biolabels. Gold nanoparticles functionalized with proteins have been used as markers to detect biological molecules for some time. They may also be used to deliver DNA in a so-called gene-gun. Arrays of nanoparticles can be prepared via dip pen nanolithography (DPN), which is described in Section 9.1.2. For example, magnetic nanoparticles can be patterned into arrays, with potential applications in magnetic storage devices.

Functionalized nanoparticles are required for many biotechnological applications. Figure 7.7 shows a technique for detecting specific gene sequences that could be used in genetic screening. First the sequence of bases in the target DNA is identified. Then two sets of gold particles are prepared: the first set has attached DNA that binds to one end of the target DNA, and the second set carries DNA that binds to the other end. The nanoparticles are dispersed in water. When the target DNA is added, it binds both types of nanoparticle together, linking them to form an aggregate. The formation of this aggregate causes a shift in the light-scattering spectrum from the solution; i.e., a colour change in the solution that can easily be detected. This technique has recently been developed to allow the electrical detection of DNA. The principle is similar to that of the colour-change detection system, except one end of the target DNA binds to a short capture oligonucleotide attached to the surface of a microelectrode, and the other end

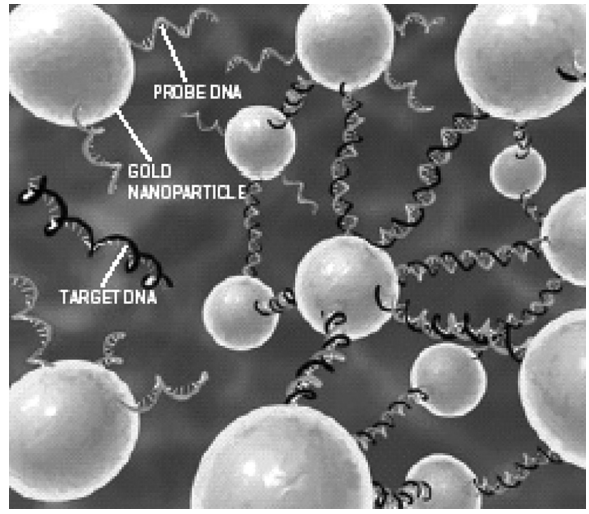

Figure 7.7 DNA-functionalized gold nanoparticle gene sequence detection system. Reproduced from *Scientific American*, September 2001, p. 63

binds to an oligonucleotide attached to Au nanoparticles. Binding of the target DNA causes Au nanoparticles to fill the gap between a pair of electrodes, an event that can be detected from capacitance or conductivity measurements. In practice the sensitivity of the device was enhanced by silver deposition on the nanoparticles. Arrays of electrode pairs were assembled to form DNA chip arrays in which each pair contained a different oligonucleotide capture strand.

7.4.3 Colloidal nanoparticle crystals

There is an immense interest in photonic band gap crystals because they can be used to confine photons or to modulate or control stimulated light emission or to construct lossless waveguides. A photonic band gap crystal or photonic crystal is a structure with a periodic variation in dielectric properties (Section 3.8.8). The propagation of electromagnetic waves in such a crystal is analogous to that of electrons in semiconductors, in particular there exist band gaps that exclude the photon propagation modes in certain frequency intervals. In principle, three-dimensional crystals could have a complete bandgap; i.e., one for which photon propagation is prevented in all spatial directions; i.e., throughout the Brillouin zone, using the nomenclature of solid-state physics. The main focus on three-dimensional structures has been on the face-centred cubic (fcc) lattice because its Brillouin zone is most closely spherical, which might favour the formation of a complete photonic bandgap. However, it has been shown for an fcc crystal formed by colloidal spheres (opal structure) that, independent of the dielectric contrast, there is never a complete band gap. The inverse structure (spheres of air in a continuous solid medium) however holds promise, because calculations indicate the possibility of a complete 3D band gap. It has even been shown that by coating the air

pores with nematic liquid crystal, a switchable photonic bandgap material can be achieved. Here the tunable localization of light or of waveguiding results from the electro-optic properties of the liquid crystal, where an electric field can be used to orient molecules in a particular direction with respect to the pore lattice.

To create a 3D photonic band gap, two conditions must be fulfilled. First, the colloidal particles must have low polydispersity (i.e., be almost the same size) in order to form a cubic crystal. Second, the number of defects in the cubic crystal must be minimized. Several strategies have been adopted to create macroscopic colloidal crystals. A common technique relies on sedimentation of particles under gravity. However, the resulting samples generally contain polycrystalline domains. Other approaches rely on surfaces to act as templates to induce order. For example, spin coating onto planar substrates can provide well-ordered monolayers, as can flow-induced ordering. A method that relies on so-called convective self-assembly has been used to create ordered crystals upon rapid evaporation of solvent. A related technique is the controlled withdrawal of a substrate from a colloidal solution, similar to Langmuir–Blodgett film deposition (Section 8.5.2.2), where lateral capillary forces at the meniscus induce crystallization of spheres, and if the meniscus is slowly swept across the substrate, well-ordered crystal films can be deposited. Convective flow prevents sedimentation and provides a continuous supply of particles to the moving meniscus. Actually, the controlled evaporation process alone is sufficient to produce films of controlled thickness that are well ordered up to the centimetre scale. An epitaxial mechanism has been employed, using a lithographically patterned polymer substrate to template crystal growth. Holes just large enough to hold one colloidal particle were created in a rectangular array. Controlled layer-by-layer growth starting from this template was then achieved by slow sedimentation of the silica spheres used. The formation of well-ordered crystal monolayer 'rafts' of charged colloid particles on the surface of oppositely charged surfactant vesicles has also been demonstrated.

As mentioned above inverse opal structures offer the greatest potential for photonic crystals. The most promising materials for the matrix seem to be certain wide band gap semiconductors, such as CdS and CdSe, because they have a high refractive index and are optically transparent in the visible and near-IR region. The preparation of porous metallic (gold) nanostructures within the interstices of a latex colloidal crystal has been demonstrated. Here a solution of gold nanoparticles fills the pores between colloidal particles, and the latex is subsequently removed by high-temperature furnace heating. A similar method has been used to fabricate inverse opal structures of titania. The same idea has been applied to form a nanoporous polycrystalline silica (deposited via low-pressure chemical vapour deposition); see Figure 7.8. In a related approach, silica spheres are coated with gold (to reinforce the colloidal crystal) then immersed in electroless deposition baths to deposit metal films within the porous template; the silica is removed in an HF rinse. These types of approach have been extended to a lost wax approach to prepare high-quality arrays of hollow colloidal particles (or filled particles) of various ceramic and polymer materials. Here a well-ordered silica colloidal crystal is taken and used as a template for polymerization in the interstices. If the pores are interconnected, the polymer forms a continuous porous matrix. By appropriate choice of polymer, either hollow or solid nanoparticles can be grown in it (hollow nanoparticles grow from the polymer matrix inwards, solid nanoparticles form within the voids). In this way it was possible to prepare colloidal crystals of solid or hollow TiO_2 particles,

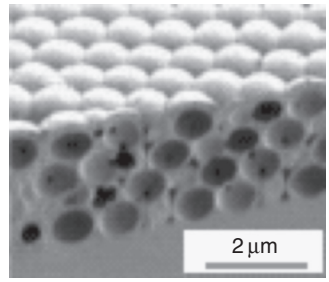

Figure 7.8 Cross-sectional scanning electron micrograph image of thin film inverse opal structure of polycrystalline silicon templated by 855 nm silica spheres. Reproduced from Y. A. Vlasov, X.-Z. Bo, J. C. Sturm and D. J. Norris, *Nature* **414**, 289 (2002)

as well as conductive polymer nanoparticles. An extension of colloidal polymerization techniques can be used to prepare defined waveguides. Crossed laser beams were used to polymerize polymer precursors within particular pores. By scanning the laser beams, a waveguide with a chosen path and shape can be fabricated.

The use of microgel particles of PNIPAM to form colloidal crystal arrays that selectively diffract light has been reported. Poly(*N*-isopropylacrylamide) in aqueous solution exhibits a volume phase transition at 32 °C; below 32 °C gels are hydrated and swollen but above 32 °C gels dehydrate and collapse. This transition has been used to vary the dimensions of PNIPAM microgel particles from 100 nm at 40 °C to 300 nm at 10 °C, a 27-fold volume change. This can be exploited to prepare a switchable selective diffraction array. Below the transition, the particles are swollen and only diffract light weakly; however, in the compact state, the diffracted intensity increases dramatically due to the enhanced contrast between particles and medium (the Bragg diffraction wavelength is unaffected). Wavelength-tunable arrays were fabricated by polymerizing PNIPAM in the presence of 99 nm polystyrene spheres. The embedded polystyrene spheres follow the swelling or shrinking of the PNIPAM hydrogel so that the wavelength of the Bragg diffraction can be tuned across the visible range of the spectrum.

7.4.4 Self-organizing inorganic nanoparticles

Within the past few years, there has been a surge of interest in composite materials consisting of a polymer filled with plate-like particles such as clay particles. Such fillers are extremely effective in modifying the properties of polymers, and orders of magnitude improvement in transport, mechanical and thermal properties have been reported. Examples of applications include low-permeability packaging for food and electronics, toughened automotive components, and heat- and flame-resistant materials. Polymer–clay nanocomposites have several unique features: First, they are lighter in weight than conventional filled polymers for the same mechanical performance. Second, their mechanical properties are potentially superior to fibre-reinforced polymers, because reinforcement from the inorganic layers occurs in two dimensions instead of one. Lastly,

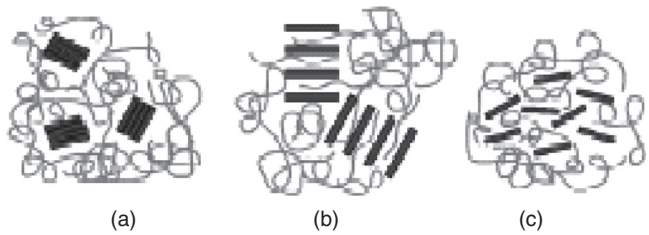

Figure 7.9 Possible structures for polymer–clay nanocomposites: (a) phase separated, (b) intercalated, (c) exfoliated. Reproduced from E. P. Giannelis, R. Krishnamoorti and E. Manias, *Adv. Polym. Sci.* **138**, 108 (1999)

they exhibit outstanding diffusional barrier properties without requiring a multipolymer layered design, allowing for recycling.

Clays are colloidal suspensions of plate-like mineral particles, with a large aspect ratio. Typically the particles are formed from silicate layers combined with layers of octahedrally coordinated aluminium or magnesium atoms. The layers lead to a lamellar phase for the clay in water. The aim in applications is to retain this structure in the polymer–clay nanocomposite; possible structures are illustrated schematically in Figure 7.9. Exfoliation and phase separation should be avoided and there is an immense literature (especially patent literature) on how to achieve this by chemical treatment of the clay particles, in particular by adsorption of organic molecules. The intercalated structure leads to enhanced barrier properties, due to the tortuous path for gas diffusion around the clay platelets.

Liquid crystal phases formed by mineral moieties have been known almost as long as organic liquid crystals. They have received renewed interest because of the ability to combine the properties of liquid crystals, in particular anisotropy and fluidity, with the electronic and structural properties of minerals. They may also be cheaper to produce than conventional liquid crystals, which require organic synthesis. Rod-like mineral systems that form nematic phases have been well studied. Sheet-forming mineral compounds that form smectic (layered) structures in solution are also known.

The colloidal behaviour of vanadium pentoxide (V_2O_5) has been investigated since the 1920s. Under appropriate conditions of pH, ribbon-like chains can be obtained via the condensation of V—OH bonds in a plane. Figure 7.10 shows a scanning electron micrograph of dried ribbons. A nematic liquid crystal forms in aqueous suspensions if the particle volume fraction, ϕ, exceeds 0.7%. A sol–gel transition occurs at $\phi = 1.2\%$, which divides the nematic domain into a nematic sol and a nematic gel. For $\phi > 5\%$, a biaxial nematic gel phase is formed. Suspensions of V_2O_5 can be aligned in electric and magnetic fields, similar to organic nematogens used in liquid crystal displays. Laponite and bentonite/montmorillonite clay particles also form nematic gels.

The previous section discussed formation of layered structures in intercalated suspensions of these types of clay. It can be argued that they are not lamellar or smectic phases since long-range order is not preserved upon swelling, where exfoliation occurs. Colloidal smectic phases have been observed for β-FeOOH, which forms Schiller layers (from the German for iridescence). The rod-like β-FeOOH particles form layers at the bottom of the flask. The spacing between the layers is comparable to the wavelength of light, hence the iridescence. A swollen liquid crystalline lamellar phase based on

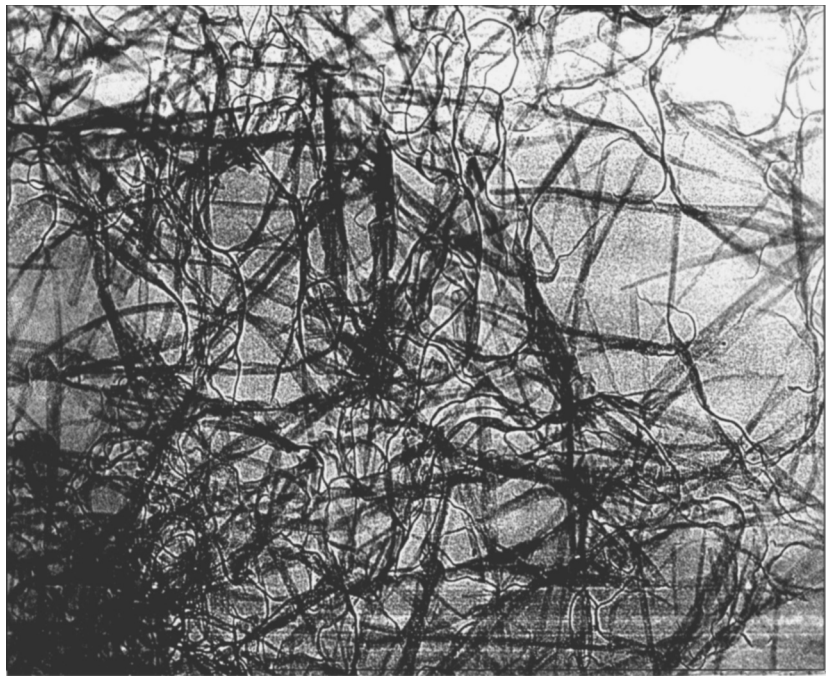

Figure 7.10 Scanning electron micrograph of a dried V_2O_5 suspension. Reproduced with permission from J. Livage

extended solid-like sheets (rather than rod-like particles) has been rationally designed using the solid acid $H_3Sb_3P_2O_{14}$. In contrast, plate-like $Ni(OH)_2$ nanoparticles (91 nm radius, 12 nm thick) and $Al(OH)_3$ nanodiscs (radius 200 nm, thickness 14 nm) self-assemble into columnar mesophases. A nematic phase has also been observed for $Al(OH)_3$ nanoparticles. The formation of a smectic phase rather than a columnar phase is expected if the polydispersity in particle radius is large enough to prevent the efficient packing of columns. In fact, at very high volume fractions in $Al(OH)_3$ suspensions, evidence was obtained for a smectic phase, which can accommodate the polydispersity in radius (although a low polydispersity of particle thickness is required).

7.4.5 Liquid crystal nanodroplets

Figure 7.11 shows an array of block copolymer micelles containing liquid crystal solubilized in the micellar core. The self-assembly of the block copolymer micelles into a hexagonal close-packed arrangement is apparent. The long-range ordering of the structures could be improved as in other soft materials by using an alignment substrate or by annealing. The ability to pattern liquid crystal nanodroplets at the nanoscale is not required for conventional display applications (which do not require a resolution beyond that of visible light) but may find applications in phased array optics. Phased array optics is a method to reconstruct a three-dimensional image on a two-dimensional

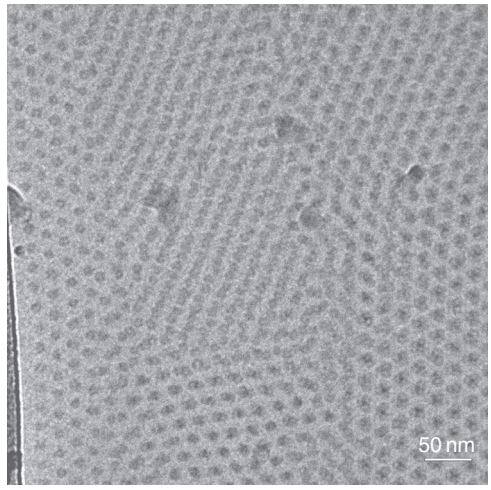

Figure 7.11 Transmission electron micrograph of quench-cooled film of poly(styrene oxide)-*b*-poly(ethylene oxide) block copolymer micelles containing liquid crystal solubilized in the poly(styrene oxide) core. Reproduced from I. W. Hamley, V. Castelletto, J. Fundin, M. Crothers, D. Attwood and Y. Talmon, *Colloid Polym. Sci.* **282**, 514 (2004)

surface. Optics allows this to be done if the phase and amplitude of the light waves from the virtual image are controlled. An array of switchable light sources 200 nm apart is sufficient to reconstruct any desired light wave pattern. It has been proposed that liquid crystals can be used as switchable birefringent phase shifters. However, no one has yet found the means to arrange the liquid crystal in nanometre-scale arrays. Patterning of liquid crystals in micelles or microemulsions is a promising way to achieve this.

7.4.6 Bionanoparticles

Viruses are natural nanoparticles which have evolved into a variety of shapes. A number of nanotech applications of viruses are now considered. First, they may be used as responsive delivery agents. Recent work has focused on the use of modified cowpea chlorotic mottle virus nanoparticles as biocompatible responsive delivery agents. At pH <6.5 the virus adopts a compact spherical structure, however at pH >6.5 the structure becomes porous, allowing the pH-controlled release of encapsulated drug molecules, for example. In non-responsive mode, viruses may be used as 'Trojan Horses' for the delivery of genes in transfection applications. Gene therapy is attracting immense attention as a means to treat diseases by modifying the expression of genetic material. Its premise is that disease can be prevented at the level of DNA molecules, thus compensating for abnormal genes. With an eleven-year history of clinical trials, and many more in progress, recent evidence that gene therapy may be efficacious in the treatment of medical conditions due to the deficiency of single genes has attracted worldwide attention.

Both viral and non-viral approaches have been used in clinical trials to treat illnesses such as cystic fibrosis and several forms of cancer. Viruses have evolved efficient ways of

targeting cells, delivering genetic material and expressing it. However, inflammatory and immunological responses induced by viruses may limit their utility for repeated administration. Numerous systems have been studied for non-viral gene delivery, including synthetic polymers such as polylysine and poly(oxyethylene)-based block and graft copolymers or biologically derived liposomes or cationic lipids or the cationic polyelectrolyte poly(ethyleneimine) (PEI). PEI has a very high cationic charge density, making it useful for binding anionic DNA within the physiological pH range and forcing the DNA to form condensates small enough to be effectively transferred across the cell membrane. Furthermore, it has been shown that PEI enhances transgene expression when DNA/polymer complexes are injected into the cytoplasm.

Magnetotactic bacteria exploit magnetic nanoparticles to navigate from regions of oxygen-rich water (toxic to them) to nutrient-rich sediment. The bacteria contain grains of magnetite aligned in chains, as shown in Figure 7.12. The chain of crystals (and hence the bacterium) aligns along a magnetic field direction, which contains vertical and horizontal components (except at the poles). In the northern hemisphere, the bacteria move downwards by moving towards the north. In the southern hemisphere, the bacteria are south-seeking. The magnetic grains of magnetite in these bacteria contain single magnetic domains. Grains that are <5 nm in size are magnetised to saturation, whereas grains that are larger than 10 nm contain several magnetic domains. Nanotechnologists can take inspiration from nature's use of chains of magnetic particles as navigational aids.

The use of chemically modified versions of the iron storage protein ferritin in high-density magnetic data storage devices is the focus of current commercialization efforts. Ferritin is a nearly spherical protein with an 8 nm diameter core of ferrihydrite ($5Fe_2O_3 \cdot 9H_2O$). The core can be removed by reductive dissolution to produce the shell protein 'apoferritin'. The core can then be 'refilled' by incubation with metal salts, and subsequent oxidation. In this way, the core can be filled with magnetite (Fe_3O_4), which unlike the native ferrihydrite is ferrimagnetic at room temperature; the resulting ferritin is called magnetoferritin.

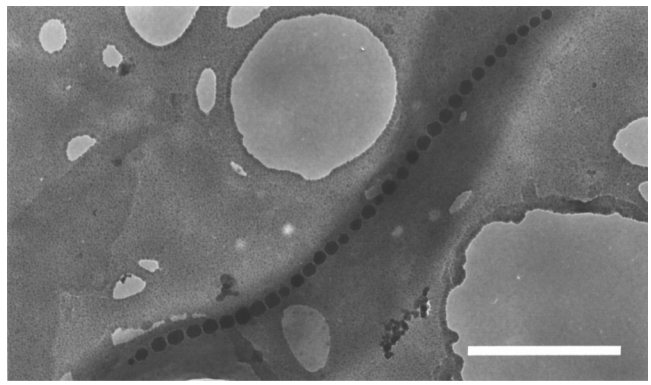

Figure 7.12 Chain of magnetite nanoparticles in a magnetotactic bacterium: scale bar = 500 nm. Reproduced from S. Mann, *Biomineralization: Principles and Concepts in Bioinorganic Materials Chemistry*, Oxford University Press, Oxford, 2001, with permission

7.4.7 Nano-objects

Nanoparticles with shapes other than simple spheres, shells or tubes have been prepared via soft material-mediated methods. The photoinduced conversion of silver nanospheres to silver nanoprisms has been reported. Photoinduced fragmentation of silver nanoparticles is believed to produce the single-crystal prism-shaped particles (whose faces correspond to planes of the crystal lattice). The growth habit of (nano)crystals can be controlled using organic agents such as surfactants (as well as through the degree of supersaturation or ionic strength), producing polyhedra with faces controlled by the growth rate of certain planes in the crystal unit cell. Nanoparticles of CdSe with rod, arrow, teardrop and tetrapod shapes may be fabricated by using surfactants to selectively control the growth of certain crystal faces. String and other superstructures of spherical nanoparticles may be prepared in the same way. Nature exploits soft materials to template the synthesis of hard nanostructures, as discussed further in Section 7.5.2, which includes examples of the intricate structures made by certain organisms. Self-assembled nanostructures may also be used to template the formation of helical nanoparticles (using peptides in solution) or of string, necklace or vesicular structures formed by block copolymers in solution.

The self-assembly of rod-coil block copolymers can, for example, be used to make mushroom-shaped nano-objects that assemble into lamellar stacks which show polar ordering.

7.5 TEMPLATED NANOSTRUCTURES

7.5.1 Mesoporous silica

The self-assembly of surfactants can be exploited to template inorganic minerals, such as silica, alumina and titania. The resulting structures resemble those of zeolites, except that the pore size is larger for the surfactant-templated materials than the pore size resulting from channels between atoms in classical zeolite structures. In conventional zeolites, the pore size is typically up to 0.1 nm, whereas using amphiphile solutions it is possible to prepare an inorganic material with pores up to several tens of nanometres. Such materials are thus said to be mesoporous. They are of immense interest due to their potential applications as catalysts and molecular sieves. Just as the channels in conventional zeolites have the correct size for the catalytic conversion of methanol to petroleum, the pore size in surfactant-templated materials could catalyse reactions involving larger molecules.

It was initially believed that the templating process simply consisted of the formation of an inorganic 'cast' of a lyotropic liquid crystal phase. In other words, preformed surfactant aggregates were envisaged to act as nucleation and growth sites for the inorganic material. However, it now appears that the inorganic material plays an important role, and that the structuring occurs via a cooperative organization of inorganic and organic material. Considering, for example, the templating of silica, a common method is to mix a tetra-alkoxy silane and surfactant in an aqueous solution. Both ionic and non-ionic surfactants have been successfully used to template structures,

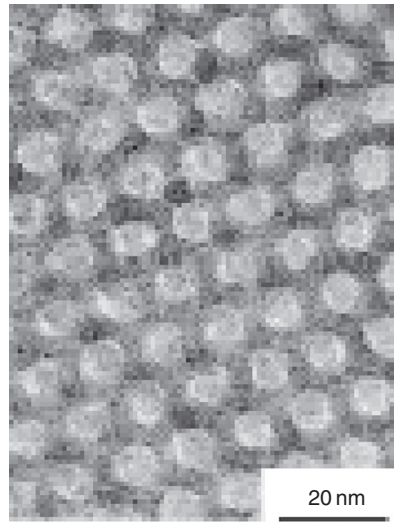

Figure 7.13 Hexagonal structure of calcined mesoporous silica, templated using an amphiphilic triblock copolymer. Reproduced from D. Zhao, J. Feng, Q. Huo, N. Melosh, G. H. Fredrickson, B. F. Chmelka and G. D. Stucky, *Science* **279**, 548 (1998)

as have amphiphilic block copolymers (these behave as giant surfactants, and enable larger pore sizes). The cooperative self-assembly process leads to a structure in which the silica forms a shell around amphiphilic aggregates, the latter being removed by calcination.

Figure 7.13 shows a hexagonal honeycomb pattern where the silica has been templated from a hexagonal-packed cylinder phase. Layered or bicontinuous structures have been prepared in a similar manner, by templating lamellar or bicontinuous phases, respectively. Similarly, highly monodisperse silica beads have been made by templating spherical micelles.

7.5.2 Biomineralization

Biomineralization involves the uptake and controlled deposition of inorganic moieties from the environment in biological systems. The main types of biominerals are the various forms of calcium carbonate (e.g., calcite and aragonite) and calcium phosphate. Calcium carbonate is the principal component of shells, which consist of an outer layer of large calcite crystals, and an inner region of layers of aragonite several hundreds of nanometres thick. Other marine organisms live within intricate exoskeletons formed from calcium carbonate. Examples include the so-called coccospheres (Figure 7.14). Calcium phosphate is the building material for bone and teeth, in the form of hydroxyapatite, which can be represented as $Ca_{10}(PO_4)_6(OH)_2$. Bone is formed by the organized mineralization of hydroxyapatite in a matrix of collagen fibrils and other proteins to form a porous structure. The mineral content controls the rigidity or elasticity of the bone. Tooth enamel also contains hydroxyapatite (more than in bone), and its ability to

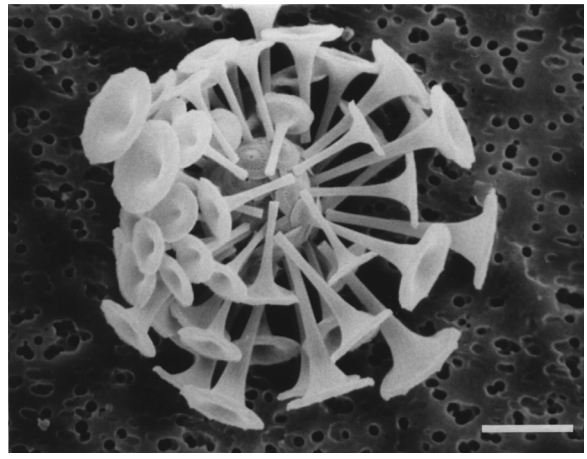

Figure 7.14 Example of a coccosphere. scale bar = 3 μm. Reproduced from S. Mann, *Biomineralization: Principles and Concepts in Bioinorganic Materials Chemistry*, Oxford University Press, Oxford, 2001

withstand abrasion results from a complex structure where ribbon-like crystals are interwoven into an inorganic fabric. A great deal of research activity is currently focused on the construction of artificial bone for replacement joints, and as scaffolds for tissue engineering. However, the porous macrostructure of bone is outside the nanodomain, and so this fascinating subject is not considered further here.

Unicellar organisms called radiolarians and diatoms produce their beautiful microskeletons (Figure 7.15) from amorphous silica. Lamellar aluminophosphates can also be

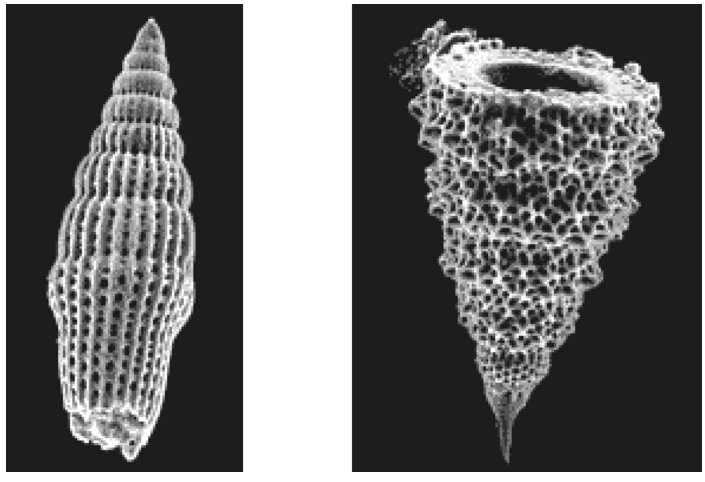

Figure 7.15 Examples of radiolarian microskeletons of length 330 μm (left) and 220 μm (right). Reproduced from www.ucmp.berkeley.edu/protista/radiolaria/radmm.html

templated to create patterns that mimic diatom and radiolarian microskeletons. Their nanoscale features are formed by the templated self-assembly of minerals via biological structures. In particular, the lace-like structures are formed from vesicles, packed together at the cell wall. The vesicles are arranged in a thin foam-like film, and biomineralization occurs in the continuous matrix.

7.5.3 Nanostructures templated by block copolymer self-assembly

Nanolithography using block copolymers is the subject of Section 8.7. The patterning of inorganic nanoparticles using block copolymer micelles adsorbed onto solute substrates is another exciting application of block copolymer self-assembly, as discussed in Section 7.4.1.

7.6 LIQUID CRYSTAL MESOPHASES

7.6.1 Micelles and vesicles

Micelles and vesicles formed by surfactants and block copolymers are widely used in systems as diverse as personal care products, agrochemicals and pharmaceuticals to solubilize fragrances, pesticides and herbicides, or drugs. Usually the aim is to solubilize organic compounds in the core of micelles in aqueous media.

The primary nanotechnology applications of micelles and vesicles result from their use as templates to synthesize nanoparticles with a multitude of structures and functionalities. Core cross-linking reactions to form organic nanoparticles containing functionalized coatings (tailored through the choice of corona chain) have also been used. In particular, cross-linking of the non-toxic biodegradable polylactide core of micelles with an end-functionalized poly(ethylene glycol) corona leads to sterically stabilized and biocompatible nanoparticles for drug delivery applications. Another approach is to cross-link the shell and remove the core, for example by ozone etching. Similarly, cross-linking the shell of a vesicle leads to hollow nanoparticles that can be used to encapsulate compounds.

As mentioned in Section 7.4.1, micelles can also be used as media for the production of inorganic nanoparticles. The synthesis of metal nanoparticles in aqueous block copolymer micelles has recently attracted a great deal of attention. Metal ions or complexes that are insoluble in water are sequestered in the micellar core. The block copolymer micelles containing the metal compounds then act as nanoreactors where, upon reduction, nucleation and growth of metal nanoparticles occurs. Applications of such metal nanoparticles are extensive, including catalysis, electro-optical materials (quantum dots) and in patterning of semiconductors. Using block copolymer micelles, it is possible to control the size of the particles by changing the copolymer composition and molecular weight. This is very important for the synthesis of magnetic nanoparticles, to ensure they are large enough to exceed the superparamagnetic limit but small enough to comprise a single domain (Section 4.1.4).

7.6.2 Lamellar phase

The lamellar phase (known as the smectic phase for low molar mass liquid crystals) is found in diverse systems, ranging from surfactants in solution to clays to block copolymers. The layered structures in clays and polymer–clay nanocomposites were discussed in Section 7.4.4. Here the focus is on recent examples of high-tech applications for lamellar phases in block copolymers.

Non-centrosymmetric structures can possess a macroscopic electric polarization, hence piezo- and pyroelectricity, as well as second-order non-linear optical activity. The fabrication of non-centrosymmetric stacks of block copolymer lamellae has been demonstrated in blends of ABC triblock and AC diblock copolymers. The structure is illustrated schematically in Figure 7.16. It is favoured over others (macrophase separated, random lamellar, centrosymmetric lamellar stack) if the asymmetry in aA and cC contact energies is large enough.

It has been proposed to exploit lamellar block copolymer structures to self-assemble all-polymer solid-state batteries, by using a triblock copolymer where the three blocks correspond to the anode, electrolyte and cathode. This has the advantage that leakage of toxic liquid electrolyte is avoided, and furthermore the processing is straightforward (e.g., spin coating of thin films). Similar applications of lamellar block copolymers in nanocapacitors and nanotransistors have also been envisaged.

Lamellar block copolymer nanostructures can be used as selective one-dimensional dielectric reflectors if the layer thickness is large enough (close to the wavelength of light) and the refractive index difference between blocks is large enough. Polystyrene–polyisoprene diblocks swollen with the corresponding homopolymers, for example, exhibit a limited angular range stop band at visible frequencies with potential applications in photonics; for instance in waveguiding.

Rod-coil diblocks can form a range of lamellar structures, as demonstrated by transmission electron microscopy images of polystyrene–poly(hexyl isocyanate) diblocks, which form wavy lamellar, zigzag and arrowhead morphologies. Distinct structures result because the rod block can tilt with respect to the layers, and the tilt can alternate between domains. The coupling of liquid crystal ordering to that of block copolymers extends considerably the range of nanostructures available to the nanotechnologist.

Inspired by a similar concept, it has been shown that ordering on multiple nanolength scales can be achieved in complexes of diblock copolymers and the amphiphilic long-chain alcohol pentadecylphenol (PDP). Hydrogen bonding of the alcohol to the

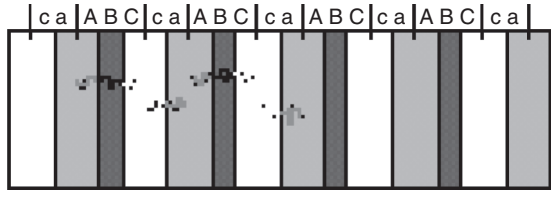

Figure 7.16 Schematic of a non-centrosymmetric lamellar structure observed in a blend of ABC triblock and AC diblock copolymers. Reproduced from T. Goldacker, V. Abetz, R. Stadler, I. Erukhimovich and L. Leibler, *Nature* **398**, 137 (1999)

–NH group in poly(4-vinylpyridine) (P4VP) produced a comb-like block, whereas no hydrogen bonding occurred to the coil-like polystyrene block. The usual ordered structures were observed due to microphase separation in the melt of the diblock, however, in addition, mesogenic ordering was observed within the P4VP–PDP phase due to formation of a lamellar structure below the liquid crystal–isotropic phase transition for the PDP. Since the lamellar–isotropic phase transition for the PDP–P4VP lamellae occurs below that for the PS–P4VP block copolymer, it is possible to switch off the lamellar ordering on one length scale independent of the other. It was shown that this transition was accompanied by a large change in the electrical conductivity (P4VP being a semiconducting side chain conjugated polymer). The potential to create switchable nanoscale structures with ordering in two and three dimensions has obvious implications in other applications such as alignment layers in liquid crystal displays, nanoscale sensors and optical waveguides.

7.6.3 ABC triblock structures

The phase behaviour of ABC triblocks is much richer than that of AB diblocks because there are two independent compositional order parameters and three Flory–Huggins interaction parameters (this expresses the energy of interaction between segments for the three different block combinations), the subtle interplay of which gives a varied morphospace. Figures 7.17 and 7.18 show examples of the intricate morphologies that are observed. A remarkable structure consisting of helices of minority polybutadiene domain wrapped around polystyrene cylinders in a PMMA matrix has even been reported.

State-of-the-art self-consistent mean field theory calculations have been used to predict a number of intricate nanostructures at the surface of ABC triblock copolymers (Figure 7.19). It should be noted that the patterns in Figure 7.19 are simulated in a 2D system. Due to confinement and surface energy effects, such morphologies may not be realizable at the surface of a bulk sample, however they could be accessed by sectioning of a glassy bulk sample. Potential exploitation of surface structures formed by ABC triblock copolymers can be envisaged when domains are selectively doped with metal or semiconductor; for example, Figure 7.6 shows patterning using a diblock copolymer. Applications include nanowire arrays for addressing nanoscale electronic devices or three-colour arrays for high-resolution displays.

7.6.4 Smectic and nematic liquid crystals

Conventional methods of fabricating liquid crystal displays are not usually regarded as nanotechnology. Present-day displays are based on nematics sandwiched in thin films between electrode-coated glass substrates. The supertwist nematic (STN) is used in low-cost small displays, for example in watches and calculators. Its principle of operation relies on the Fréedericks transition, in which the orientation of molecules (on average defined by a director) is switched by application of an electric field. In the STN, the orientation of the director in the off state is induced to follow a helix by the use of perpendicularly oriented grooves in the glass plates used to sandwich the liquid crystal.

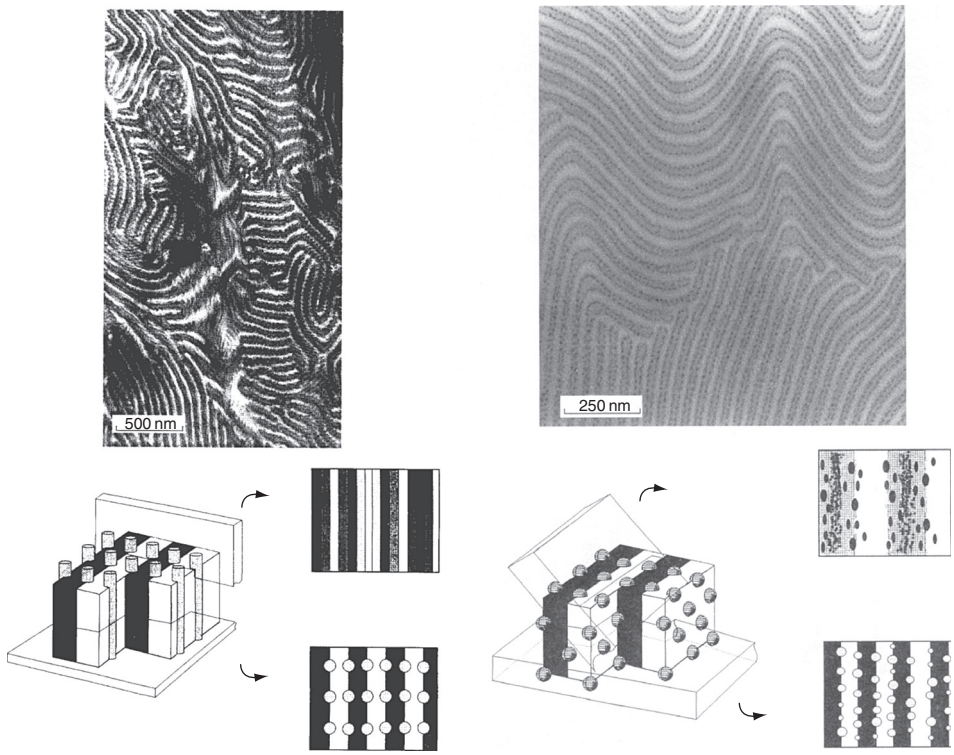

Figure 7.17 Examples of morphologies observed for polystyrene-*b*-polybutadiene-*b*-polymethylmethacrylate triblock copolymers with a minority midblock component. Left: cylinders at a lamellar interface, Right: spheres at a lamellar interface ("ball at the wall" morphology). The upper images are transmission electron micrographs. The lower figures are schematic diagrams. Reproduced from R. Stadler, C. Auschra, J. Beckmann, U. Krappe, I. Voigt-Martin and L. Leibler, *Macromolecules* **28**, 3080 (1995)

In the on state, the molecules align along the electric field lines, perpendicular to the glass plates. TFTs operate on the same principle, but each element of the display is individually addressed using a thin film transistor.

The fabrication of a liquid crystal display on a single substrate, which could ultimately lead to flexible or paintable displays has recently been demonstrated based on an array of encapsulated liquid crystal cells. Stratified polymer structures self-assemble through phase separation of a photopolymerizable prepolymer and a nematic liquid crystal. Horizontal stratification creates the walls of the cells and vertical stratification (using a different wavelength of UV) produces lids. At present, the technique has been used to fabricate micron-sized polymer cells, although extension to the nanoscale using harder radiation should be feasible.

Usually a nematic phase is cloudy due to light scattering from fluctuating micron-sized domains with different orientations (creating refractive index variations, since the refractive index of liquid crystal phases is anisotropic). Nanometre-scale phase-separated structures formed in a lyotropic structure of surfactant micelles in a liquid crystal matrix have been shown to lead to a transparent nematic phase. In the nanoemulsion, the

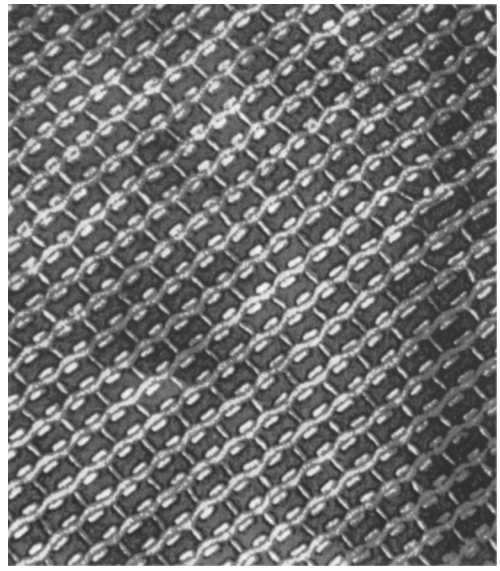

Figure 7.18 'Knitting pattern' morphology observed by TEM on a polystyrene-*b*-poly(ethylene-co-butylene)-*b*-poly(methylmethacrylate) triblock copolymer (stained with RuO_4). Reproduced from U. Breiner, U. Krappe, E. L. Thomas and R. Stadler, *Macromolecules* **31**, 135 (1998). Also used as cover of *Physics Today*, February 1999

droplets of surfactant disrupt the long-range orientational order of the nematic phase, leading to optical isotropy and transparency, although the local nematic ordering is retained. Mixing spherical colloidal particles with liquid crystal likewise produces a phase-separated structure as colloidal particles are expelled from nematic droplets

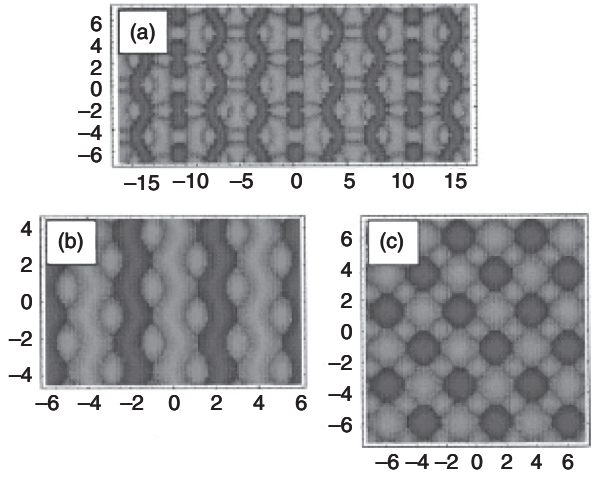

Figure 7.19 Examples of predicted morphologies for linear ABC triblock copolymers, from self-consistent mean field calculations. Reproduced from Y. Bohbot-Raviv and Z.-G. Wang, *Phys. Rev. Lett.* **85**, 3428 (2000)

below the isotropic–nematic phase transition temperature. The particles are expelled because the trapping of defects in the nematic phase by colloidal particles has too high an energy penalty. The colloid particles therefore separate into an interconnected network (the struts of which are several nanometres thick). The result is a waxy soft solid with a high storage modulus.

7.6.5 Discotic liquid crystals

Columnar phases formed by discotic liquid crystals such as those based on triphenylenes form one-dimensional conductors, due to the overlap of π^* orbitals of the aromatic moieties which are surrounded by a hydrocarbon insulator coating. Each column thus acts as a nanowire, and applications in molecular electronics have resulted, in particular in gas sensors. They could also be used in molecular electronic devices, for example in electroluminescent displays or in three-dimensional integrated circuits.

7.7 SUMMARY AND OUTLOOK

Self-assembly is responsible for nanostructure formation in colloidal, amphiphilic, polymeric and biomolecular materials. In this chapter, the principles of self-assembly in synthetic and biological systems were first considered. Then selected examples of self-assembly routes to the production of nanostructures and nanodevices were presented. A key theme is that self-assembly in soft materials (synthetic and biological) can be used to template nanostructures in inorganic matter, either in bulk or at a surface. The range of structures that can be fabricated in equilibrium depends (following the Gibbs phase rule) on the number of components in the system. In the case of ABC triblock copolymers this leads to a large number of possible nanostructures with different symmetries. An additional complexity in phase behaviour results from the coupling of distinct types of order, for example orientational order of liquid crystals with translationally ordered block copolymer nanostructures.

Out-of-equilibrium processes can also be exploited, for example in nanoscale motors or actuators. Actually, out-of-equilibrium structures may also be useful, since they could be captured when templating a hard material. It has to be kept in mind that the rich structural diversity and access to out-of-equilibrium structures are both different aspects of the weak ordering due to non-covalent interactions that characterizes soft materials.

Many developments are under way to exploit self-assembling soft materials in nanotechnology. The first commercial nanostructures are likely to be nanoparticles fabricated in micellar or vesicular nanoreactors, and mesoporous templated materials for catalysts and separation media. Uses of more intricate structures such as those formed by ABC triblock copolymers are still some way off. Downstream applications of biomineralization (in prostheses, artifical bone and teeth) are less distant. The development of drug delivery systems using functionalized nanoparticles is also the subject of intense research activity at present. This is only a flavour of the many different

approaches being investigated. The use of block copolymer films in nanolithography (Section 8.6.2) and to pattern nanoparticles into regular arrays are the focus of much attention.

Arguably the most important nanodevice is the nanomotor, and self-assembly routes to the production of simple oscillating 'motors' have already been developed. To fabricate directional motors with a renewable energy source, inspiration is being taken from nature, where ATP synthesis underpins distinct linear and rotory motors. This is discussed in more detail in Chapter 9. Supramolecular chemistry also has much to offer here, although this is outside the scope of the present chapter. Other nanodevices will contain passive nanostructures which can be built using self-assembly, examples including waveguides and optical filters. Nanowires and ferroelectric piezo- and pyro-electric structures can also be produced. Self-assembled nanocapacitors and nanotransistors can also be envisaged, although as yet there has been little research in this area. Using a combination of self-assembled nanostructure elements from the broad palette available, together with a suitable power source (e.g., nanostructured polymer solid-state battery) a customized nanodevice could readily be put together. The prime limitation is that certain non-periodic structures require atomic or molecular manipulation, outside the realm of self-assembly.

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