Chemical Processing by Self-Assembly

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Introduction

Self-assembly is a spontaneous process, guided by information content intrinsic to the assembling units, in which multiple levels of structural organization are built into a product (Kuhn and Ulman, 1995). Owing to the complexity of structures formed and the nominal ease of spontaneous organization, self-assembly is increasingly being examined as a practical chemical processing method. It is akin to crystallization except that the complexity of the structural elements involved is greater in self-assembly and length-scales beyond a single lattice constant emerge in the product. In some cases, self-assembly can result in intricate, interlocking and useful architectures of matter. The resultant structures are being actively explored as new materials, surface treatments, catalysts, membranes, photonic materials, and electronic devices, to name a few areas of current engineering exploration. Self-assembly is one of the key mechanisms by which nature builds products from biological molecules such as proteins to such larger structures as cells and extracellular matrices, and the spatial arrangement of atoms is determined, in large part, by information built into the assembling units.

Table 1. Processes Incorporating Self Assembly

- Adsorption of multicomponent polymers
- Cooperative supramolecular self-assembly of surfactant-inorganic mesostructures
- Grafting of polymers on interfaces
- Langmuir-Blodgett deposition
- Layer-by-layer deposition or sequential adsorption
- Micellar control of reactions
- Microcontact printing
- Organizing colloids into arrays and crystals
- Self-assembly of monolayers
- Spin and dip coating of supramolecular solutions and dispersions
- Surface directed ordering of molecules at interfaces (liquid crystals)
- Surface modification by monolayer or multilayer deposition
- Templating
- Vesicle fusion

The ability to form structures spontaneously from the bottom up, using principles akin to biological assembly, has inspired considerable research among chemists, physicists, and chemical engineers to develop useful products (Whitesides et al., 1991). The high level of scientific activity in this field creates several kinds of major opportunities for chemical engineering research. The overall opportunity might be characterized as a shift from *product* to *processing* research in self-assembly. As self-assembly attempts to evolve from laboratory techniques and provocative demonstrations of structure, to practical, larger-scale, applied processing methods, a broad spectrum of important engineering research problems is being generated.

Opportunities for new chemical engineering research in self-assembly are the focus of this article. This requires, among other matters, taking self-assembly seriously as a processing method and asking, "What are the barriers to its development and widespread implementation?" This review takes a processing perspective, appropriate to motivate this underdeveloped field of chemical engineering research. A recent review (Schreiber, 2000) from a surface science perspective describes the current state of laboratory growth methods and structural characterization comprehensively, for the case of self-assembled *monolayers*. An up-to-date review on three-dimensional self-assembled *structures* has yet to be written. This article aims at *processing* 2-D and 3-D self-assembled structures.

An important characteristic of self-assembly processing, which changes both the chemistry and chemical engineering research perspective, is that the fundamental objects participating in the process are, more often than not, neither simple atoms nor simple molecules. Rather, they are modular, prefabricated, complex molecules or objects with some internal structure. This internal structure is the information content of the assembler. Colloidal crystallization of structured particles typifies the process of developing organized assembly of complex, multimolecular objects. The rules of chemical bonding (interaction potentials) and chemical kinetics for reactions among objects such as these to form stable, useful products remain to be thoroughly explored to form a good basis for process development.

Brief summary and critique of the state-of-the-art of self-assembly processing

Numerous processes developed for producing chemical products, surface layers, or new materials by self-assembly are given in Table 1—a substantial, but not exhaustive, list. What is included and omitted, as well as why it is warranted are discussed briefly. Adsorption of polymers consisting of identical units—*homopolymers* (not on the list)—is a widespread and effective practical method to modify materials surfaces. It, however, is a random process without any particular guidance to the assembly coming from the molecular structure, and, therefore, it lacks an important ingredient in the definition of self-assembly. On the other hand, in the adsorption of *multicomponent polymers*, such as block copolymers or hydrophobically modified polymers, some pieces of the molecule are driven by their chemical nature to stick to interfaces, while others are not. The resulting molecular arrangement is directed by information (internal structure) in the adsorbing molecules.

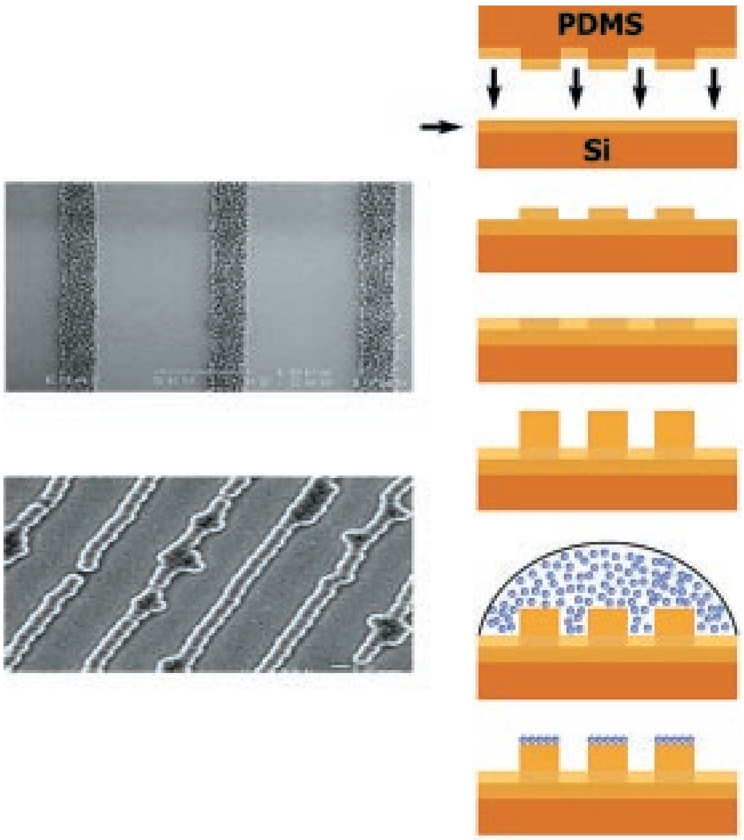

Figure 1. Extension from molecular to microscale systems. Selective self-organization of charged colloid particles using patterned multilayers as templates. Initial patterning done with microcontact printing, followed by layer-by-layer assembly, with the final step incorporating electrostatic assembly of nanoparticles. SEM and drawing courtesy of Paula Hammond, Massachusetts Institute of Technology.

Some of the processes in Table 1 have been known for quite some time (e.g., Langmuir-Blodgett deposition); others have been developed in the last decade (e.g., microcontact printing). Note that by definition, in our parlance, a self-assembly process, while being largely controlled by the chemical architecture of the assemblers, may have elements that are neither spontaneous nor inherent in the assembling entities. That is, some of them are *directed assembly* processes, which may incorporate nonthermodynamic influences (dipping, printing, spinning, quenching, etc.) or effects of external influences (templates, surfaces, fields, etc.). In fact, the effective use of these influences will be one of the most important issues in developing practical self-assembly processes. This article does not make a sharp distinction between purely *self*-assembly processes and *directed*-assembly processes. In both cases, the information content of the assembling objects plays a major role.

The practical history of Langmuir-Blodgett deposition as a processing method (Swalen et al., 1987) offers a sharp focus, and possibly a sobering shadow, on the future of self-assembly processing. Langmuir-Blodgett processing has never been an important practical technology, despite its widespread utility and unique capability of controlling structure in *laboratory-scale materials assembly*, owing among other things to the difficulty in scaling up the process via continuous, parallel or repetitive processing. As we shall see, continuous processing has been achieved in a few examples of self-assembly processing.

One promising self-assembly method that seems to lend itself to scale-up and to continuous processing, and also possesses great versatility in the range of components that can be used in the process, is layer-by-layer growth (LbL), pioneered by Decher and coworkers, and now much more broadly explored (Decher, 1997). It works by successive dipping cycles of substrates into solutions of molecules with some interactive complementarity (usually of opposite charge). Möhwald and coworkers have generalized this method to LbL on particle surfaces (Caruso et al., 1998; Caruso and Möhwald, 1999) developing the capability, after destruction of the templating particle (usually by dissolution), to make self-assembled capsules with controlled structure, contents and wall properties (mechanical and transport). Destruction of an *organic* template to leave a self-assembled inorganic material has proven a very effective route to new porous materials for catalysts, sorbents, and membranes (Asefa et al., 1999; Melde et al., 1999; Freemantle, 2000).

Microcontact printing (MCP) is another burgeoning laboratory-scale method incorporating self-assembly (Kumar et al., 1994). In the basic application of this methodology, a stamp is "inked" with a self-assembled layer. The stamp is then used in MCP processing to transfer the self-assembled material to another surface. The possibilities for making MCP an efficient, versatile, even continuous process seem very achievable, based as it is on classical printing technology. Clearly, many of the processes in Table 1, MCP included, are not purely self-assembly, or even directed-assembly, processes, but involve the intervention of some other processing techniques in concert with self-assembly. A very likely outcome of much of current nanoscale processing research is self-assembly used as one method in a multistep process. This would characterize such methods as micellar or microemulsion controlled reactions, as well as a range of "hybrid" self-assembly processes. Figure 1 shows the product of a hybrid

LbL-MCP process, followed by the deposition of a layer of colloidal particles (Chen et al., 2000). Other hybrid processes include ink-jet printing followed by a self-assembly process such as vesicle fusion (Cremer and Boxer, 1999), and biological production of self-assembled products (Cha et al., 2000; Belcher et al., 1996; Yu et al., 2000).

Most of the current self-assembly processing methods function primarily to create surface and thin-film structures (LB, LbL, multicomponent polymer adsorption, etc.). This 2-D emphasis derives both from the many applications for surface modification and for the templating assistance, which surfaces generally offer self-assembly processes. Nevertheless, much more work is needed in the direction of 3-D self-assembly methods. As work in colloidal crystallization has shown, not only is 3-D assembly of preformed, supermolecular objects a route to materials with interesting new structures and properties (Velev et al., 2000) (Figure 2), but also studying the crystallization of objects reveals considerable new insight into the interobject potentials (Davis et al., 1989).

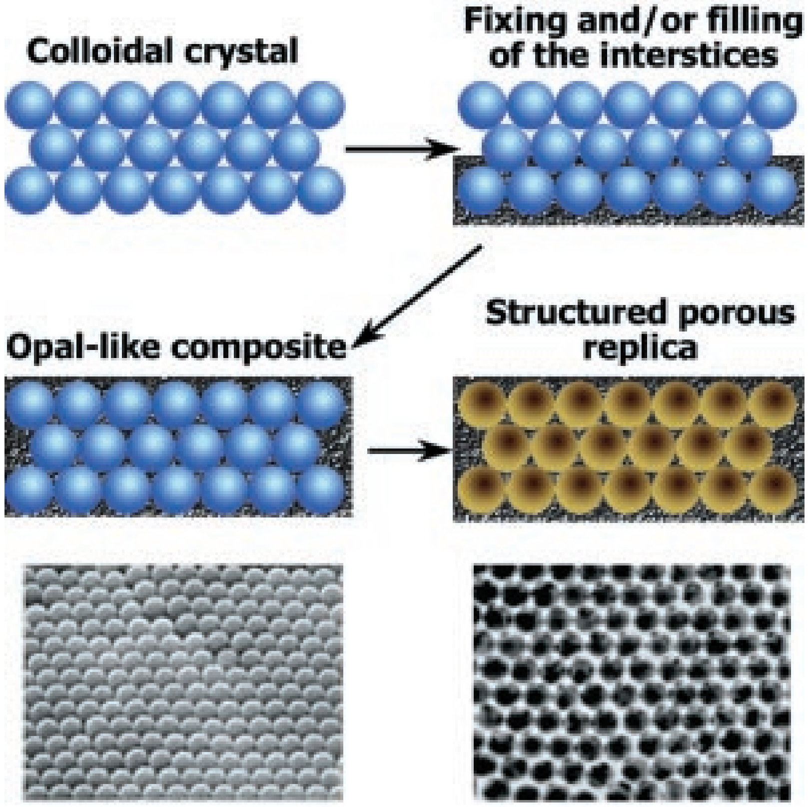

Figure 2. Synthesis of porous materials by templating upon close-packed colloidal crystals.
Courtesy of Orlin Velev and Eric W. Kaler, University of Delaware.

Processes competitive with self-assembly

An issue that must be addressed is competing processes: What competitive processes are available to achieve similar targets? Structuring at the nanoscale is not available exclusively via self-assembly. While the "bottom-up," additive approach embodied in self-assembly, has much to recommend it, "top-down," subtractive processes, such as nanolithography by X-ray, electron beam, and UV also have considerable potential yet to be tapped. Furthermore, subtractive processes have a track record of past accomplishment. Direct-write processes, which are automated layer-by-layer depositions, including ink-jet printing (Sachs et al. 1992), stereolithography, or 3-D printing (Griffith and Halloran, 1996), are also advancing rapidly, based in part on advances in robotics (Lewis, 2000). More conventional processes, such as lamination and multilayer extrusion (Cesarano and Calvert, 2000), are also achieving a greater degree of spatial control. Sol-gel processing and certain combustion/aerosol processes also are achieving some success in creating controlled nanostructured products.

Thus, there are serious competitors to self-assembly processing. Engineering research in self-assembly processing should be realistic about comparative advantages of alternative processes and creative about inventing combinations of new technologies for nanoscale processing.

New issues in self-assembly processing

Several identifiable directions should be taken toward scientific and technological advances in the chemical sciences to make self-assembly processing an important, widely used processing tool. Because each direction discussed below is important, it is not possible to prioritize the current state of the field.

Precision Synthesis of Precursors. The ability to form a desired state of organization spontaneously depends on the internal structure of the assemblers. It is then clear that information must be built into the assembling objects with some degree of fidelity. There are various avenues for achieving this. Size, shape (in rigid objects), conformation (in flexible objects), sequence (in multicomponent macromolecules), and spatial relationships among subunits all can be "read" in molecular recognition interactions. In synthetic molecules, small amphiphiles, such as surfactants or lipids, are classes of molecules that can be synthesized with precision, that is, they can be made and isolated as pure compounds. The ability to make micellar and bilayer membrane structures by self-assembly is a direct consequence of the precise architectures of these molecules.

Only biological systems currently achieve precise syntheses of molecules of more than a few hundred daltons. There are two broadly thought-provoking points in realizing current self-assembly research. One is that *precision synthesis* and fidelity of information content *is essential* for effective self-assembly of intricate, functional systems. This should motivate a broad array of useful chemical synthesis and process research to produce the starting materials for nonbiological self-assembly. Protein folding, the unimolecular self-assembly process by which proteins (multicomponent macromolecules with precise sequence distributions) take their functional forms, is far from fully understood. It is certain, however, that the final state of a protein folding process is determined by the primary sequence of amino acids in the macromolecular backbone. Precision synthesis of the sequence controls the assembly. Folding processes of nucleic acids are also increasingly recognized to be functionally important, while information is built into polysaccharides by control of architectural features such as branching. Successful development of self-assembly processes will place a premium on new chemical or directed biological routes to pure, precise macromolecular synthesis and production or particle formation. Furthermore, it will be fruitful to understand, in much more detail, the sensitivity of various synthetic self-assembly processes to the lack of precision in the architecture of the assemblers.

A second lesson that may be extracted arising from consideration of biological self-assembly is understanding how nature achieves precision synthesis. Biological systems do not synthesize perfectly; rather, considerable effort is expended in detecting and correcting errors en route to a pure product. Its chemical processing analogs are online measurement, control, and post-reaction separation processes. To achieve the necessary control over molecular architecture, it will be necessary to explore both chemical and biological synthesis routes with a realistic eye toward process efficiency.

Scale-Up of Self-Assembly Processes. As mentioned earlier in the context of Langmuir-Blodgett deposition, scale-up of self-assembly processes to technologically significant scales has not been pursued to an appreciable degree. That is perhaps natural given the state of development of the field. Nevertheless, lack of ways to scale up can be the demise of a promising processing route in a technological arena. Some of the most innovative developments in self-assembly processing to date have been achieved by chemists, where advances in assembly on nonplanar surfaces have led to the ability to assemble macroscopic, 3-D structures spontaneously (Jacoby, 2000; Gracias et al., 2000). A great opportunity exists for some tools of process systems research to be applied to self-assembly processing and nanoscale engineering in general. Success in enlarging the capacity of self-assembly processes by continuous, parallel or repetitive processing would be very valuable.

Kinetics and Mechanisms of Self-Assembly Processes. Another important issue is the matter of kinetics. Self-assembly science is grounded in processes that tend toward desirable equilibrium structures. Chemical processes generally should go as fast as possible, consistent with product quality. It is difficult to envision the processing research called for above proceeding fruitfully without data on the rates of self-assembly processes. Our view is that, for design and development purposes, we need to understand fully the trajectories, through time and structural intermediates, of self-assembly processes.

This need for research in self-assembly kinetics and the related issue of mechanisms has several facets. The acquisition of such data will stretch and eventually expand the tools that we have to observe self-assembly in progress. Research on self-assembly kinetics requires data in realtime, pushing the field toward methods that are faster and more highly time-resolved. Accurate kinetic data are a necessary prelude to predictive models of the evolution of self-assembly processes. As the complexity and number of components in these processes increase, predictive models will become more important tools in process and product design. We believe that it is fair to make the analogy between self-assembly and chemical reaction processes. Thorough understanding of chemical bonding, reaction mechanisms, pathways and kinetics is crucial to reactor design. Analogs in self-assembly are intermolecular or interparticle potentials, trajectories, and rates of assembly.

Rates of Self-Assembly Processes. Chemical engineers are seldom satisfied with the rates of uncatalyzed chemical reactions for technological purposes. Biological self-assembly is, in some situations, promoted or directed by protein or templates. It is reassuring in some respects that self-assembly proceeds down a free energy gradient to a thermodynamically determined endpoint. However, metastable states of varying duration may intervene. Equilibration is unhurried, but chemical manufacturing is not. It is challenging to think of how one might design a catalyst for a self-assembly process. Physical or chemical templating, e.g., a type of epitaxial growth, is one possible route, which in self-assembly has been explored more for its effect on structure than on rate (Ball, 1997). External fields can profoundly affect the rates of self-assembly processes (Koppi et al., 1993) and should be explored more extensively in this vein. Perhaps more than in simpler chemical reaction processes, the size and complexity of objects involved in self-assembly are such that diffusion limitations are more the rule than the exception, motivating a need for new research in transport phenomena applied to this field.

Characterization and Process Control. Practical processes must be controlled to produce valuable products; in the case of self-assembly, these are products of intricate internal structure. Real-time structural analyses present instrumental challenges that must be addressed. Since self-assembly often produces structured products over several length and time scales, techniques capable of measuring, with resolution, over multiple length and time scales are needed. Informative online measurement is a prerequisite for process control. Characterization of defects is particularly important for the applications envisioned. Furthermore, self-assembly processing of nanostructured products is a driver for new research in control of distributed processes (March 2001 Perspective, Christofides, 2001). Control of distributed systems such as self-assembly will also rely heavily on the development of tractable, predictive models.

Concluding remarks

It has been remarked that new directions in science are launched by new tools more often than by new concepts (Dyson, 1997). “Self-assembly is a blend of concepts and tools; the field will advance more rapidly as we turn concepts into techniques.” Research in the chemical sciences and technology over the next few years, pursued with a clear view to the barriers and competition facing self-assembly, is likely to produce important new progress, not only for self-assembly processing, but for the optimum routes to nanostructured chemical products.

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