Meso-Scale Self-Assembly

David H. Gracias, *Harvard University, Cambridge, MA*
Insung Choi, *Harvard University, Cambridge, MA*
Marcus Weck, *Harvard University, Cambridge, MA*
George M. Whitesides, *Harvard University, Cambridge, MA*

This paper describes the application of self-assembly to the formation of structured aggregates (both static and dynamic) of millimeter sized objects. We argue that MEso-scale Self-Assembly (MESA) provides a framework for fabricating two- and three- dimensional structures (with objects ranging in size between 10 nm and 10 mm), and illustrates broadly important principles underlying the behavior of complex, natural systems.

1 Introduction

Self-Assembly is the spontaneous organization of molecules or objects, under steady state or equilibrium conditions, into stable aggregates, by non-covalent forces; these aggregates are not necessarily at the global minimum in energy [14, 15]. Meso-Scale Self-Assembly (MESA) refers to self assembly carried out with objects ranging in size from 10 nm to 10 mm using forces having lateral extension with similar size [8, 6, 1, 9, 12, 17, 13, 7, 4, 11]. MESA bridges the gap between molecular self-assembly (e.g. crystallization [16]; and protein-ligand recognition [10]) and the conventional fabrication of macroscopic machines. This paper briefly outlines the most important concepts governing self-assembly at these length scales. It also describes the application of MESA in (a) fabricating artificial crystals and three dimensional structures [9, 12, 17], (b) mimicking molecular self assembly [4, 11, 3, 5], and (c) designing dynamical systems that show tailored complexity [2].

2 Forces

We begin by describing two static systems; in these systems, the capillary interactions between individual units are responsible for MESA. (i) One system uses MESA to form 2D aggregates. It employs selective patterning of the faces of the object into hydrophilic and hydrophobic sets. These objects self assemble, while floating at the interface between a hydrophobic liquid (perfluorodecalin, PFD) and a hydrophilic one (water) [6, 1]. In this system, PFD wets the hydrophobic faces and forms "positive" menisci (menisci that extend above the plane of the interface); water wets the hydrophilic faces and forms "negative" menisci (menisci that extend below the plane). Menisci of the same shape interact attractively with each other, while a mismatch in the shape of the menisci results in weak or repulsive interactions between the objects. Since capillary forces have decay lengths on the order of millimeters to nanometers, they can be used to assemble objects across this range of sizes. (ii) The second system uses MESA to form three-dimensional (3D) aggregates. In this system liquid films (e.g. of low melting-point alloys [9], or polymeric adhesives [12]) coat the faces of the assembling units. These films have a high interfacial free energy in contact with water. When two faces come into contact, the films coalesce; this coalescence minimizes the exposed area of the interface and decreases the free energy of the system.

We also describe a system based on dynamical self-assembly [2] that incorporates a combination of attractive and repulsive forces. In this system, millimeter-sized magnetic disks are placed at a liquid-air interface, and subjected to the magnetic field produced by a rotating permanent magnet. The attractive forces occur between the magnetic units and the rotating magnet. The repulsive forces are due to hydrodynamic interactions associated with vortices in the fluid in the vicinity of the individual spinning magnets.

3 Two-Dimensional MESA

We assembled two-dimensional (2D) aggregates using pieces made of PDMS, an organic polymer: polydimethylsiloxane; (density = 1.05 g/mL) at the PFD (density = 1.91 g/mL) /water (density = 1.00 g/mL)
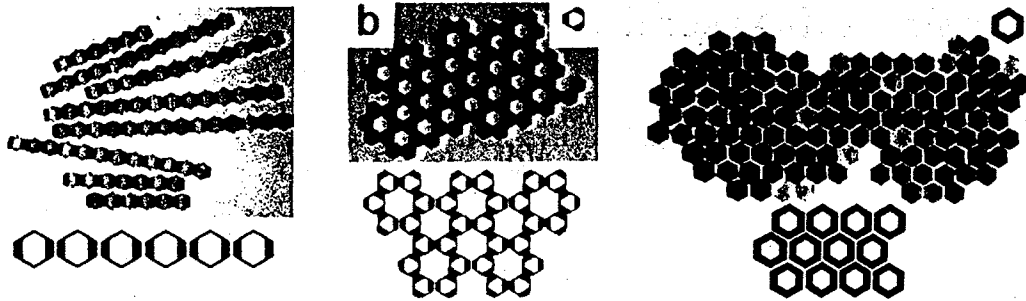
Figure 1: *Photographs of self-assembled arrays of hydrophobically patterned hexagons, floating in the plane of the PFD / water interface, and agitated by an orbital shaker. All the hexagons have centrosymmetric patterns of hydrophobic faces; the dark faces are hydrophobic, while the light ones are hydrophilic. (A) Two faces (opposite) of individual hexagons are hydrophobic; this pattern results in a linear array on assembly. (B) Alternate faces of individual hexagons are hydrophobic; this pattern generates a porous 2D array. (C) All the faces of individual hexagons are hydrophobic; this pattern generates a 2D, close-packed array.*


⊔⊔⊔⊔⊔⊔ 1 cm

Figure 2: *3D assemblies containing 300 cubes. All the faces of the individual cubes were coated with a hydrophobic polymer; assembly was carried out in water.*

interface [6, 1, 7, 4, 11]. The PDMS objects assembled upon agitation using an orbital shaker. We chose this interface for four reasons: (a) PDMS does not swell in contact with either liquid; (b) capillary forces at the interface are strong (interfacial energy=0.05 J/m^2); (c) PDMS has a density intermediate between that of water and PFD, and the pieces therefore float at the interface; (d) a thin film of PFD remains between the faces of the objects when they assemble, and acts as a lubricant; this film allows the objects to move laterally relative to one another, and minimizes the free energy of the system. Figure 1 shows photographs of aggregates formed with different hexagonal units at the PFD/water interface.

4 Three-Dimensional MESA

MESA also provides an alternate strategy for the fabrication of 3D microstructures. We assembled large,

regular arrays (crystals) of millimeter sized polymeric polyhedra. The faces of these polyhedra were coated with either a photocurable adhesive [12] or molten solder [9]. When these liquid-coated polyhedra were suspended in water and agitated, collisions between them allowed contact and coalescence of the liquid films; this coalescence minimized the interfacial area between the hydrophobic liquid and water, and provided the thermodynamic driving force for the self-assembly. In experiments using pieces coated with photocurable adhesive, after self-assembly was complete, the structures were exposed to UV radiation; this exposure cured the lubricant and gave the aggregates sufficient mechanical strength that they could be manipulated and characterized. Figure 2 shows assembled 3D structures that contain 300 cubes; these structures formed from suspensions of 1000 cubes, using a photocurable adhesive. Figure 3 shows 3D porous structures formed by the as-
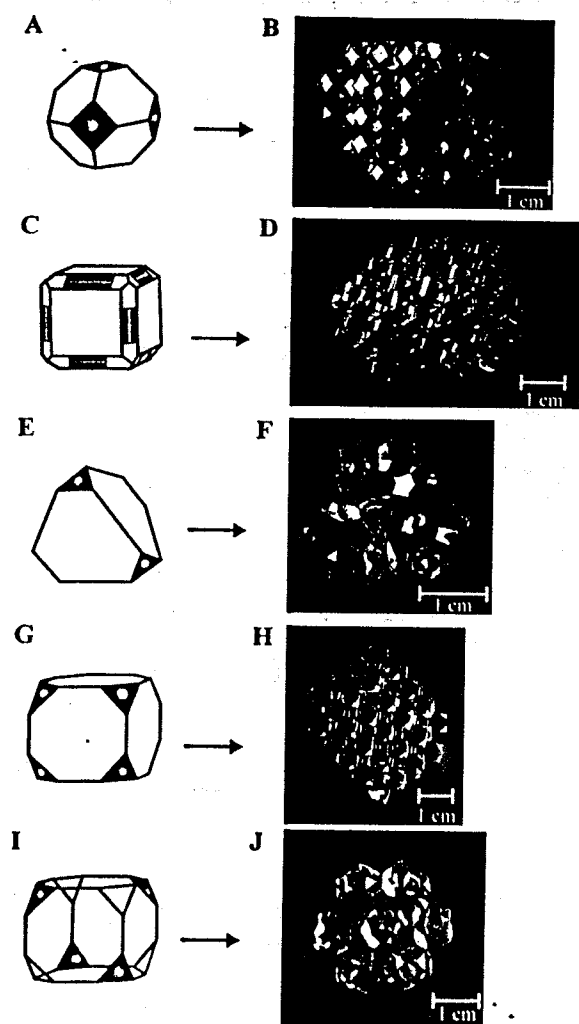
Figure 3: *3D self-assembly of porous structures using a high surface tension, low-melting point solder. Polyhedra on the left, (dark regions represent areas covered with solder) assembled into the structures shown on the right.*

sembly of polyhedra whose faces were covered with a solder having high interfacial tension with water.

5 Molecule-Mimetic Self-Assembly: Hierarchical and Templated MESA

One of the most interesting applications of MESA is as a vehicle with which to abstract and illustrate important concepts in self-assembly modeled on those exhib-

ited by molecules and to use them to join mesoscale objects. Examples of processes that have been abstracted from organic and biological chemistry and used in MESA include hierarchical [4] and templated [3] self-assembly, and DNA recognition [5]. We describe results of these experiments carried out at the PFD / water interface through the interaction of hydrophilic and hydrophobic menisci as described earlier.

The optical photographs in Figure 4 illustrate the translation of the molecular concepts of hierarchical and templated self-assembly into the mesoscopic world. The results shown in Figure 4A demonstrate hierarchical self-assembly. Two interactions of different strengths were responsible for the self-assembly. Initially, a strong capillary interaction between hydrophobic faces formed structures containing four components; a weaker interaction between the concave hydrophobic faces subsequently caused aggregation into larger structures. Figure 4B illustrates templated MESA. These objects interacted among themselves through concave hydrophobic regions; the self-assembly was directed using round, hydrophilic objects (the templates). On addition of the templating structures, the system formed the inclusion structures shown in Figure 4B; inclusion of these templates strengthened and extended the hexagonal lattice in these structures. We observed that the formation of the cyclic structures began with the pre-orientation of the trefoil objects around the circular template, followed by the self-assembly of these trefoil objects.

6 Biomimetic MESA: Models of DNA Recognition

Figure 5A, B, and C are photographs illustrating a model of sequence-specific assembly: this model is based on sequence specific molecular recognition in DNA and RNA. In particular it is based on a long strand, a specific sequence of which can be recognized by a short probe with a complementary sequence. These strands are based on individual objects containing hydrophobic lock and key functionalities that are connected via a PDMS thread. The two strands associated by pairing at the complementary sequences, with probabilities that clearly illustrate the principle, but are much lower than corresponding molecular systems.

This process is the first, primitive step toward modeling the formation of double-stranded DNA by the
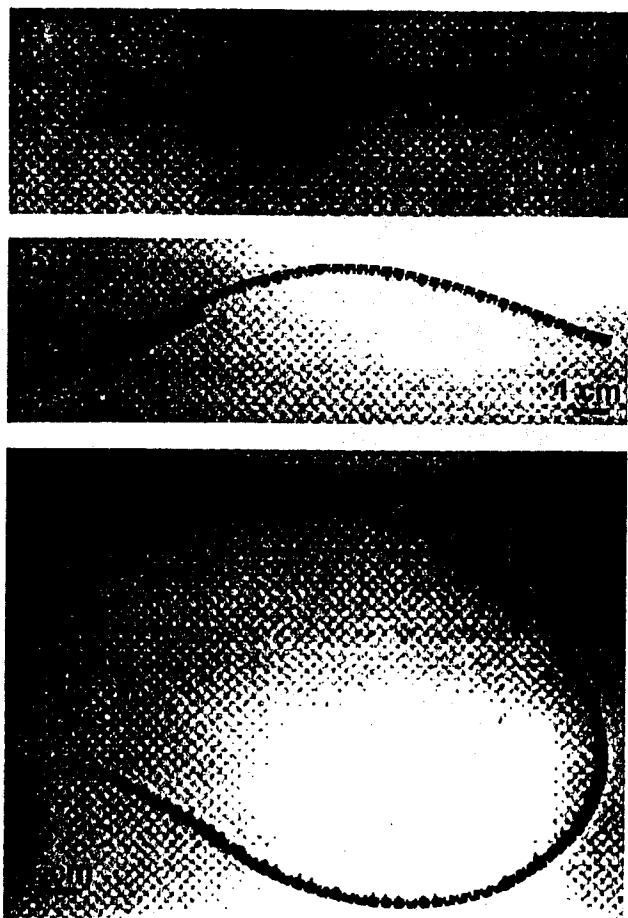
D. H. Gracias, I. Choi, M. Weck, and G. M. Whitesides
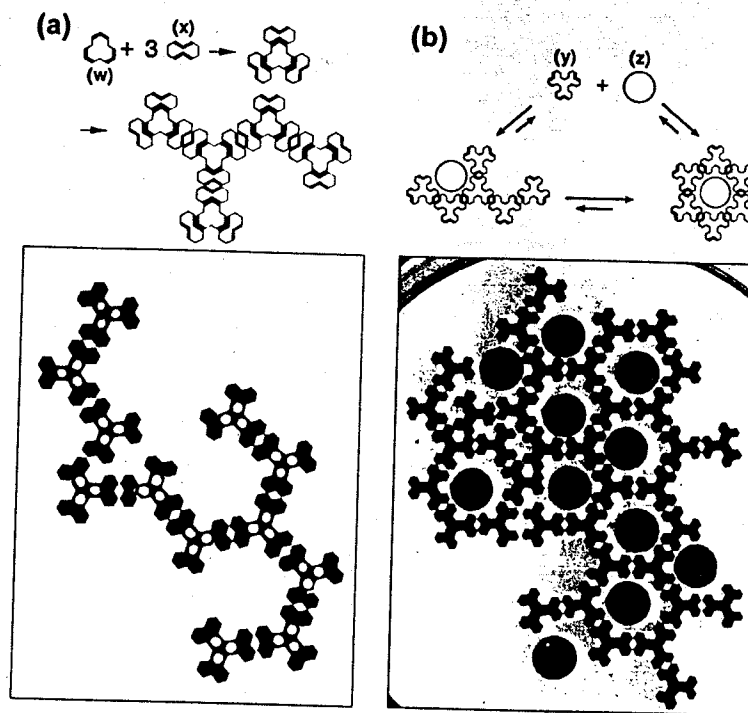
Figure 4: *(A) Hierarchical MESA in 2D. Initially four pieces (one (w) and three (x)) aggregate via strong capillary interactions at the hydrophobically patterned faces (dark regions). A weaker capillary interaction between two concave hydrophobic faces enables these small aggregates to grow into larger structures. (B) Templated MESA in 2D. Eleven circular pieces (z), act as templates around which 37 pieces (y), assemble into cyclic hexamers through capillary interactions at the hydrophobic patterned faces (dark regions).*

association of short sequences of single-stranded DNA. Although this model has obvious limitations, it contains several features analogous to molecular systems, including cooperativity, directionality, and sequence specificity.

7 Dynamic Self-Assembly

We have also examined dynamic self-assembly systems, that is, systems that develop order only when dissipating energy. These systems are particularly interesting for their possible relevance to issues of complexity and emergence and ultimately, perhaps to understanding very complex systems, such as the cell. Here we describe the formation of dynamic patterns of unexpected regularity and complexity by millimeter-sized magnetic disks subjected to a rotating magnetic field
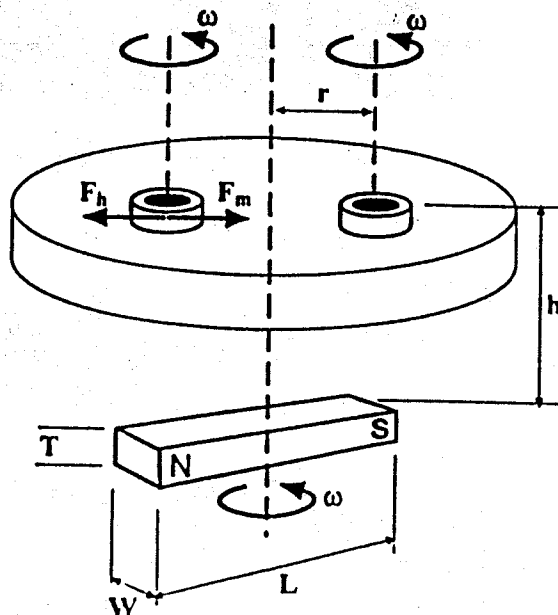
and spinning at the liquid-air interface. Circular disks made up of PDMS doped with magnetite (1 mm inner diameter, 400 μm thick) were placed in a dish filled with a liquid (typically ethylene glycol/water or glycerin/water with kinematic viscosities 1-50 cp). A bar magnet (5.6 cm x 4 cm x 1 cm) was then rotated below the dish (2.4 cm below the air-liquid interface), at an angular velocity of 200-1200 r.p.m. Figure 6 is a schematic diagram of the experimental set-up. Figure 7 shows the dynamic patterns formed with different numbers of disks. A variety of patterns were observed, ranging from unnucleated (n<5) to nucleated (n>5) to bistable patterns (n=10, 12). The wealth of phenomena displayed by this system makes it a good one to study complexity: the interactions involved are simple enough to be studied in detail but the patterns are far from obvious.

Figure 6: *The scheme of the experimental setup for the dynamic self-assembly. A bar magnet rotates below a dish filled with liquid. Magnetically doped disks are placed on the interface, and are fully immersed in the liquid except for their top surface. The disks spin around their axes. A magnetic force (F_m) attracts the disks towards the center of the dish, and hydrodynamic force (F_h) pushes them apart from each other.*

Figure 5: *Examples of a two-dimensional model for sequence-specific self-assembly. In all three cases, a long strand and a short probe were placed at the water/PFD interface and swirled at a frequency of 60 r.p.m. on an orbital shaker. These objects interacted through hydrophobic lock and key structures. Self-assembly between the long strand and the probe at a pre-determined recognition site took place with high probability, in less than two hours. Figures show the self-assembled structures based on sequence-specific recognition between (a) a 22-membered single strand and a seven-membered probe, (b) a larger 50-membered single strand and an eight-membered probe, and (c) the largest single strand examined (100-membered) and a nine-membered probe.*

Acknowledgments

References

[1] A. Terfort, N. Bowden, and G. M. Whitesides. Three-dimensional self-assembly of millimeter-scale components. *Nature*, 386:162–164, 1997.

[2] B. A. Grzybowski, H. A. Stone and G. M. Whitesides. Dynamic self-assembly of magnetized, millimeter-sized objects rotating at the liquid-air interface. *Submitted.*

[3] I. S. Choi, M. Weck, B. Xu, N. L. Jeon and G. M. Whitesides. Mesoscopic templated self-assembly at the fluid-fluid interface. *Langmuir.* (In Press).
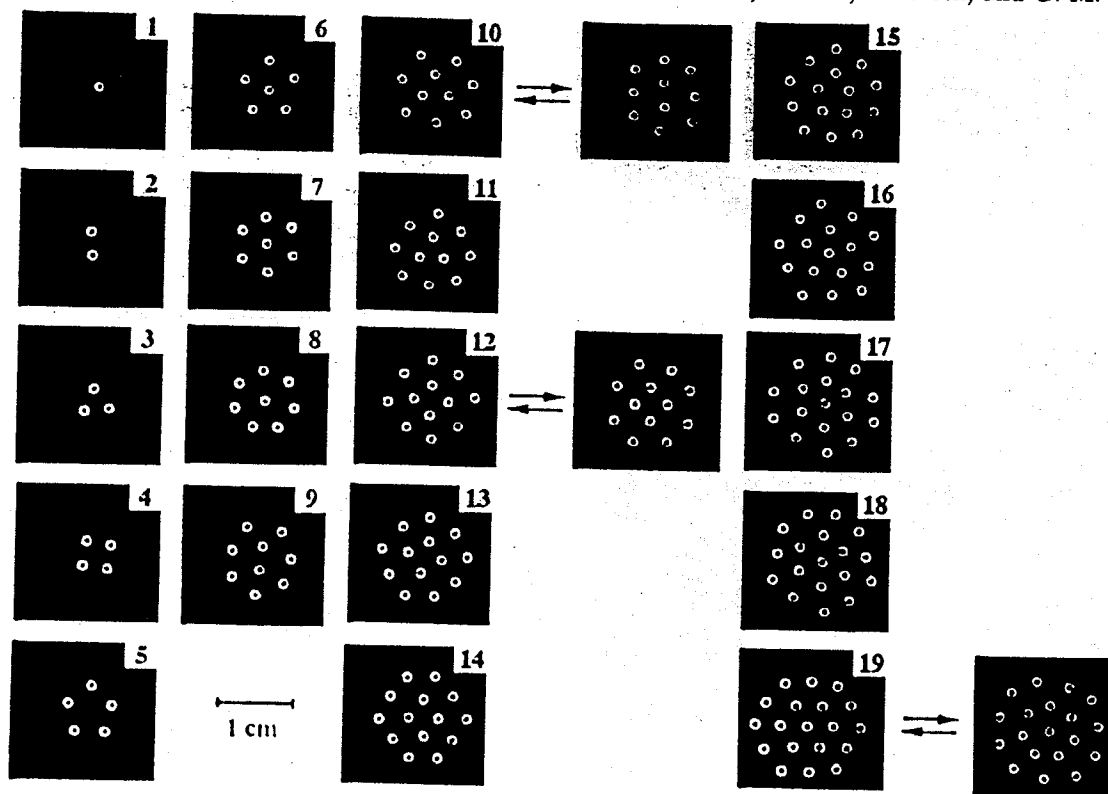
Figure 7: *The dynamic patterns formed by various numbers (n) of disks rotating at the ethylene glycol-air interface, 27 mm above the plane of the external magnet. The disks are composed of polyethylene shell (white) of outer diameter 1.27 mm, filled with PDMS doped with 25 % w/w of magnetite (black core). All disks spin around their centers at $\omega = 700$ r.p.m, and the entire aggregate slowly (<2 r.p.m.) precesses around its center. For $n<5$, the aggregates do not have a "nucleus"-all disks are precessing on the rim of a circle. For $n>5$, nucleated structures appear. For $n=10$ and $n=12$, the patterns are bistable in the sense that the two observed patterns interconvert irregularly with time. For $n=19$, the hexagonal pattern (left) appears only above ω 800 r.p.m., but can be "annealed" down to 700 r.p.m. by slowly decreasing the spinning rate. Without annealing, a less symmetric pattern exists at $\omega = 700$ r.p.m.*

[4] I.S. Choi, N. Bowden and G. M. Whitesides. Macroscopic, hierarchical, two-dimensional self-assembly. *Angewandte Chemie International Edition*, 38:3078–3081, 1999.

[5] M. Weck, I. S. Choi, N. L. Jeon and G. M. Whitesides. Assembly of mesoscopic analogs of nucleic acids. *Journal of the American Chemical Society.* (In Press).

[6] N. Bowden, A. Terfort, J. Carbeck and G. M. Whitesides. Self-assembly of mesoscale objects into ordered two-dimensional arrays. *Science*, 276:233–235, 1997.

[7] N. Bowden, I. S. Choi, B. A. Grzybowski and G. M. Whitesides. Mesoscale self-assembly of hexagonal plates using lateral capillary forces: Synthesis using

the "capillary bond". *Journal of the American Chemical Society*, 121:5373–5391, 1999.

[8] P. A. Kralchevsky and K. Nagayama. Capillary forces between colloidal particles. *Langmuir*, 10:23–36, 1994.

[9] T. L. Breen, J. Tien, S. R. J. Oliver, T. Hadzic and G. M. Whitesides. Design and self-assembly of open, regular, 3d mesostructures. *Science*, 284:948–951, 1999.

[10] M. M. C. A. L. Lehninger, D. L. Nelson. . *Principles of Biochemistry 2nd Ed.* Worth Publishers, 1993.

[11] I. S. Choi, N. Bowden and G. M. Whitesides. Shape-selective recognition and self-assembly of mm-scale components. *Journal of the American Chemical Society*, 121:1754–1755, 1999.

[12] T. L. B. J. Tien and G. M. Whitesides. Crystalliza-tion of millimeter-scale objects with use of capillary forces. *Journal of the American Chemical Society* , 120:12670–12671, 1998.

[13] N. B. Y. X. L. Isaacs, D. N. Chin and G. M. Whitesides. *Self-assembling Systems on Scales from Nanometers to Millimeters: Design and Discovery*. D. N. Reinhoudt, John Wiley and Sons, New York, 1999.

[14] J.-M. Lehn. *Supramolecular Chemistry: Concepts and Perspectives: A Personal Account.* VCH: Weiheim, 1995.

[15] M. V. M. M. Mrksich and G. M. Whitesides. *Using Self-Assembled Monolayers to Study the Interactions of Man-Made Materials with Proteins; 2nd ed.* Landes Co.: Austin, TX, 1997.

[16] J. W. Mullin. *Crystallization.* London, Butterworths, 1961.

[17] W. T. S. Huck, J. Tien and G. M. Whitesides. Three-dimensional mesoscale self-assembly. *Journal of the American Chemical Society*, 120:8267–8268, 1998.