

Molecular engineering of surfaces using self-assembled monolayers

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ABSTRACT

The self-assembly of molecules into structurally organized monolayers (SAMs) uses the flexibility of organic chemistry and coordination chemistry to generate well-defined, synthetic surfaces with known molecular and macroscopic properties. The process of designing monolayers with a specified structure gives a high level of control over the molecular-level composition in the direction perpendicular to a surface; soft lithographic technique gives useful (if lower) resolution in the plane of the surface. Alkanethiolates adsorbed on gold, silver, mercury, palladium and platinum are currently the best-defined systems of SAMs. They provide substrates for a number of applications—from studies of wetting and electron transport to patterns for growing mammalian cells. SAMs have made organic surfaces a central part of surface science. Understanding the principles by which they form, and connecting molecular-level structure with macroscopic properties, opens a wide range of areas to study and exploitation.

Keywords: *self-assembled monolayers, SAMs, organic films, alkanethiolates, molecular electronics, surface science, nanotechnology*

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Introduction: surfaces and interfaces; the role of SAMs

Surfaces and interfaces—the regions separating two homogeneous phases (gases, liquids, and solids)—are a distinct state of matter: they are where the *gradients* in properties are highest¹ (in homogeneous phases, gradients are, on the average, zero). The words “surface” and “interface” are often used interchangeably in surface science; the former emphasizes the geometrical separation between phases; the latter the finite thickness of the region over which the change occurs between phases. (We will use both terms, with these connotations.) The environments of atoms or molecules at surfaces are different than those in bulk matter, as are their free energies, bonding, structures, and mobilities.^{2,3} These differences between

surfaces, liquids, and solids make surfaces intensely interesting. Surfaces are also often the parts of solid phases that are the most accessible to investigation.

Historically, much of the interest in surfaces originated in their ubiquitous relevance to technologies: heterogeneous catalysis, wetting, adhesion, lubrication, fracture toughness, corrosion, colloid stabilization, detergency, and biocompatibility are examples.⁴ Early research focused on the atomic and electronic structures of metals, metal oxides, and derivatives (usually as single crystals),^{5,6} and developed a variety of sophisticated spectroscopies to determine these structures.⁷ This work required studying the surfaces in ultrahigh vacuum (UHV), since they have high interfacial free energies, and adsorb atoms or molecules from any gas or liquid to which they are exposed.^{8,9} Curiously, a major stimulus and justification for this work was the promise of “heterogeneous catalysis by design,”¹⁰ the discrepancy between UHV and the high pressures used in practical catalysis is only now beginning to be addressed.¹¹

For many years, surface science largely ignored *organic* surfaces, although they were acknowledged to be important for biology, and for polymer and materials science (*inter alia*). The central problem was the absence of structurally well-defined organic surfaces to use as substrates. Early studies of organic surfaces by Timmons, Zisman and others^{12,13} had characterized the adsorption and organization of amphiphilic molecules such as fatty acids on metals and metal oxides. Because organic surfaces have low interfacial free energies, these studies could be carried out under *ambient* conditions—a great experimental convenience. Kuhn also used amphiphilic molecules to form self-organized monolayers at the air-water interface, and transferred these monolayers to air-solid interfaces (a technique invented by Irving Langmuir and Katherine Blodgett, and which led to the so-called Langmuir-Blodgett, or LB, monolayers).^{2,14,15} Some LB films are well-ordered, but they are also difficult to prepare, mechanically fragile, and idiosyncratic in their properties. LB monolayers are probably too complicated ever to be technologically important. Other systems of organic monolayers—particularly those formed by hydrolysis and cross-linking of organic trichlorosilanes (for example, $C_nH_{2n+1}SiCl_3$, which generate alkyl-siloxane SAMs)—were (and are) widely used in industrial applications where structural irregularities are less important.¹⁶ The structures of these (and other) systems of adsorbed organic mono- and bilayers are usually, at best, semicrystalline, and are

often glassy or disordered; experimentally, they are also difficult to prepare reproducibly.

Two discoveries in the early 1980s changed surface science. They were (i) the invention of the scanning tunneling microscope (STM) by Binnig and Rohrer,¹⁷ and (ii) the discovery and characterization of self-assembled monolayers (SAMs) formed by the chemisorption of alkanethiols on gold.^{18,19} The introduction of the STM caused a revolution: it was a fundamentally new type of tool, with the ability to image, characterize and even manipulate single atoms and molecules on metallic surfaces. Its many descendants, most notably the atomic force microscope (AFM),^{20,21} could examine an extended range of forces, properties, and surfaces. These techniques removed the requirement for UHV to study the structure of many surfaces and reduced the importance of single crystals for substrates. SAMs provided a method to *synthesize* organic surfaces with known, reproducible structures. Alkanethiolate SAMs shifted the focus of surface science from metals and metal oxides to surfaces composed of organic molecules, and allowed studies of surfaces in contact with water or other liquids, and of biologically relevant surfaces (Figure 1). The ability to control the composition of the surface made it possible to examine structure-property relationships, and to design and synthesize surfaces having properties important in materials science, nanoscience, and biology.

We focus this review on organized organic surfaces, and especially on SAMs of alkanethiolates on silver and gold. We highlight both what is known about these systems, and what is not known. We have five objectives: (i) to emphasize that SAMs allow the rational and flexible synthesis of structurally well-defined organic surfaces; (ii) to point out that despite extensive work on synthesis and characterization, there remain many points about these remarkable systems that are still not fully understood and controlled; (iii) to show that the availability of these surfaces has made it possible to relate the microscopic, molecular-level structure of an interface to its macroscopic properties as a material, and to test hypotheses about these relationships; (iv) to illustrate several classes of applications of SAMs that depend on understanding their properties—specifically, the use of SAMs in studies of electron transport across ultrathin organic films, in soft lithography, and in the design and fabrication of surfaces showing selective adsorption of biomolecules and tailored interactions with cells; and (v) to sketch the extension of SAMs to applications in other areas of science and technology.

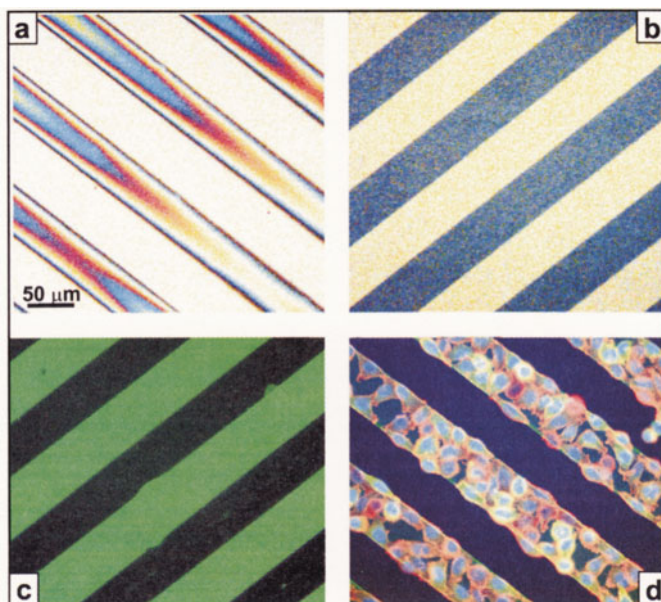


Fig. 1. Alternating 50 nm lines of SAMs demonstrate contrasting properties at adjacent regions of a gold surface. (a) A solution of glycerol in water only wets regions with hydrophilic terminal groups (colored stripes). (b) A hydrophobic SAM prevents corrosion of gold by a chemical etchant; bare gold is removed to expose the dark, underlying silicon substrate. (c) Fibronectin, stained green, does not adsorb onto protein-resistant SAMs. (d) HeLa cells cannot spread onto protein-resistant SAMs. Here, the fibronectin is stained green, the actin red and the nuclei blue.

Bridging molecules to surfaces using alkanethiolate SAMs

In 1983, Nuzzo and Allara¹⁸ described the structure of long-chain alkyl disulfides chemisorbed on gold. This study and later ones involving alkanethiols¹⁹ ($\text{CH}_3(\text{CH}_2)_{n-1}\text{SH}$, here abbreviated as C_nSH) initiated work on SAMs (Figure 2). (Before 1983, the ability of sulfur-containing organic molecules to adsorb on the surface of clean metals, metal oxides, and metal sulfides was well-known in fields ranging from electrochemistry to ore flotation,²² but the structure of these adsorbed layers had not been established.)

Two characteristics of SAMs of alkanethiolates on gold distinguished them from organic assemblies formed from amphiphiles, e.g. fatty acids, on metal oxides. First, the thiols formed single, highly organized layers at the surface *reproducibly*; and second,

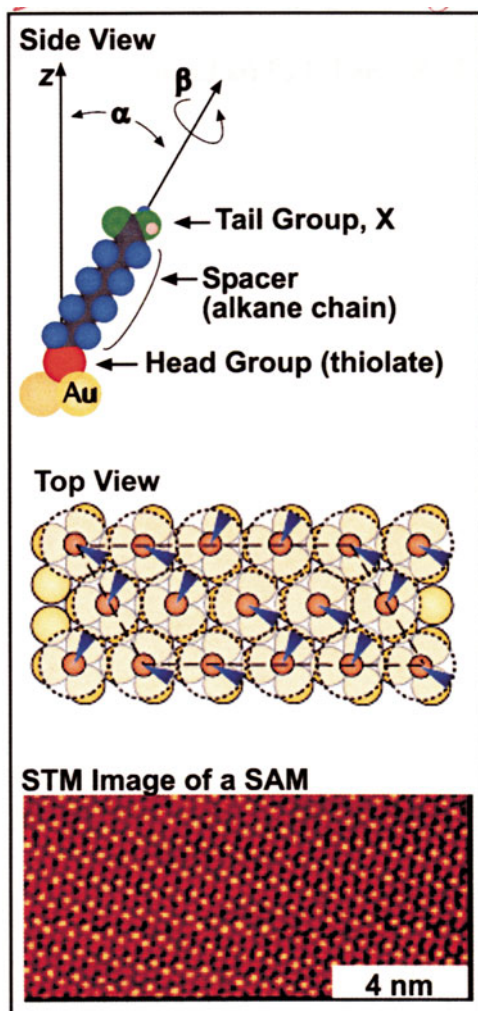


Fig. 2. Structure of a SAM of alkanethiolate on gold. The most extensively studied SAMs are *n*-alkanethiolates on gold. The molecular units of these and related SAMs have three components: (1) a chemical moiety or “head” group (here, a thiol group) that binds to a substrate,²³ (2) hydrocarbon spacer group (here, a C10 alkane chain), and (3) a terminus or “tail” group X (here, $-\text{CH}_3$). The gold-thiolate bond has the highest energy in the system (17.7 kcal)²⁴ and orients the molecules with their head groups toward the solid surface, leaving the tail groups free. The thiols bind in the three-fold hollows in the gold lattice; this conformation spaces the sulfur atoms by $\sim 5 \text{ \AA}$ and determines the lattice spacing of the molecular crystal.²⁴ This lattice spacing is slightly larger than the van der Waals diameter of the alkane chains, and the chains tilt 30° (α) to maximize the attractive interactions between chains. The strength of the van der Waals interactions induces the alkane chains to align

ω -functionalized alkanethiols (XC_nSH , where X is $-\text{CH}_3$, $-\text{COOH}$, $-\text{PO}_3^{2-}$, $-\text{OH}$, *etc.*) formed monolayers having the terminal group, X, exposed. Molecular assemblies formed from fatty acids always minimized the surface free energy by forming a hydrocarbon-terminated surface, but the strong affinity of the thiol group (a “soft” ligand) for gold often made it possible to form well-defined interfaces that presented a wide range of structures, including ones that were polar, electroactive, or biologically relevant.

Developing the relationships between the molecular structure of the surface and its macroscopic properties required developing new protocols and techniques. Surface reflectance infrared spectroscopy,²⁷ transmission electron microscopy,²⁸ scanning probe microscopy,^{29,30} contact angle goniometry,³¹ contact angle titration,^{32,33} ellipsometry, X-ray photoelectron spectroscopy,³⁴ and electrochemistry³⁵⁻³⁸ established the broad characteristics of the formation and structure of SAMs of alkanethiolates on gold.

SAMs of organic thiolates on late transition metals (coinage metals – silver and gold – but also copper, platinum, palladium and alloys) have major advantages as subjects for surface science: (i) Neither single-crystalline substrates nor UHV are required to prepare, manipulate and examine them. (ii) Their structures can be prepared by design, simply by the synthesis of the constituent organic molecules. (iii) Only very small quantities of organic materials are needed to form a SAM ($\sim 10^{14}$ molecules, or ~ 1 nanomole, covers 1 cm^2 of surface); they can thus be used with ligands that are scarce or difficult to synthesize. (iv) They offer broad access to organic surfaces, and in particular they make it straightforward to prepare surfaces that present the complex organic ligands needed in biological studies. (v) A wide range of approaches—from surface spectroscopies and electrochemistry to physical-organic chemistry and biophysics—can be used to characterize them. (vi) The methods used to prepare them are applicable to large, heterogeneous, and non-planar surfaces, including many surfaces—especially colloids and nanoparticles—generated in nanotechnology.

in an all-trans conformation. Although schematics often display a single row of a SAM with all the molecules tilting in the same directions, the two-dimensional crystal is a more complex two-chain structure common to organic crystals of hydrocarbon chains.²⁵ The blue wedges in the top view indicate the CCC plane of the alkane chains projected onto the surface. The unit cell of this model is overlaid on the top view. The STM image is a SAM of C_{10} on $\text{Au}(111)$.²⁶

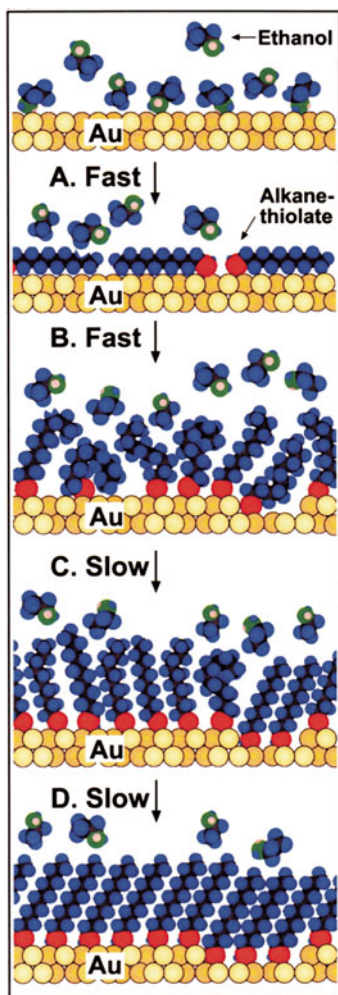


Fig. 3. Formation of a SAM. Although the mechanism by which *n*-alkanethiols form SAMs on gold has been studied extensively on single crystals of Au(111) in UHV,^{23,26,41} the most accessible and common method for forming SAMs is the absorption of alkanethiols from an ethanolic solution onto polycrystalline gold surfaces (prepared by deposition from the vapor phase). Unless the gold films are transferred in vacuum, adventitious materials present in the atmosphere quickly adsorb onto the surface of the gold when they are transferred from an evaporator into solution. The thiols must displace the adsorbed materials and solvent from the surface. The majority of the thiols that form the SAM adsorb quickly (A-B): low mass coverage produces a striped layer followed by a dense upright layer (B). These transformations happen in 5–6 minutes, during which time 90% of the surface is covered.⁴³ The bond formed by chemisorption of the thiol onto the gold substrate has two effects: (1) it induces a local strain in the gold surface that is relieved by releasing gold atoms onto the surface to form a pit or

SAMs of alkanethiolates on late transition metals also have disadvantages: (i) They are not thermally or mechanically stable.³⁹ (ii) They are not relevant to large-scale heterogeneous catalysis, or, generally, to semiconductor microelectronics. (iii) There is no convenient, available substrate that truly is (and *remains!*) atomically flat on which to support them (liquid mercury supports alkanethiolate SAMs,⁴⁰ but these systems are less convenient to prepare and use than those on solid metals).

Preparation of SAMs

The preparation of SAMs by adsorption of C_nSH on gold is experimentally very easy: a gold film—usually prepared by evaporation of gold onto a flat substrate—is exposed to a solution of the alkanethiol in a solvent for a short time (minutes to hours), then removed. During this process, the alkanethiols adsorb on the gold, order, and lose the thiol hydrogen.⁴¹ Although it is often assumed that this hydrogen desorbs from the surface as H_2 , its fate has not been proved.^{24,25} The product that is formed is probably best understood as a gold(I) thiolate ($RSAu$) adsorbed on metallic gold ($Au(0)$). The C_nS-Au bond is predominantly covalent, and has little polar character.⁴² Both kinetic and thermodynamic factors influence the formation of SAMs²⁵ (Figure 3).

“vacancy island”; and (2) it increases the mobility of the gold-thiolate complex on the surface. The vacancy islands coalesce during the formation of the SAM and the gold adatoms move to the step edges of the surface; the entire process leaves the surface inherently rougher than the original gold surface. The alkanethiolate-gold complexes nucleate small crystalline regions of the monolayer; these regions grow as additional thiols adsorb.^{24–26,41} The next step, during which the alkane chains unfold to their all-trans configuration, is 3–4 times slower than the initial coverage. The reordering of the alkane chains maximizes the van der Waals interactions between molecules (C). Additional alkanethiols adsorb and complete the well-packed monolayer. Finally, in a process that takes up to 7 hours, the gauche defects in the tail group largely disappear (D).²⁵ The process leaves a surface with steps in the gold, and with a variety of grain boundaries and other defects, but with the great majority of the molecules of alkanethiolate present in crystalline grains.

Structure of SAMs

The most common structures of SAMs of *n*-alkanethiolates on gold and silver are increasingly well-established, based on extensive experimental evidence and theoretical models.^{24,25} The majority of chains of *n*-alkanethiolates on gold are *trans*-extended and tilted approximately 30° from the vertical, provided that $n > 11$ (for $n < 10$, the polymethylene chains are less ordered); the structure of SAMs derived from alkanethiols on other metals are comparable, although the tilt angles differ (Ag,^{44,45} 0–12°; Pd,⁴⁶ 14–18°; Cu,⁴⁵ ~12°; and Pt,⁴⁷ <15°). Alkanethiols (C_nSH) and dialkyl disulfides (C_nSSC_m) form SAMs with similar structures on gold and silver;^{48,49} the sulfur–sulfur bond is cleaved at the gold surface.

The most extensively studied SAMs are those formed from molecules comprising an alkanethiol functionalized with a terminal group or “tail group”, X (abbreviated XC_nSH), because this class of molecules: (i) is relatively easy to synthesize and (ii) makes it easy to tailor the structure and properties of the ambient interface of the SAM.^{50,51} A convenient fiction of the field is that the organization of these types of molecules within the SAM is similar to simple alkanethiols. For small tail groups, such as —CN, —OH, —COOH, —NH₂, this approximation may be reasonably accurate.⁵¹ Molecules resembling lollipops or mushrooms—that is, molecules with a large tail group, such as some organometallic complexes and many biomolecules, attached to a skinny alkanethiol—probably cannot organize into well-ordered monolayers. The steric constraints of the head group reduce the density of the packing of the chains and prevent the molecules from aligning. The Langer group has described a system in which the loose packing and flexibility of these molecules is harnessed to change the density of a surface—showing that, while often ignored, this effect can be technologically useful if properly understood.⁵²

The effects of geometrical constraints on molecular organization are qualitatively understood in the formation of micelles, membranes, and vesicles.⁵³ Others also have developed intuitive models for predicting the types of structures formed by adsorption of surfactants at interfaces by considering the shape of molecules.⁵⁴ There is, however, no equivalent theory for the structures of SAMs on surfaces.

Microscopic examination of the organization of SAMs suggests that a number of types of defects exist even for the best-behaved molecules (Figure 4). The adsorption and organization of thiols on

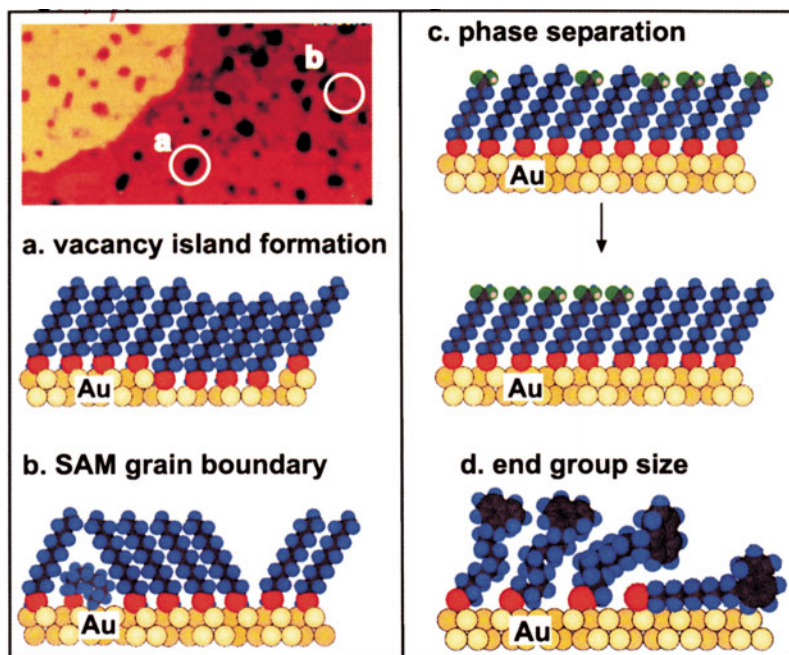


Fig. 4. Defects and heterogeneities in SAMs. Defects intrinsic to the formation of a SAM include (a) vacancy islands, which form due to the effect of the gold-thiolate bond on the lattice,^{24,41,43} and (b) molecular grain boundaries between crystals of SAMs, which nucleated at different sites.^{26,41} These defects cannot be avoided during the formation of the SAM, but can be minimized by annealing. There are several defects that are due to experimental design: (c) SAMs are mobile and phase separation of the tail groups in a mixed SAM occurs;⁵⁸ and (d) molecular structure distorts packing, forcing the SAM into structures that are not well-ordered.

the surface generate two types of defects: (1) disordered boundaries between crystalline regions (grains) within the SAM, and (2) pits, or vacancy islands, in the surface of the gold.⁵⁵ Atomic steps and grain boundaries in the gold substrate also complicate the structures of SAMs.⁵⁶ The effect of nano-scale heterogeneities on the order of the alkane chains is poorly characterized, and the structure and reactivity in these disordered regions may be substantially different than those of the crystalline regions. For many applications of SAMs as materials (*e.g.*, in studies of wetting, adhesion, and stabilization of nanoparticles), defects in the SAMs appear to be secondary in importance.⁵⁷ In others (especially studies of electronic transport through SAMs), they may be critical in determining current-voltage characteristics.

Applications of SAMs

SAMs provide a uniquely convenient and controllable system with which to synthesize and study the macroscopic materials properties of organic surfaces. Some applications, such as wetting and micro/nanofabrication, use simple tail groups ($-\text{CH}_3$, $-\text{COOH}$, $-\text{OH}$) and rely on the structure and function of SAMs that are already well-characterized and accepted. Other applications (in organic/molecular electronics, nanotechnology, and biology) require SAMs that contain a diverse range of chemical structures, including organometallic complexes, aromatic hydrocarbons, biomolecules, and ligands for proteins. The structures of these SAMs are more complex than those of simple alkanethiolates, and most of these SAMs have not been characterized rigorously.

SAMs for modifying the wetting properties of surfaces

The most clearly understood of the properties of SAMs is wetting. Contact angle goniometry provides a simple method of measuring wettabilities. Various procedures allow the preparation of mixtures of polar and non-polar functional end groups,^{59,60} patterns of these groups,⁶¹ and step and smooth gradients of these groups.^{62,63} These procedures provide relatively well-defined systems for preparing surfaces with heterogeneities at all scales—from the molecular (0.5 nm) to mm-scale—and for relating this structure to an important macroscopic property.³¹

SAMs as ultrathin resists in micro/nanofabrication

Photosensitive polymers, called resists, are essential components in photolithography, a fabrication process ubiquitous in micro- and nanoelectronics. Patterns of resist—defined by exposure to ultraviolet light through chrome photomasks, or by scanning beams of electrons—are typically 50–1000 nm thick and protect the underlying surface during subsequent processing steps such as metal film deposition, etching, and ion implantation. SAMs are useful as etch resists for patterning metal films on surfaces for exploratory research because they offer simple, inexpensive methods for patterning surfaces; SAMs are particularly helpful for generating prototypes of micro- and nanostructures on substrates that are not

used commonly in microelectronics⁶⁴, *e.g.*, plastic or non-planar substrates.

The use of SAMs in combination with microcontact printing to fabricate functional microstructures is now an established methodology^{65,66} (Figure 5). Some nanostructures (50–100 nm) have been produced using this method.^{67–69} More stable designs for the elastomeric stamps used in printing,^{70,71} and new systems of SAMs (*e.g.*, alkanethiols on Pd⁷²), should improve the utility of microcontact printing for fabricating nanostructures.⁷³ Two advantages of printing methods are: (1) they allow parallel patterning over large areas (Figure 6a);^{56,74} and (2) they enable rapid prototyping of microstructures when used with photomasks prepared on transparent films by high resolution imagesetting. It is possible to generate microstructures with critical dimensions of $< 10 \mu\text{m}$ in a single day;^{74–76} this interval is more attractive for exploratory research than the days or weeks required to make chrome photomasks using conventional laser- or e-beam writing.

Scanning probe methods (dip-pen lithography,^{77,78} nano-scribing²⁶) also can write patterns of SAMs with dimensions of 10–100 nm (Figure 6b). These techniques offer excellent spatial resolution, but are slow: writing times required to pattern large areas ($> 1 \text{ cm}^2$) are hours to days. The demonstration of arrays of SPMs, operating in parallel, suggests one possible solution to this problem;^{79,80} such arrays could be useful for storing information in memory devices and for generating arrays of biomolecules for use when sample sizes are very limited (*e.g.*, single-cell analysis).

SAMs as model systems for organic/molecular electronics

An application of SAMs that demands fewer defects than those in biology is as structures with which to examine the mechanisms of electron transport in organic molecules.^{81–83} This subject is part of the broader field of organic and molecular electronics.^{84,85} SAMs are thin enough that electron tunneling through them generates measurable currents, and the materials and chemical and interfacial properties of the SAM determine the current-voltage relationships.^{88–91} Careful characterization of the SAMs in these systems is one element of developing structure-property relationships and mechanisms for electron transport through them.

A common experimental configuration for studying electron tunneling comprises a SAM sandwiched between two electrodes. One electrode usually supports the SAM on a metal film, while the

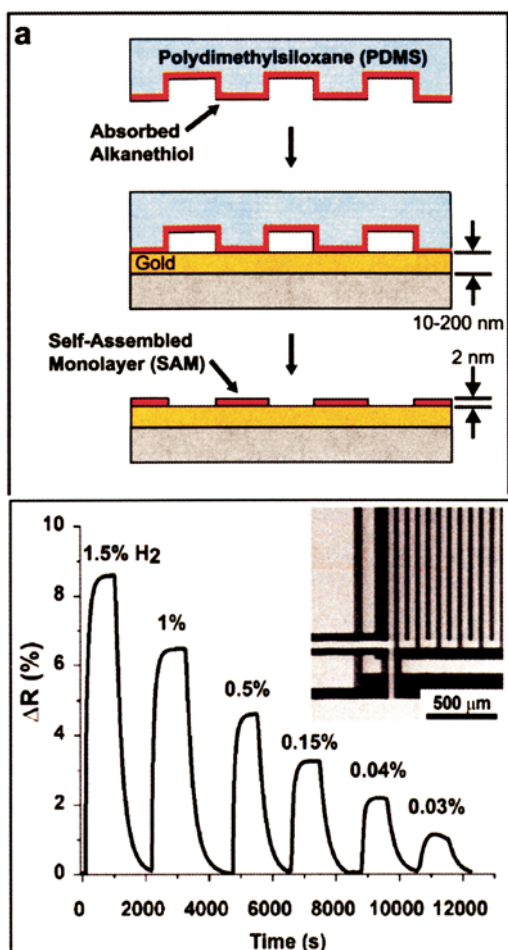


Fig. 5. *Soft Lithography.* “Soft lithography” is the collective term for the tools and techniques for patterning SAMs and other materials (organic, ceramic, polymeric) on surfaces. We use the term “soft” to refer to either the element used for pattern transfer (mold or stamp) or the organic material patterned; this usage comes from physics where the term “soft matter” describes organic materials. Soft lithographic techniques—based on molding, printing, and embossing—are used primarily for replication; the mold or stamp is prepared by casting a prepolymer against a topographically patterned surface, or master, made by high resolution printing, photolithography, or electron-beam lithography. (a) Microcontact printing is especially useful for producing patterns of SAMs on surfaces. The technique, developed in the early 1990s, uses an elastomeric stamp to transfer alkanethiols (or other molecules) dissolved in the stamp to the surface of the metal film.^{67,86} A SAM forms only in the regions contacted by the stamp. Immersion of the substrate into a solution containing a second thiol creates a surface with adjacent regions of different surface composition. Alternatively, immersion of the substrate into a wet chemical etchant yields

second electrode is: a metal film evaporated onto the SAM or transferred onto it by floating,⁹² a drop of mercury supporting a second SAM^{81,90,93} (Figure 7a), an STM^{26,94} or cAFM tip,^{95–97} or wires crossed on the surfaces of a SAM.^{94,98} An alternative system for measuring electron transport through one molecule consists of a SAM bridging two planar nanoelectrodes formed by electromigration, nanofabrication, or controlled fractures.^{99–101} A SAM of a short-chain ($n < 12$) alkanethiolate also can act as a supporting matrix to hold individual molecules for current-voltage spectroscopy by STM; small numbers (1–2) molecules, inserted randomly at grain boundaries in the SAM,^{102,103} can be examined in this configuration. Electrochemistry allows electron transfer across a single SAM to be examined; here, a species accepting or donating an electron is in an aqueous solution in contact with the SAM.^{104,105}

For some measurements, these different types of experiments have yielded data that are roughly compatible. For example, the value of β – the parameter characterizing the rate of decay of the tunneling current (I) as a function of distance (d) through a potential barrier ($I = I_0 e^{-\beta d}$) – determined for alkanethiolates is consistent among many experimental methods ($\beta = 0.75\text{--}1.0 \text{ \AA}^{-1}$).⁸² Other potentially interesting electronic characteristics, such as negative differential resistance^{107–111} and electronic switching^{108,112} have been reported, but both the reproducibility of these measurements and the yields of working devices are distressingly low.¹¹³ The uncertainty of the results limits the theoretical models that can be tested using them.

The SAMs used in these experiments are not flat, perfectly ordered structures. Even when the fabrication of a SAM-on-gold electrode starts with a planar gold surface, the final system has many steps in the gold^{41,43,89} (Figure 3). Poorly understood phenomena related to the conditions of fabrication and measurement in these systems may define, in part, their electronic characteristics.¹¹⁴ Some of these phenomena may include: (i) formation of bridging filaments of metal at the very high electric fields ($\sim 10^9 \text{ V m}^{-1}$) often present during electrical measurement;

*metallic micro- or nanostructures on the surface where the SAM was patterned. This technique is useful for fabricating functional devices on substrates that are uncommon in microelectronics, e.g., plastic and non-planar substrates. Part of a palladium wire patterned by microcontact printing and selective wet etching is shown here; the resistivity of the wire changes as a function of hydrogen concentration.*⁷³

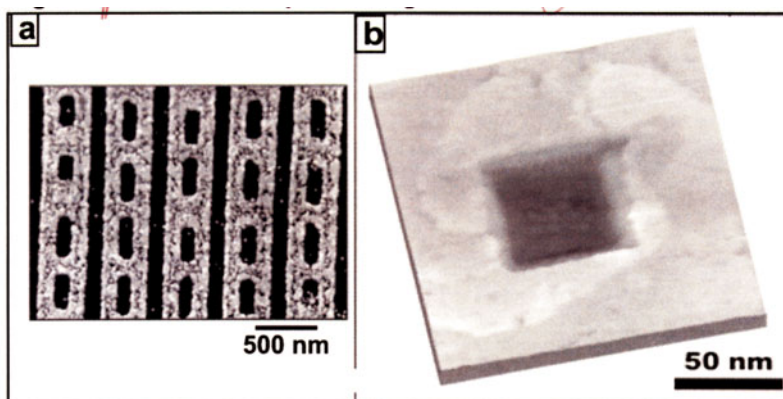


Fig. 6 Nanoscale patterning of SAMs. (a) Scanning electron microscope images of gold patterns produced by soft lithography. Micro-contact printing of alkanethiols onto the gold surface protected those areas during the subsequent etching of the gold film.⁸⁷ (b) Atomic force micrograph of a square region scratched into a monolayer of alkanethiol.²⁶

(ii) chemical changes in the interfaces caused by highly reactive metal atoms deposited onto organic molecules;^{115–117} and (iii) local disruption or destruction of SAMs by passivating films or metal intercalation. Other processes, such as oxidation of the metal or adhesion layer, may also affect the nature of the interface, and thus, its electronic characteristics.¹¹⁸

SAMs of thiolates on metals, and related systems of SAMs on semiconductors^{92,119,120} (Si/SiO₂ and GaAs), still seem, to us, to be

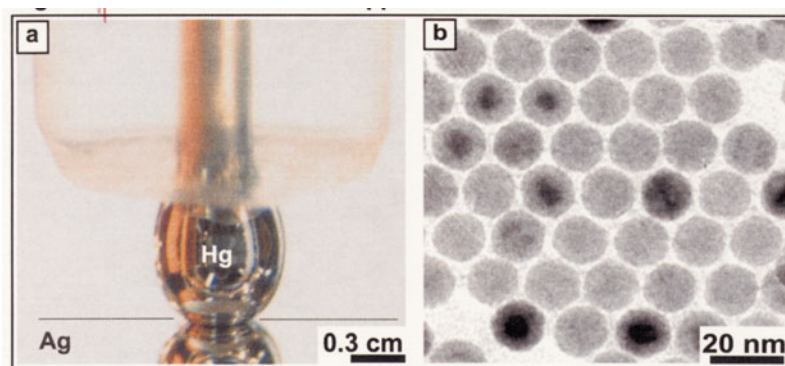


Fig. 7. Applications of SAMs in nanoscience. (a) SAM on a mercury electrode in contact with a SAM on a silver film. Electron transport is measured across the Hg/SAM//SAM/Ag junction.¹⁰⁶ (b) Transmission electron micrograph of iron oxide nanocrystals coated with oleic acid. The SAM prevents direct contact between the nanocrystals and determines the spacing between them.

the most reliable that are now available for the study of electron transport through organic matter. The probable sensitivity of conductivity to the nanoheterogeneity of SAMs means, however, that an accurate understanding of these systems will require thorough, painstaking characterization of the sort that they have only occasionally received.

SAMs as functional elements in nanotechnology

Nanoscience is a name that unifies a broad range of physical (and, increasingly, biological) sciences. Nanostructures are, in a sense, “all surface”; that is, their dimensions are sufficiently small that all of their constituent atoms can be considered to be interfacial. The composition at the surface can determine or modify many of the properties of these structures, and, in fact, controlling interfacial properties is at the core of nanoscience.

SAMs themselves are prototypical nanostructures, since they are only 1–3 nm thick in the direction normal to the supporting substrate.¹²¹ SAMs can be used as “nanospacers” to determine the separation between nanoparticles deposited on surfaces (Figure 4b); the spacing in turn determines the degree to which adjacent particles interact optically,¹²² electronically,¹²³ and magnetically.¹²⁴ The composition and nature of bonding of the SAM also influences the optical (local refractive index) and electronic (surface states) properties of nanostructures.^{125,126}

SAMs are now commonly used in the synthesis of metal and semiconductor colloids—an increasingly important class of nanoscale structures—to determine their size, shape, and solubility.^{127–130} SAMs passivate the surface of nanoparticles, during and after growth. They prevent aggregation and play an active role in determining the kinetics of growth along the crystal planes of the nanoparticles.¹³¹ A range of functional groups can be presented on the surface of nanoparticles by using $X(\text{CH}_2)_n\text{SH}$ to form SAMs; these ligands can mediate the interactions between nanoparticles, capture molecular targets such as proteins, or permit the transport of particles into cells.^{132–134}

SAMs as interfaces for biochemistry and biology

SAMs are particularly appropriate as substrates for biological systems: here, the ability to present the large, delicate, water-

soluble ligands often required in biological studies is more important than the defects that these ligands might induce in the underlying polymethylene structures. A range of synthetic techniques—most conveniently, the *in situ* reaction of organic amines with a preformed SAM presenting carboxylic anhydride groups¹³⁵—makes the preparation of relevant surfaces straightforward.¹³⁶

Biological studies benefit from a fortunate coincidence: the systems of SAMs on gold films most useful in biology are also perfectly suited for analysis by surface plasmon resonance (SPR) spectroscopy, quartz crystal microbalances, ellipsometry, and mass spectrometry.^{137,138} These tools are useful for characterizing binding events at surfaces, and for determining the composition and mass coverage of the surface; they provide, however, only limited information about the supramolecular structure of the SAM. New protocols are now needed to develop better, more intuitive models to connect the molecular structure of SAMs decorated with complex biomolecules or ligands in water to their biological activity.

Among the important applications of SAMs in biological studies are these: (i) SAMs terminating in oligo(ethylene glycol) groups $(-(\text{OCH}_2\text{CH}_2)_n\text{OH})$ ($n = 3-6$) form so-called “inert” surfaces: that is, they prevent the adsorption of proteins from solution and the attachment of cells.^{139,140} (ii) SAMs terminating in appropriate ligands make possible a wide variety of biological sensors.¹⁴¹ (iii) Mixed SAMs presenting different surface densities of ligands are useful in examining oligovalency and polyvalency, and in comparing the kinetics and thermodynamics of protein-ligand association/dissociation at interfaces and in solution.^{144,145} (iv) Patterning of SAMs into regions that *allow* cell attachment, and regions that *prevent* it, provides a broadly useful method of manipulating the position and shape of mammalian cells^{146,147} (Figure 8a). Patterns imposed on cells influence their passage through the cell cycle, and allow the design of systems containing multiple different types of cells in predetermined geometries.¹⁴⁸ These patterns have also been important in answering questions about the biochemical response of cells to mechanical stimuli.¹⁴⁹ Electrochemical methods that desorb the SAMs allow these patterns to be erased, and are the basis for new types of assays based on cell motility and other phenotypic behaviors^{143,150,151} (Figure 8b).

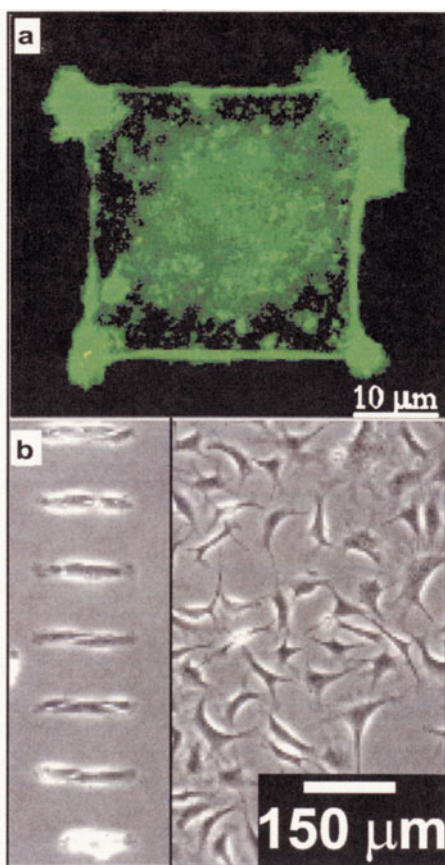


Fig. 8. Applications of SAMs in biology. (a) Fibroblast cells grew constrained to fibronectin-coated adhesive islands with distinct geometric shapes, which were created using microcontact printing technology. Cells extended new lamellipodia preferentially in the corner regions of the islands.¹⁴² (b) Optical micrographs of bovine capillary endothelial cells confined in an array on the surface by the pattern of the underlying SAM (left) and the system 10 min. after a mild electrochemical pulse released the SAM that prevented the cells from spreading (right).¹⁴³

Current assessment

SAMs combine the accessibility of solid surfaces and the flexibility of organic chemistry. They are unique in their ability to generate well-defined, synthetic surfaces. The process of *designing* monolayers with a specified structure and properties has been limited, however, to systems derived from the most extensively studied

SAMs—alkanethiolates on coinage metals and alkylsiloxanes on silicon/silicon dioxide; the breadth of structural information about SAMs prepared from other classes of molecules is small. Other surface chemistries form SAMs that appear to have the robustness of thiols on gold (*e.g.*, phosphates/ Al_2O_3 or TiO_2 ,¹⁵² alkynes and alkenes/Si,¹⁵³ isonitriles/metals⁹⁶), but have been studied less intensively. The great diversity of organic molecules and organo-metallic complexes should provide new opportunities for exploring alternative chemistries to attach molecules to surfaces,¹⁵⁴ and for extending the variety of structures in SAMs.

Two factors that strongly influence the structure and properties of SAMs are often overlooked in the idealised models of alkanethiolate SAMs: the physical shape of the constituent molecules and the defects formed in the close-packed structure. It is not obvious that the structure accepted for SAMs of alkanethiolates on planar surfaces is the best model for SAMs formed for applications in nanotechnology and biology. In nanotechnology, the highly curved surfaces of nanoparticles probably prevent SAMs from forming with the same close-packed arrangement observed on flat surfaces—the tail groups are too small to fill the available space; in biology, the large ligands and biomolecules likely reduce the density of molecules at the surface and induce more disordered surfaces than SAMs of alkanethiolates. Both intrinsic defects in SAMs (grain boundaries, vacancy islands) and those generated by subsequent processing (metal solvation, chemical degradation) seem to influence the electronic characteristics of devices formed with SAMs, but the character and influence of the defects in those systems is poorly understood.

Tools for patterning SAMs

SAMs give the highest level of control over structure and properties of surfaces in the *out-of-plane* direction—to within a few angstroms in the best cases—because the molecular components are synthesized with a well-defined structure. The present tools for patterning SAMs *in* the plane of the surface, such as soft and scanning probe lithographies, can generate surfaces with defined lateral features ranging in size from 10 nm to 10 μm . Despite the range and sophistication of these existing techniques, new capabilities are still required, including: (i) more convenient, rapid and inexpensive methods for “top-down” patterning with resolution of 10–1000 nm; and (ii) procedures for positioning two functional

groups on the surface at known, precisely defined *molecular* distances (1–10 nm) from one another.

The application of SAMs as etch resists for defining metallic micro- and nanostructures has had remarkable utility in exploratory research and rapid prototyping, but the microelectronics industry has not integrated SAMs (or the tools for patterning them) into commercial manufacturing processes. Some of the challenges that remain are: (i) eliminating distortions in patterns formed by soft lithography that result from deformations of the stamps and diffusion of the ink, (ii) increasing the writing speeds of scanning probe methods, and (iii) eliminating pinhole defects that develop in metallic structures during wet chemical etching. Recent advances in the techniques and materials used may improve these systems to meet the standards required, at least, in new or non-traditional electronics applications such as organic electronic displays.^{70–73,155–157}

Commercialization of SAMs

SAMs are beginning to emerge as components in commercial technologies other than microelectronics. Current early-stage companies in biotechnology and nanotechnology are using SAMs in sensors and assays to direct the placement and presentation of biological ligands, macromolecules (proteins, DNA), and whole cells.¹⁵⁸ These devices are used for bioassays, high-throughput drug discovery, and rapid diagnostics. Commercial tools for printing and writing the necessary SAMs are also now available.¹⁵⁸

Outlook

As technology pushes to small scales, bottom-up processing with well-defined chemical structures becomes increasingly important. SAMs provide an exemplary system of self-assembled materials where the structure and composition of the individual components (molecules) determine their macroscopic properties. When combined with a top-down technique such as soft lithography, they join molecular-scale ordering with micron-scale patterning. They also offer a two-dimensional bridge between individual molecules in solution and three-dimensional assemblies of molecules (crystals) in the solid state, and between the nanoscale and the macroscale. Self-assembly is a powerful technique that harnesses the flexibility of chemical synthesis to control surfaces; it is certain to gain in importance in the years and technologies to come.

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