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Material Matters™

Chemistry Driving Performance

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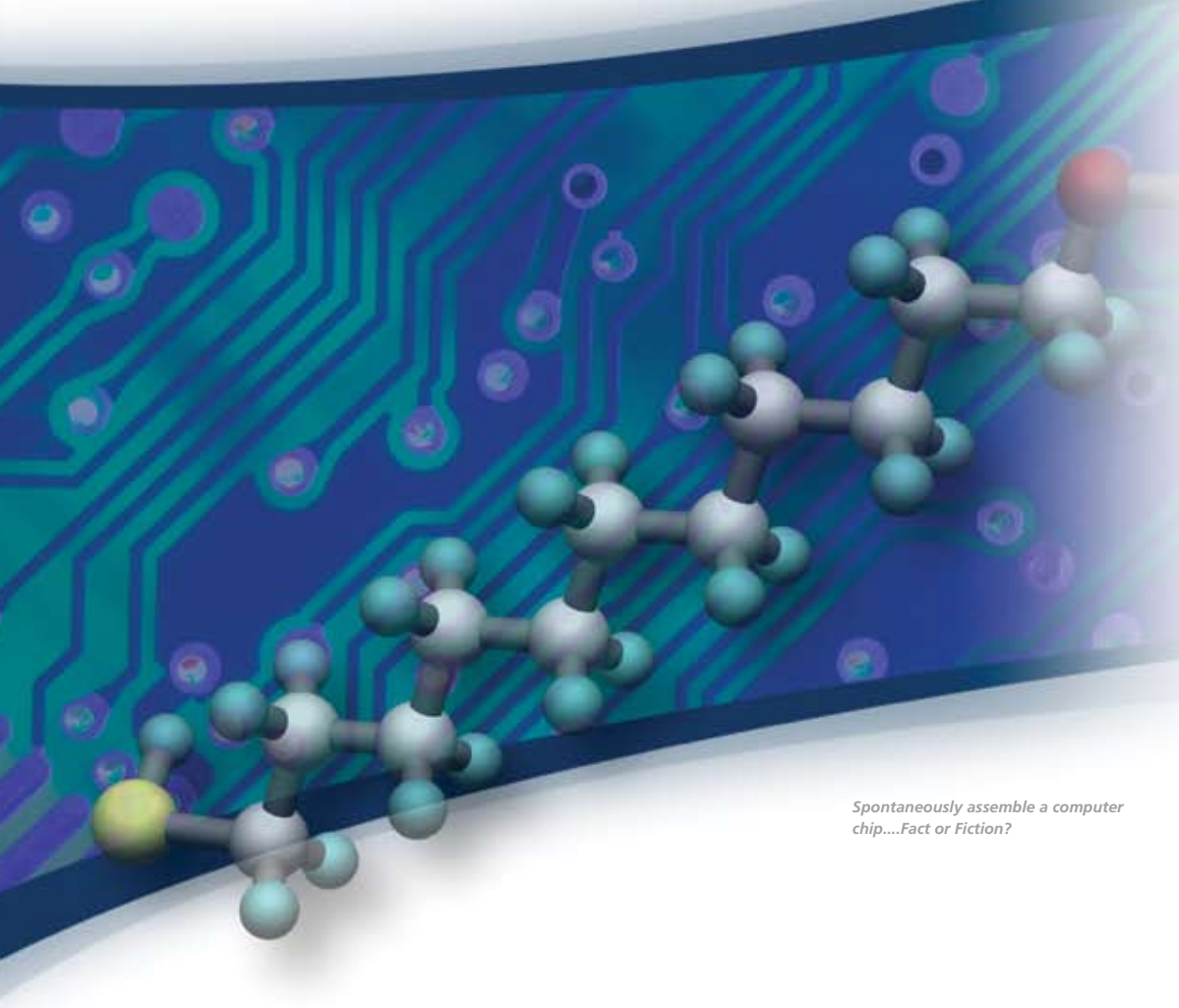
Molecular Self-Assembly



Spontaneously assemble a computer chip....Fact or Fiction?

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Introduction

Welcome to the second issue of *Material Matters*™. This thematic issue focuses on self-assembly and its application for the production of nanodevices. The ability to organize matter using self-assembled monolayers (SAMs) is part of the broader approach of Molecular Self-Assembly as introduced by Dr. Jasty of Sigma-Aldrich Materials Science.

Scientists from Assemblon discuss the importance of purity in enhancing the integrity and kinetics of SAMs formation. The Weiss group from Penn State University illustrates the principle of microdisplacement printing, a SAMs technique to fabricate precise, complex patterns at the nanoscale. Prof. Bao of Stanford University surveys the latest developments in the application of SAMs for the fabrication of organic thin film transistors. Borrowing a basic concept of biomolecular recognition, polyvalent interactions, the team at Sensopath Technologies engineers robust Nanotethers™ as the SAMs molecules for biosensor and other applications. We invite you to participate in the Sigma-Aldrich Biosensor program. Finally, in keeping with the theme of a technical guide, this issue of Material Matters includes a step-by-step protocol for the preparation of SAMs. Products that accelerate your research in the fundamental science of SAMs, and the application of SAMs for the fabrication of nanodevices are highlighted. For product details, please visit us on the Web: **sigma-aldrich.com/matsci.**

We invite your comments, questions and suggestions about *Material Matters*™ and materials of interest to you: matsci@sial.com.

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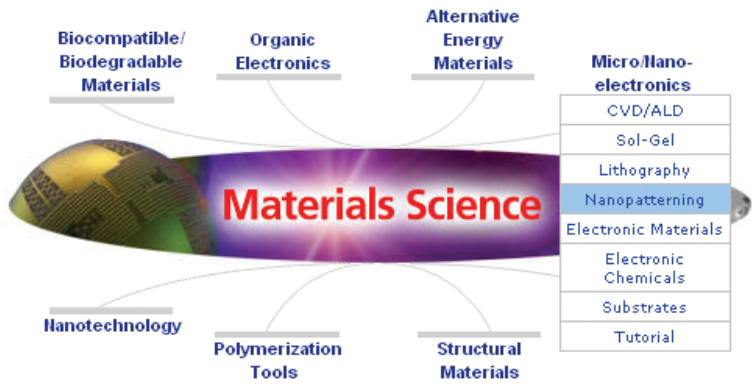

About Our Cover

What would it take to spontaneously assemble a computer chip, or for that matter any complex structure? Starting with constituent molecules such as the one featured on our cover, (11-Mercaptoundecyl)tri(ethylene glycol), and with recent advances in micro- and nanoscale science, scientists from numerous disciplines, chemistry, physics, biology, engineering, and mathematics to name a few, have begun to investigate the self-assembly process in hopes of learning to create, design and control self-assembling systems.

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Introduction to Molecular Self-Assembly

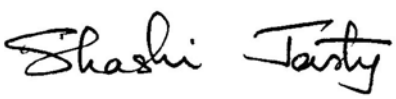
Dr. Shashi Jasty, Sigma-Aldrich Materials Science

Molecular self-assembly is the assembly of molecules without guidance or management from an outside source. Self-assembly can occur spontaneously in nature, for example, in cells such as the self-assembly of the lipid bilayer membrane. It usually results in an increase in internal organization of the system. Many biological systems use self-assembly to assemble various molecules and structures. Imitating these strategies and creating novel molecules with the ability to self-assemble into supramolecular assemblies is an important technique in nanotechnology.

In self-assembly, the final (desired) structure is 'encoded' in the shape and properties of the molecules that are used, as compared to traditional techniques, such as lithography, where the desired final structure must be carved out from a larger block of matter. Self-assembly is thus referred to as a 'bottom-up' manufacturing technique, as compared to lithography being a 'top-down' technique.

On a molecular scale, the accurate and controlled application of intermolecular forces can lead to new and previously unachievable nanostructures. This is why molecular self-assembly (MSA) is a highly topical and promising field of research in nanotechnology today. With many complex examples all around us in nature (ourselves included), MSA is a widely observed phenomenon that has yet to be fully understood. Biomolecular assemblies are sophisticated and often hard to isolate, making systematic and progressive analyses of their fundamental science very difficult. What in fact are needed are simpler MSAs, the constituent molecules of which can be readily synthesized by chemists. These molecules would self-assemble into simpler constructs that can be easily assessed with current experimental techniques.

Of the diverse approaches possible for Molecular Self-Assembly, two strategies have received significant research attention – Electrostatic Self-Assembly (or layer- by-layer assembly) and "**S**elf-**A**ssembled **M**onolayers (SAMs). Electrostatic self-assembly involves the alternate adsorption of anionic and cationic electrolytes onto a suitable substrate. Typically, only one of these is the active layer while the other enables the composite multilayered film to be bound by electrostatic attraction. The latter strategy of Self Assembled Monolayers or SAMs based on constituent molecules, such as thiols and silanes, is the theme for this second issue of *Material Matters*™. For SAMs, synthetic chemistry is used only to construct the basic building blocks (that is, the constituent molecules), and weaker intermolecular bonds such as Van der Waals bonds are involved in arranging and binding the blocks together into a structure. This weak bonding makes solution, and hence reversible, processing of SAMs (and in general, MSAs) possible. Thus, solution processing and manufacturing of SAMs offer the enviable goal of mass production with the possibility of error correction at any stage of assembly. It is well recognized that this method could prove to be the most cost-effective way for the semiconductor electronics industry to produce functional nanodevices such as nanowires, nanotransistors, and nanosensors in large numbers.



Self-Assembled Monolayers: Advantages of Pure Alkanethiols

Dr. Maxi Boeckl and
Dr. Daniel Graham,

Senior Scientists,
Asemblon, Inc.

Self-Assembly: From Nature to The Lab

In the 1980's, scientists discovered that alkanethiols spontaneously assembled on noble metals. This new area of science opened the doors to a simple way of creating surfaces of virtually any desired chemistry by placing a gold substrate into a millimolar solution of an alkanethiol in ethanol. This results in crystalline-like monolayers formed on the metal surface, called self-assembled monolayers (SAMs).[1]

Over the years, the mechanism of the self-assembly process has been well studied and elucidated. Researchers have found that a typical alkanethiol monolayer forms a $(\sqrt{3} \times \sqrt{3})R30°$ structure[2] on gold with the thiol chains tilted approximately 30 degrees from the surface normal.[3–6] The exact structure of the monolayer depends on the chemistry of the chain.

Self-assembly forms the basis for many natural processes including protein folding, DNA transcribing and hybridization, and the formation of cell membranes. The process of self-assembly in nature is governed by inter- and intra-molecular forces that drive the molecules into a stable, low energy state. These forces include hydrogen bonding, electrostatic interactions, hydrophobic interactions, and van der Waals forces.

As with self-assembly in nature, there are several driving forces for the assembly of alkanethiols onto noble metal surfaces. The first is the affinity of sulfur for the gold surface. Researchers have found that the sulfur-gold interaction is on the order of 45 kcal/mol,[3] forming a stable, semi-covalent bond; in comparison, the C—C bond strength is ~83 kcal/mol.

The next driving force for assembly is the hydrophobic, van der Waals interactions between the methylene carbons on the alkane chains. For alkanethiol monolayers, this interaction causes the thiol chains to tilt in order to maximize the interaction between the chains and lower the overall surface energy. A well-ordered monolayer forms from an alkane chain of at least 10 carbons. With carbon chains of this length, hydrophobic interactions between the chains can overcome the molecules' rotational degrees of freedom.[6,7]

A simple alkanethiol molecule is shown in **Figure 1**. (next page) An alkanethiol can be thought of as containing 3 parts: a sulfur binding group for attachment to a noble metal surface, a spacer chain (typically made up of methylene groups, $(CH_2)_n$), and a functional head group. As mentioned above, the sulfur atom and the carbons in the methylene groups act as the main driving forces for assembly of the alkanethiols. The head group then provides a platform where any desired group can be used to produce surfaces of effectively any type of chemistry.

By simply changing the head group, a surface can be created that is hydrophobic (methyl head group), hydrophilic (hydroxyl or carboxyl head group), protein resistant (ethlylene glycol head group), or allows chemical binding (NTA, azide, carboxyl, amine head groups). This enables a researcher to custom design a surface to serve any desired function.

For questions, product data, or new product suggestions, please contact the Materials Science team at matsci@sial.com.

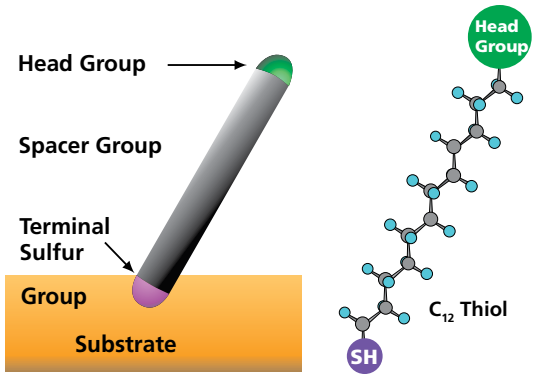


Figure 1. Schematic diagram of a thiol molecule.
The sulfur group links the molecule to the gold surface. The head group can be designed to provide virtually any surface chemistry, binding capacity, or property.

Self-Assembly: Purity Matters

SAMs are typically made from a 1 mM solution of the desired alkanethiol in ethanol. Initial monolayer formation is very fast, with monolayer coverage being achieved within seconds to minutes. This initially formed monolayer is not well ordered and contains many gauche defects within the chains. Over time, the layers become more ordered and well packed. Reported assembly times vary throughout the literature, but typically are 12 hours to 2 days.

The formation of a well-assembled monolayer can depend on the purity of the alkanethiol being used. The presence of even low levels of contaminants can result in a disordered, non-ideal monolayer. Many typical impurities in thiol compounds are thiolated precursor molecules that were not separated during the purification process. These precursor molecules can either be straight chain alkanethiols that lack the head groups of the final product, or they can be molecules used to introduce the thiol functional group to a precursor molecule (such as thioacetic acid). Since these compounds also contain thiol functionalities, they can compete with the alkanethiol of interest for available surface locations. Competitive adsorption can be particularly problematic for alkanethiols with complex or bulky head groups. Bulky head groups can reduce the driving force for assembly by disrupting the close packed arrangement of the alkane chains. With this reduced driving force for assembly, the straight chain or small thiol contaminants can out-compete the alkanethiol of interest on the surface.

These effects were noticed in early alkanethiol self-assembly research and several detailed studies were performed on the preferential adsorption of one alkanethiol versus another. Adsorption from a dilute solution in ethanol of a mixture of two alkanethiols, one with a polar the other with a nonpolar head group, showed that adsorption of the alkanethiol with the nonpolar head group was favored.[7] Bain *et al*. also noticed that alkanethiols with equivalent head groups, but longer chains adsorbed preferentially over shorter alkanethiols. [4] When one tries to intentionally obtain a mixed monolayer, where two or more head groups are present at a desired ratio, it is very difficult to predict the relative surface concentration from the solution concentration and a calibration curve is typically necessary.[4] An example is given by Nelson *et al.*, who studied mixed monolayers of biotinylated alkanethiol mixed with either mercaptohexadecane or (1-mercapto-11-undecyl)tetra(ethylene glycol) and correlated the solution concentration to the surface concentration using electron spectroscopy for chemical analysis (ESCA) and Time-of-Flight Secondary Mass Spectrometry (ToF-SIMS).[8] This study demonstrated how the surface and solution composition in mixed monolayers can vary significantly and why a calibration curve is necessary when engineering mixed monolayer surfaces.

As a demonstration of the effects of thiol impurities in SAM formation, **Table 1** shows ESCA surface composition data from a series of SAMs prepared from thiol solutions that were purposely spiked with "impurities". For this experiment, solutions of (1-mercapto-11-undecyl)tetra(ethylene glycol) (PEG_4 thiol, Aldrich Prod. No. **674508**) were mixed with 0%, 1% and 10% (v/v) thioacetic acid (TAA). All monolayers were prepared from 1 mM solutions in absolute ethanol. The percentages shown for the various thiol components are volume percentages.

The first observation noted from Table 1 is the increase in the atomic percentage of gold with increasing amount of thioacetic acid in the assembly solution. The gold signal comes from the gold substrate underlying the monolayer. This gold signal is attenuated by the overlying monolayer film. A thinner or more disordered overlayer causes a decrease in signal attenuation (increase in the gold signal). This suggests that the addition of even 1% thioacetic acid to the assembly solution caused a marked decrease in the monolayer thickness. Thioacetic acid is a small molecule which if inserted into the monolayer would disrupt the local monolayer order causing the noted decrease in the layer thickness.

Table 1. ESCA composition data from PEG_4 thiol monolayers with and without "impurities". All data is shown in atomic percent. Two analysis spots are shown for each sample.

Sample† (soln percentage)	C 1s	O 1s	S 2p	Au 4f
PEG_4thiol (100%)	64.5	19.1	1.3	15.1
PEG_4thiol (100%)	65.3	20.9	1.2	12.6
PEG_4thiol/TAA (99%/1%)	55.9	17.3	2.3	24.5
PEG_4thiol/TAA (99%/1%)	56.2	17.3	2.8	23.7
PEG_4thiol/TAA (90%/10%)	45.6	12	4.3	38.1
PEG_4thiol/TAA (90%/10%)	46.2	13.6	4	36.2

†PEG_4 thiol = (1-mercapto-11-undecyl)tetra(ethylene glycol); Aldrich Prod. No. **674508** TAA = thioacetic acid

Table 2 shows the data from Table 1 rescaled without the gold signal. This allows comparison of the atomic percentages with that expected based on the solution mixture atomic composition. As seen in Table 2, the experimental values compare well with the calculated values. The atomic percentage of sulfur is typically observed to be lower than expected due to attenuation by the overlying monolayer. This is the case for the 100% PEG_4thiol. The fact that the sulfur data from the other two monolayers is close to the predicted numbers, suggests that the layers are disordered (consistent with the gold atomic percentages) or that there is a high amount of thioacetic acid on the surface (which has a high relative percentage of sulfur vs. the other atoms).

It is interesting to note that when looking at Table 2, one might think that since the relative percentages of carbon and oxygen do not change significantly from sample to sample, that the surfaces are still pure PEG_4 thiol. It is only the high percentage of sulfur that sets the samples apart and indicates that an impurity is likely present.

Overall, this data demonstrates that even small amounts of contaminants in a solution can cause significant differences in the monolayer composition and structure. The best way to avoid these problems is to use molecules with the highest possible purities.

Table 2. ESCA composition data from PEG_4 thiol monolayers with and without "impurities" rescaled without gold signal. All data is shown in atomic percent. Two analysis spots are shown for each sample. The values in bold are the calculated atomic percentages based on the solution mixture ratio of the compounds used.

Sample†	C 1s	O 1s	S 2p
PEG_4thiol (100%)	76.0	22.5	1.5
PEG_4thiol 100%	74.7	23.9	1.4
PEG_4thiol (100%-predicted)	76.0	20.0	4.0
PEG_4thiol/TAA (99%/1%)	74.0	22.9	3.0
PEG_4thiol/TAA (99%/1%)	73.7	22.7	3.7
PEG_4thiol/TAA (99%/1%-predicted)	75.7	20.1	4.2
PEG_4thiol/TAA (90%/10%)	73.7	19.4	6.9
PEG_4thiol/TAA (90%/10%)	72.4	21.3	6.3
PEG_4thiol/TAA (90%/10%-predicted)	73.4	20.5	6.1
TAA (100%-predicted)	50	25	25

†PEG_4 thiol = (1-mercapto-11-undecyl)tetra(ethylene glycol); Aldrich Prod. No. **674508** TAA = thioacetic acid

Results similar to these were seen when thioacetic acid was present in PEG_3 and PEG_6 thiol samples. Both of these samples showed a higher than expected gold and sulfur signals indicating the layers were disordered and a sulfur contaminant was present. The most important property of poly(ethylene glycol) alkanethiols (PEG_n thiols) is the ability to form a non-fouling self-assembled monolayer, but the presence of just small amounts of carboxylic acid-terminated PEG_n thiols (possibly introduced from poly(ethylene glycol) starting material) leads to significant protein adsorption, making the surface more fouling than bare gold itself, as shown by Roberts *et al*.[9]

The interference of thiol contamination with monolayer formation has also been reported for the assembly of thiolated DNA on gold.[10] It was found that the presence of a thiol contaminant, dithiothreitol, impeded the assembly of the thiolated DNA onto the gold surface. The authors showed that when contaminated thiolated DNA was used for the assembly, the atomic percentages of characteristic DNA elements (P, N) did not increase with increasing assembly times as they did with purer samples. Increased assembly times instead resulted in increased amounts of the contaminant molecules on the surface. Samples prepared from relatively pure DNA showed logical trends for the DNA elements in a time series assembly.

Self-Assembly: Unlimited Opportunities

SAMs have been used for studies and applications in many areas. A few examples include surface wetting, non-fouling property, electrochemistry, surface passivation, protein binding, DNA assembly, corrosion resistance, biological arrays, cell interactions, and molecular electronics. These and other topics have been summarized in previous review articles.[11-13]

SAMs have truly opened the doors toward direct surface engineering. Only the imagination limits the possibilities available to the interested researcher. **Figure 2** shows schematic diagrams of several possible applications for alkanethiol monolayers. These types of applications will likely rely on high purity alkanethiols with head groups such as those listed in **Table 3**.

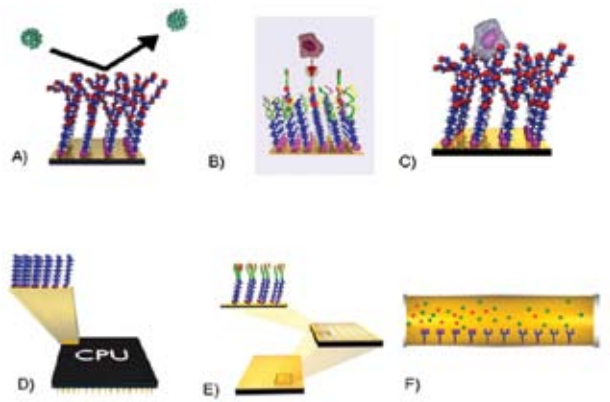


Figure 2. Possible applications for alkanethiol monolayers. A) Non-fouling surfaces B) SAMs with specific binding receptors C) Cell supports for native cell growth and studies D) Molecular electronics E) Microarrays F) Separations.

Table 3: Some head group examples useful for the applications shown in Figure 2.

Application	Common Head Group
Non-fouling surfaces	PEG_n, Mannose
Specific binding receptors	Biotin, NTA, Peptide, Carbohydrates
Cell supports	Peptide
Molecular electronics	CH_3, SH
Microarrays	DNA, Peptide, PEG_n
Separations	NTA
Surface reactions	Azide, COOH, NH_2, OH, SH

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(1) Nuzzo, R. G.; Allara, D. L. *J. Am. Chem. Soc.* **1983**, 105, 4481. (2) Strong, L.; Whitesides, G. M. *Langmuir* **1988**, 4, 546. (3) Dubois, L. H.; Nuzzo, R. G. Annu. *Rev. Phys. Chem.* **1992**, 43, 437. (4) Bain, C. D.; Whitesides, G. M. *J. Am. Chem. Soc.* **1989**, 111, 7164. (5) Bain, C. D.; Whitesides, G. M. *Angew. Chem. Int. Ed.* **1989**, 28, 506. (6) Porter, M. D.; Bright, T. B.; Allara, D. L.; Chidsey, C. E. D. *J. Am. Chem. Soc.* **1987**, 109, 3559. (7) Bain, C. D.; Evall, J.; Whitesides, G. M. *J. Am. Chem. Soc.* **1989**, 7155. (8) Nelson, K. E.; Gamble, L.; Jung, L. S.; Boeckl, M. S.; Naeemi, E.; Golledge, S. L.; Sasaki, T.; Castner, D. G.; Campbell, C. T.; Stayton, P. S. *Langmuir* **2001**, 17, 2807. (9) Roberts, B. J.; Naeemi, E.; Ratner, B. D. *JURBIE* **2004**, 4, 103-107. (10) Lee, C.-Y.; Canavan, H. E.; Gamble, L. J.; Castner, D. G. *Langmuir* **2005**, 21, 5134. (11) Love, J. C.; Estroff, L. A.; Kriebel, J. K.; Nuzzo, R. G.; Whitesides, G. M. *Chem. Rev.* **2005**, 105, 1103. (12) Chaki, N. K.; Vijayamohanan, K. *Biosensors & Bioelectronics* **2002**, 17, 1. (13) Ulman, A. *Chem. Rev.* **1996**, 96, 1533.

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4		**451878** (95%)		
5	**P7908** (98%)			
6	**234192** (95%)	**451088** (97%)	**674974** (90%)	**H12005** (96%)
7	**H4506** (95%)			
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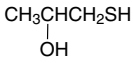
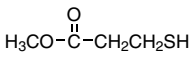
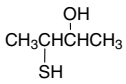
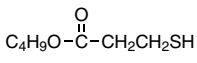
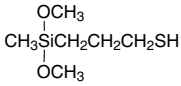
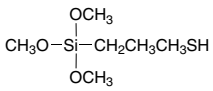
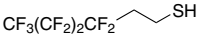
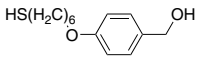
Alkane Thiol	Structure	Purity, %	Product No.	
1-Mercapto-2-propanol		95	328375-1G 328375-5G	22.60 61.80
Methyl 3-mercaptopropionate		98	108987-100G 108987-500G 108987-5G	29.50 79.50 20.60
3-Mercapto-2-butanol, mixture of isomers		97	264792-1G 264792-5G	28.00 93.30
Butyl 3-mercaptopropionate		98%	381454-100ML 381454-500ML	22.90 54.30
3-(Dimethoxymethylsilyl)-1-propanethiol		95	446173-10ML 446173-50ML	18.00 50.00
(3-Mercaptopropyl)trimethoxysilane		95	175617-25G	18.70
1*H*,1*H*,2*H*,2*H*-Perfluoro-1-hexanethiol		98	16494-250MG	130.00
4-(6-Mercaptohexyloxy)benzyl alcohol		96.5	673560-50MG	157.00

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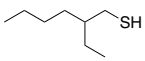
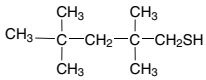
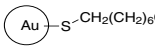
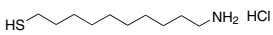
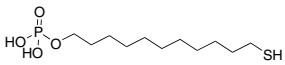
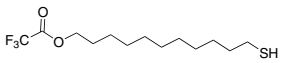
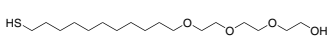
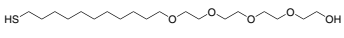
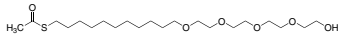
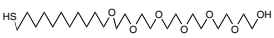
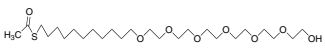
Alkane Thiol	Structure	Purity, %	Product No.	
2-Ethylhexanethiol		96	669148-25G 669148-100G	34.60 112.50
tert-Nonyl mercaptan, mixture of isomers		97	171034-250ML 171034-1L	26.90 74.60
tert-Dodecylmercaptan, mixture of isomers	$C_{12}H_{25}SH$	98.5	471585-100ML 471585-500ML 471585-2L	16.00 28.80 55.40
1*H*,1*H*,2*H*,2*H*-Perfluorodecanethiol		97	660493-25G 660493-5G	157.00 58.70
11-Amino-1-undecanethiol, hydrochloride		99	674397-50MG	264.00
11-Mercaptoundecyl phosphoric acid		99	674311-50MG	300.00
11-Mercaptoundecyl trifluoroacetate		99	674230-50MG	314.50
2,2′-(Ethylenedioxy)diethanethiol	$HSCH_2CH_2OCH_2CH_2OCH_2CH_2SH$	95	465178-100ML 465178-500ML	18.00 57.60
11-Mercaptoundecyl)tri(ethylene glycol)		95	673110-250MG	113.00
(1-Mercaptoundec-11-yl)tetra(ethylene glycol)l		95	674508-250MG	129.00
(1-(Methylcarbonylthio)undec-11-yl)tetra(ethylene glycol)		95	674176-250MG	91.90
(1-Mercaptoundec-11-yl)hexa(ethylene glycol)		96.5	675105-250MG	270.80
Hexa(ethyleneglycol)mono-11-(acetylthio)undecylether		95	675849-250MG	75.10

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Displaceable Monolayers and Microdisplacement Printing: 1-Adamantanethiol Assembly and Applications

Thomas J. Mullen, J. Nathan Hohman, Dr. Arrelaine A. Dameron,

Jennifer R. Hampton, Susan D. Gillmor, and Prof. Paul S. Weiss (photo)

Departments of Chemistry and Physics, The Pennsylvania State University

Introduction

Self-assembly techniques at the supramolecular 1–100 nm scale have been extensively studied for applications ranging from biocompatible systems to microelectronics.[1, 2] As the dimensions of patterned surface structures decrease, the difficulty and intricacy of fabricating and measuring these structures increases.[3, 4] Employing a library of molecules with a range of distinctive chemical and physical properties allows the design and the fabrication of thin films for specific applications. 1-Adamantanethiol (1-AD), an example in this spectrum of molecules with distinct chemical and physical properties, forms self-assembled monolayers (SAMs) on Au{111} that are displaceable when exposed to other thiolated molecules from solution, vapor, or contact[5, 6] due to weak intermolecular interactions in 1-AD SAMs. This process is called microdisplacement. The process can be applied to intelligent self- and directed- assembly[7, 8] to fabricate nanoscale-separated SAMs and improve chemical patterning techniques.

Experimental

All SAMs were fabricated using 1-adamantanethiol (1-AD, Aldrich Prod. No. **659452**), 1-dodecanethiol (C12, Aldrich Prod. No. **471364**), and 1-octanethiol (C8, Aldrich Prod. No. **471836**) on commercially available Au{111} that was evaporated onto freshly cleaved mica substrates and annealed using a hydrogen flame just prior to deposition. A single component 1-AD SAM was created by immersing a gold substrate into a 10 mM ethanolic 1-AD solution for 24 h. Subsequently, the gold substrate with the single-component 1-AD SAM was rinsed in neat ethanol and blown dry with nitrogen twice.

To fabricate separated C12 and 1-AD SAMs, a single-component 1-AD SAM was immersed in a 1 mM ethanolic C12 solution for a displacement time of 20 min and then rinsed in neat ethanol and blown dry with nitrogen twice. Representative scanning tunneling microscopy (STM) images were acquired for both the single-component 1-AD SAMs and the separated C12 and 1-AD SAMs within 24 h of SAM fabrication. From the STM images, the lattice structure, the domain boundaries, and the molecular order of the SAMs were investigated. All STM measurements were performed under ambient conditions using a custom beetle-style STM.[9] Images were recorded in constant-current mode and at high tunneling gap impedances (~10^{12} GΩ) to ensure large tip-sample separation for minimal contact between the probe tip and the monolayer.

Microdisplacement-printed SAMs were fabricated by contact of a C8 coated patterned elastomeric stamp with a preformed single-component 1-AD SAM.[7, 8] An elastomeric polydimethylsiloxane (PDMS) stamp was fabricated, cleaned, and exposed to a 10 mM ethanolic solution of C8 for 10 s and blown dry with nitrogen using a modified method described by Graham *et al.*[10] The stamp with C8 ink was contacted to the single-component 1-AD SAM for 5 min, and then the sample was rinsed in neat ethanol and blown dry with nitrogen twice. Lateral force microscopy (LFM) images were acquired within 1 h of pattern fabrication using a Thermo Microscopes Autoprobe CP Research Atomic Force Microscope (Veeco, Santa Barbara, CA). Silicon nitride tips with a spring constant of 0.05 nN/m were used as received from Mikromasch (Portland, OR).

Results and Discussion

Ordered 1-AD monolayers were formed when a Au{111} substrate was exposed to an ethanolic 1-AD solution.[5] **Figure 1 (A)** displays a representative STM image of a single-component 1-AD SAM predominantly showing two flat terraces with several monatomic substrate step edges as well as depressed regions attributed to substrate vacancy islands.

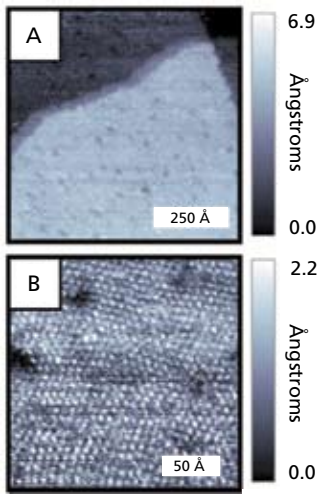

Figure 1. Scanning tunneling microscopy image of a 24 h 1-adamantanethiolate (1-AD) SAM on a Au{111} substrate. Image parameters: Vsample = -0.75 V, Itunnel = 3.0 pA. A) **Resolution:** 750 Å × 750 Å; shows several monatomic step edges and substrate vacancy islands. B) Resolution: 200 Å × 200 Å; molecular resolution shows the 1-AD lattice.

Both of these features are commonly observed in thiol SAMs. Additionally, 1-AD SAMs show depressed domain boundaries resulting from rotational domains of the 1-AD molecules. This is in contrast to alkanethiolate SAM systems, which exhibit protruding domain boundaries associated with regions of molecules with differing tilts, rotational and translational boundaries, and stacking faults.[11-13] **Figure 1 (B)** shows a representative STM image with molecular resolution of a single-component 1-AD SAM, showing individual molecules arranged in a hexagonally closed-packed structure with nearest-neighbor spacing of 6.9 ± 0.4 Å. This lattice spacing is considerably larger than the nearest-neighbor spacing for alkanethiolate SAMs and can be attributed to the bulky carbon cage of 1-AD molecules compared to the relatively compact (predominantly all-trans) alkyl chains of

alkanethiolates. A (7×7) unit cell can be assigned to the 1-AD SAM with respect to the Au{111} substrate.[5] Typical alkanethiol SAMs exhibit a (√3×√3)R30° unit cell. This implies that there are 1.8 times more molecules in an alkanethiol SAM than in a 1-AD SAM in the same area of Au{111}. For example, in a (7√3×7√3)R30° unit area of Au{111}, which is the unit area where the 1-AD and alkanethiolate unit cells overlap, there are 49 alkanethiolate molecules (21.4 Å2/molecule) and 27 1-AD molecules (38.9 Å2/molecule).

Nanoscale-separated SAMs offer excellent opportunities to investigate the influence of intermolecular interactions on the assembly of thin films, which is essential for the further development of chemical patterning techniques.[14, 15] **Figure 2 (A and B)** show representative STM images of separated C12 and 1-AD SAMs formed via C12 solution displacement of preformed 1-AD SAMs.

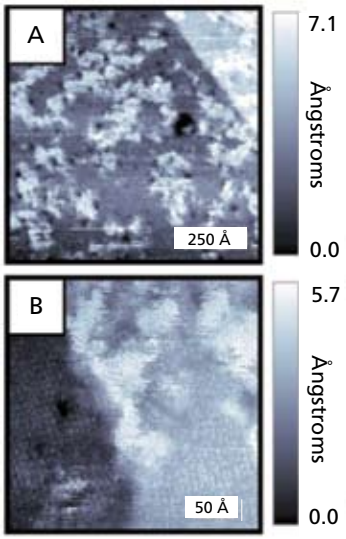

Figure 2. Scanning tunneling microscopy image of a separated 1-dodecanethiolate (C12) and 1-adamantanethiolate (1-AD) SAM on a Au{111} substrate. Image parameters: V_{sample} = -1.20 V, I_{tunnel} = 1.0 pA. **A) Resolution:** 1000 Å × 1000 Å; shows distinct domains of both lattice types: C12 - more protruding molecular domains; 1-AD - less protruding molecular domains; the most depressed regions are substrate vacancy islands. **B) Resolution:** 300 Å × 300 Å; shows the molecular order of each lattice type.

The apparent heights and the differences in lattice spacing were employed to differentiate between the C12 and 1-AD lattice types. The most protruding lattice with smaller molecular spacing that originates at the substrate defects was attributed to C12, while the less protruding lattice with larger molecular spacing was attributed to 1-AD. Substrate step edges and substrate vacancy islands (the most depressed regions) were observed throughout the separated SAM. The fractional C12 coverage of the separated C12 and 1-AD SAM was controlled by the C12 displacement time (i.e. longer C12 displacement times result in larger C12 domains). At long C12 displacement times, the resulting SAM was completely composed of C12 molecules, although the C12 domains were significantly smaller when compared to a single-component C12 SAM.

Microcontact printing (μCp) is a technique for chemically patterning a substrate by contact with an elastomeric stamp that is inked with the molecules to be patterned.[16] Molecules on the stamp are transferred from the stamp to the substrate only in places where the stamp and substrate are in contact. However, this process is limited to molecules that are not susceptible to lateral diffusion across the surface. Microdisplacement printing (μDp), is an alternative patterning technique not limited by lateral diffusion. In μDp, a preformed 1-AD monolayer is used that is sufficiently labile to be displaced by patterned molecules through competitive adsorption while preventing lateral diffusion of the patterned molecules.[7,8] **Figure 3** displays a LFM image of a patterned Au{111} substrate fabricated by μDp.

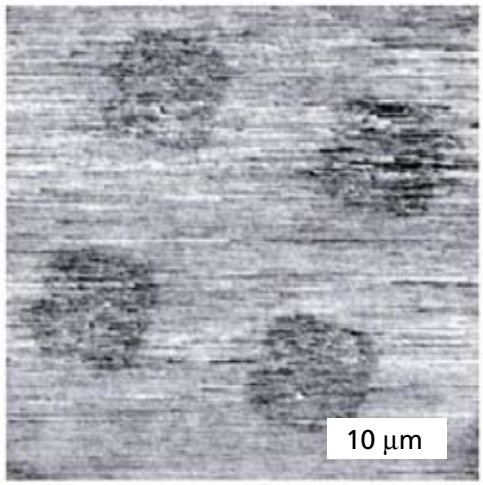

Figure 3: Lateral force microscopy (LFM) image of a patterned Au{111} substrate made by microdisplacement printing. The low-friction (shown as dark) squares are the stamped octanethiol molecules, and the high-friction (shown as light) background is the preformed 1-adamantanethiolate SAM. Image parameters: 40 μm × 40 μm, Scan rate = 1.0 Hz, Force setpoint = 4 nN.

The low-friction (shown as dark) squares are stamped C8 molecules, and the high-friction (shown as light) background is the preformed 1-AD SAM. This pattern could not be formed using traditional μCp printing. μDp also eliminates the need for solvent exposure after stamping. Solvent exposure is often required in μCp to prevent degradation of the pattern over time, but the precision of the pattern is reduced due to molecular exchange. With microdisplacement printing, the 1-AD SAM is still present in places where the elastomeric stamp did not contact the surface; thus, a solvent exposure step is not necessarily required. Multiple stamping steps can also be used to create proximate structures, circumventing the difficulty in the precise registration of neighboring patterns in conventional printing.[8]

Conclusions

Highly ordered, one-molecule-thick films of 1-adamantanethiol (1-AD) can be fabricated on Au{111} substrates. Exploiting the labile nature of 1-AD SAMs, precise nanoscale-separated SAMs can be fabricated and can enhance common chemical patterning techniques by hindering the lateral movement of molecules across a patterned surface.

Acknowledgments

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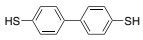
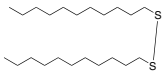
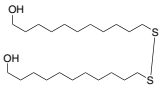
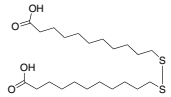
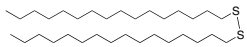
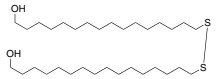
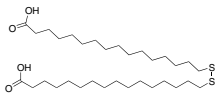
(16) Wilbur, J. L.; Kumar, A.; Kim, E.; Whitesides, G. M., *Adv. Mater.* **1994**, 6, 600.

Thiol Products

Product Description	Structure	Purity,%	Product No.	
1-Adamantanethiol		95	659452-5G	55.50
Biphenyl-4,4′-dithiol		95	673099-1G	95.00

Alkane Disulfides

Alkane Disulfide	Structure	Purity,%	Product No.	
Undecyl disulfide		99	674303-250MG	180.00
Hydroxyundecyl disulfide		99	674257-250MG	220.00
Carboxy undecyl disulfide		99	674451-250MG	157.00
Hexadecyl disulfide		99	674419-500MG	157.00
Hydroxyhexadecyl disulfide		99	674478-100MG	220.00
Carboxy hexadecyl disulfide		99	674443-250MG	220.00

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Product Description	Coating Thickness/Particle Size	Prod. No.	
99.999% Gold coated silicon wafer, 4″× 500 µm wafer	1000 Å	643262-1EA	123.50
99.999% Gold coated microscope slide, 3″×1″× 0.7 mm slide	100 Å	643203-5EA	243.50
99.999% Gold coated microscope slide, 3″×1″× 0.7 mm slide	1000 Å	643246-5EA	371.50
Gold coated glass cover slip, 22 mm x 22 mm square	100 Å	643254-12EA 643254-24EA	391.00 416.50
Gold coated glass cover slip, 15 mm diameter	100 Å	643289-24EA	480.50
Gold coated mica, 1″x 3″ slide	2000 Å	643297-1EA	737.00
Gold colloid	3.5–6.5 nm	G1402-25ML	63.40
Gold colloid	8–12 nm	G1527-25ML	63.40
Gold colloid	17–23 nm	G1652-25ML	63.20
Gold, nanopowder, 99.9+%	50–130 nm	636347-1G	203.00
Gold, wire, 1.0 mm diameter, 99.999%	1.0 mm†	349305-1.5G 349305-375G	260.50 83.90
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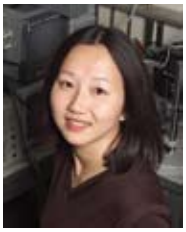
Self-Assembly In Organic Thin Film Transistors For Flexible Electronic Devices



Professor Zhenan Bao

Department of Chemical Engineering,
Stanford University

Introduction

Flexible electronic circuits and displays based on organic active materials are future generations of products that may eventually enter mainstream electronics market. The advantages in using organic active materials are their ease in tuning electronic and processing properties by chemical design and synthesis, low cost processing based on low temperature processes and reel-to-reel printing methods, mechanical flexibility, and compatibility with flexible substrates.[1]

Organic thin film transistors (OTFTs) are the basic building blocks for flexible integrated circuits and displays. A schematic structure is shown in **Figure 1**.[2]

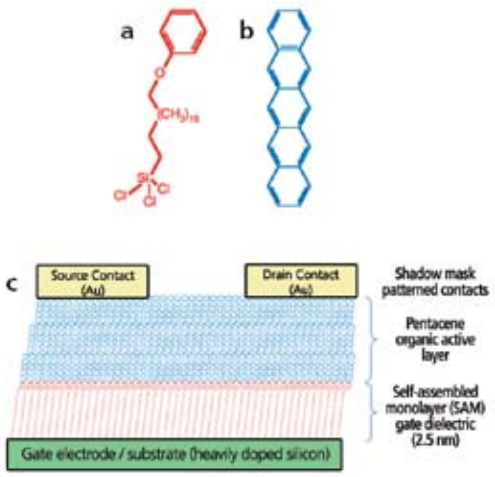


Figure 1. Schematic structure of an organic thin film transistor. (a) Chemical structure of the silane molecule used as the self-assembled monolayer dielectric layer (b) Chemical structure of pentacene used as the semiconductor layer (c) schematic structure of the device. Reproduced with permission from the Nature Publishing Group.

During the operation of the transistor, a gate electrode is used to control the current flow between the drain and source electrodes. Typically, a higher applied gate voltage leads to higher current flow between drain and source electrodes. A fast switching transistor should have a high charge carrier mobility and a high on/off current ratio for the semiconductor material. For the pixel switching transistors in liquid crystal displays, mobility greater than 0.1 cm^2/Vs and on/off ratio greater than 10^6 are needed.

Both self-assemblies and self-assembly processes play important roles in improving device performance as well as enabling low cost processing methods for the fabrication of these devices. In this article, a briefly survey is given on the applications of self-assembly in OTFTs.

Surface modification with self-assembled monolayers (SAMs)

Drain and source electrode surface modification with SAMs

For organic transistors to function well, charge injection from the electrode needs to be efficient. This requires the work function of the electrode to match well with the energy level of the organic semiconductor such that the energy barrier for charge injection is low. For organic transistors, typically high work function electrodes (Au, Pd, or indium tin oxide) have been used for p-channel organic semiconductors, in which holes are injected and transported through the organic material. It has been found that electrode surface modification with a self-assembled monolayer can be used to improve the charge injection into the organic semiconductor.[3] For example, when Au electrodes are used, they can be functionalized with various thiol SAMs to tune their work functions. Moreover, the morphology of organic semiconductors is significantly different when deposited on SAM modified Au compared to bare Au. This observation has been used to tune the morphology of the organic semiconductor at the Au/organic interface to improve its charge injection.[4]

Dielectric surface modification

Surface treatment of dielectric layer is an important way to improve organic transistor performance. Since most of the charge carriers induced in the semiconductor layer are confined to the first 5 nm of organic semiconductor from the semiconductor/dielectric interface, the dielectric surface chemical and physical characteristics thus play a significant role on the charge carrier transport. For example, Si-OH groups on SiO_2 surface (a typical dielectric material) is known to trap electrons. Capping SiO_2 surfaces with octadecyl trichlorosilane (OTS) molecules can significantly reduce electron traps and improve mobility of n-channel semiconductors (electrons are the major charge carriers).[5]

Additionally, dielectric surface treatment with SAMs also affects the nucleation and growth of organic semiconductors.[6] For example, pentacene is an organic semiconductor with the highest reported thin film charge carrier mobility. Its charge carrier mobility changes significantly depending on the types of hydrophobic SAM surface treatment. This difference is related to the morphological difference of the first pentacene monolayer formed on different surfaces.[6]

SAMs as the active dielectric or semiconductor layers

Dielectric layer

The dielectric layer for organic transistors should be as thin as possible, pinhole-free, and ideally with a high dielectric constant for low voltage operation. A well-ordered densely packed SAM may be the thinnest possible high quality dielectric layer. As shown in Figure 1, a SAM is used as the active dielectric layer for high performance low voltage organic transistors.[2] Other SAMs, as well as self-assembled multilayers, have also been reported as high performance dielectric layers **Figure 2**.[7,8] SAM initiators have been used for initiating surface polymerization to form dielectric layers **Figure 3**.[9]

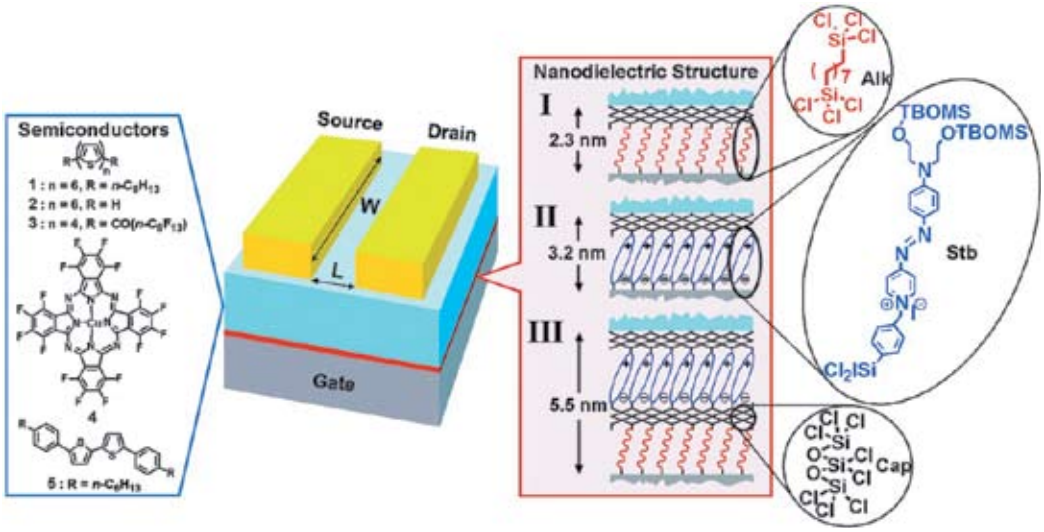


Figure 2. Schematic representation of the components of an OTFT showing the molecular structures of various organic semiconductors (*left*) and self-assembled nanodielectries **I-III** (*right*). Nanodielectric layers were deposited from solutions of silane precursors.

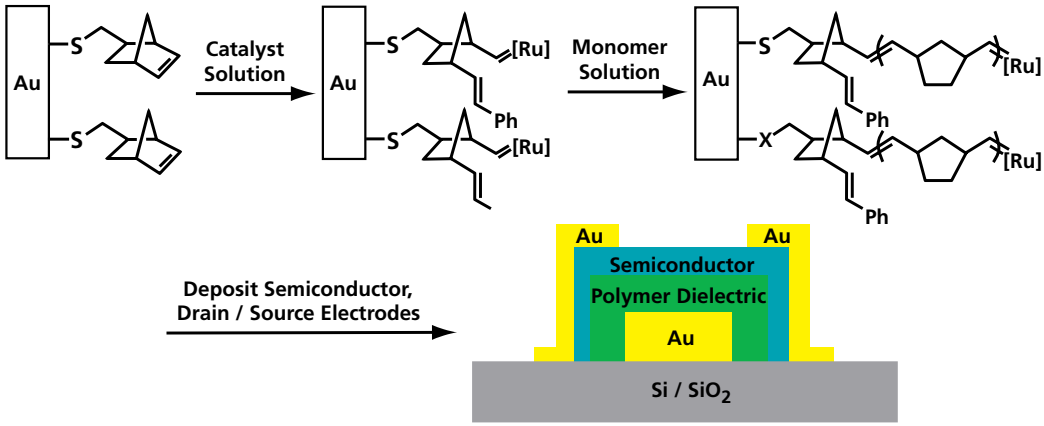


Figure 3. Modification of a gold gate electode for the surface initiated polymerization reaction to grow a dielectric layer.

Semiconductor layer

To facilitate charge transport, the organic semiconductor layer usually comprises of pi-conjugated oligomers or polymers, in which the pi-pi stacking direction should ideally be along the current flow direction. This requires the semiconductor molecules to self-assemble into desirable orientation upon either vapor or solution deposition. These well-ordered molecular layers can be formed by (1) proper molecular design of chemical structures that favor crystallization into large ordered domains or (2) self-assembly into mono and multi layers.[10,11]

Regioregular poly(3-hexylthiophene) is one of the few polymer semiconductors that spontaneously assemble into well ordered structures upon solution deposition by drop casting or spin coating **Figure 4**.[12] It is among the few reported polymer semiconductors with a mobility greater than 0.1 cm^2/Vs.[13,14]

Layer-by-layer deposition is a potentially useful method for organic semiconductor deposition. It allows precise control of the layer thickness, roughness, chemical composition, and molecular orientation. This method has been used to prepare self-assembled multilayers of copper phthalocyanine derivatives. Ion-assisted doping has been observed for these devices.[11]

Self-assembled monolayers for patterning

For organic transistors, the active semiconductor layer has to be patterned in order to minimize cross talk between devices. Additionally, both the drain and source electrodes need to be patterned so that they are separated by at most a few micrometers depending on application requirements.

In addition to various printing methods, such as ink-jet printing, screen printing, and offset printing,[15-17] SAM modified surfaces have been used for selective deposition of organic semiconductors through patterned wettability or templated growth **Figure 5**.[18,19] Patterned SAM layers can be patterned by conventional photolithography or microcontact printing.[20] In addition to pattern organic semiconductors, patterned SAM can be used as an etch resistant layer to prevent etching of an Au film underneath a thiol SAM to generate Au electrodes.[21] Patterned SAM layers have also been used to initiate electroless plating of patterned metal electrodes on plastic substrates.[22]

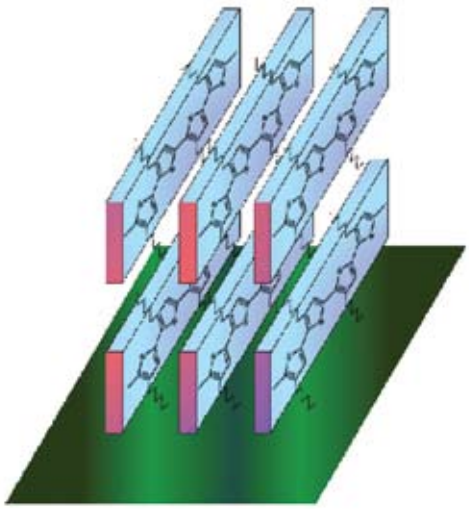


Figure 4. Regioregular poly(3-hexylthiophene) spontaneously assemble into ordered structures upon solution deposition. The pi-pi stacking between polymer chains facilitates change transport.

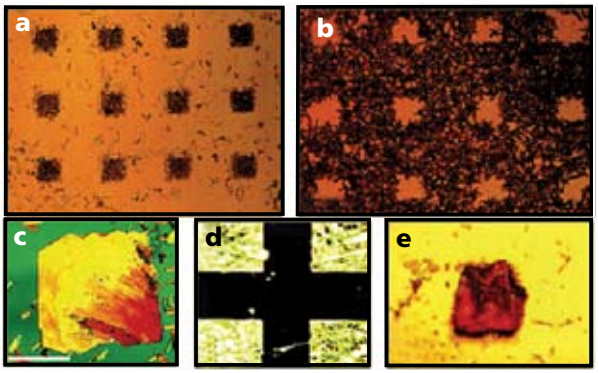


Figure 5. Optical micrographics of patterned arrays of organic semiconductor crystals nucleated selectively on to self-assembled terphenyl thiol template patterens: (a) and (b) anthracence crystals, scale bar = 200 µm; (c) large oriented sigle crystal of anthracene, scale bar = 50 µm (d) patterned anthrancene crystalline films, scale bar = 300 µm; (e) patterned single crystal of 5-chlorotetracence, scale bar = 100 µm

In summary, both self-assemblies and self-assembly processes are crucial as active materials as well as low cost fabrication methods for organic flexible electronic devices. Significant progress has already been made in this field. Nevertheless, as the demand for performance and precision in patterning increases, self-assembly processes will become increasingly important.

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Alkyl Silanes – Linear Chain

$CH_3(CH_2)_{n-2}CH_2\text{-}SiR_3$

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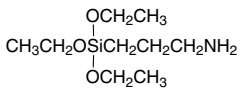
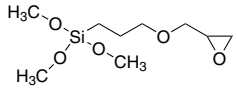
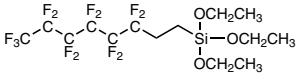
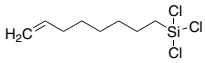
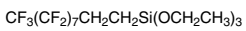
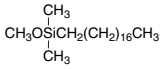
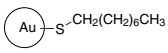
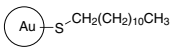
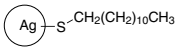
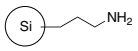
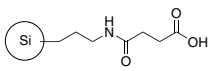
n\-R	-OCH3	-OCH2CH3	-Cl
3	**175617** (95%)		
5			**533386** (99%)
6			**446963** (97%)
8	**376221** (96%)	**440213** (96+%)	
10			**448591** (97%)
12		**44237** (95+%)	**280569** (98%)
16	**52360** (85%)		**52356** (80%)
18	**376213** (90%)		**104817** (90%), **74762** (85+%)

Additional Silanes for Self-Assembly

Silane	Structure	Purity, %	Product No.	
(3-Aminopropyl)triethoxysilane		99	440140-100ML 440140-500ML	37.60 139.00
(3-Glycidyloxypropyl)trimethoxysilane		98	440167-100ML 440167-500ML	26.80 88.70
1*H*,1*H*,2*H*,2*H*-Perfluorooctyltriethoxysilane		97	667420-25G 667420-5G	220.00 68.10
Octenyltrichlorosilane, mixture of isomers		96	539279-25ML	162.00
1*H*,1*H*,2*H*,2*H*-Perfluorodecyltriethoxysilane		97	658758-25G 658758-5G	178.50 45.30
Methoxy(dimethyl)octadecylsilane		>90	40955-100ML 40955-25ML	325.00 119.00

Functionalized Nanoparticles for Self-Assembly

Product Description	Structure	Product No.	
Octanethiol functionalized gold nanoparticles, 2 % (w/v) in toluene		660426-5ML	357.50
Dodecanethiol functionalized gold nanoparticles, 2 % (w/v) in toluene		660434-5ML	357.50
Dodecanethiol functionalized silver nanoparticles, 0.25 % (w/v) in hexane		667838-25ML	126.00
3-Aminopropyl functionalized silica nanoparticles, 3 % (w/v) in ethanol		660442-25ML	141.50
3-Aminopropyl-(3-oxobutanoic acid) functionalized silica nanoparticles, 2.5 % (w/v) in DMF		660450-25ML	188.50

Functionalized Polyelectrolytes

Polyelectrolytes are defined as materials for which properties in solvents with high dielectric constant are governed by electrostatic interactions over distances larger than typical molecular dimensions.[1,2] These materials have been successfully applied in electrostatic self-assembly techniques[3] for thin film deposition of electrically conducting polymers,[4] conjugated polymers for light emitting devices,[5] nanoparticles,[6] and nonlinear optical (NLO) materials.

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(1) *Specialty Polymers;* Dyson, R.W., Ed.; Chapman and Hall, **1987**; p 110; Aldrich Prod. No. Z22,414-6. (2) For a discussion of the differences between polyelectrolytes and ionomers, see: Eisenberg, A.; Kim, J-S. *Introduction to Ionomers;* John Wiley, **1998**; Aldrich Prod. No. Z41,033-0. (3) *Handbook of Polyelectrolytes and Their Applications, 3 Volumes,* Tripathy, S. et al., Eds.; American Scientific Publishers, **2002**; Aldrich Prod No. Z54,718-2. (4) Sayre, C.N.; Collard, D.M. *J. Mater. Chem.* **1997**, 7, 909. (5) Cheung, J. et al. *Polym. Prepr.* **1993**, 34, 757. (6) Schmitt, J. et al. *Adv. Mater.* **1997**, 9, 61.

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Association of Sulfur with Gold

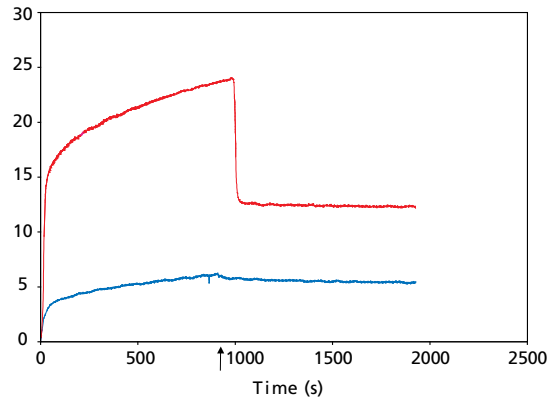
Self-assembled monolayers or SAMs of thiols and organic disulfides on gold surfaces were described by Nuzzo and Allara in 1983[1] as a considerable improvement over difficult to maintain Langmuir-Blodgett monolayers. Extensive studies by these authors and by the Whitesides group at Harvard University led to a generally accepted conclusion that the bonding state of an adsorbed thiol or disulfide on gold was an Au-thiolate (Au_0-S-) with a binding energy somewhere between the binding energy for electrostatic interaction and a covalent bond, based on X-ray-photoelectron spectroscopy (XPS), Auger electron spectroscopy, temperature-programmed desorption and high-resolution electron energy loss spectroscopy [2–5]. There is also indication that the disulfide association is much faster and more stable than a simple monothiol association with the gold surface, a point we will return to later in this article, and that the S-S bond of a disulfide may be cleaved during adsorption to the Au(111) surface[5] to yield the thiolate. On the other hand, an in-depth X-ray diffraction study by Fentner *et al.*[6] suggests that the monolayer spacing (2.2 A°) of alkane thiols on Au(111) is close enough to imply the existence of a disulfide bond between adjacent alkane thiols. It is then possible to hypothesize that the sulfur atoms may intercalate between the gold atoms, thus accounting for the deprotonation of the thiol to thiolate or disulfide and concomitant presence of Au_0, as well as enhanced binding energy and enhanced stability of the sulfur-gold association beyond a simple electrostatic interaction.

More is Better

Polyvalent interactions are one of the basic concepts of biological molecular recognition. Multiple ligand binding, represented by polyvalent antibodies or oligomeric binding subunits is characteristic of many bacterial toxins, as well as several enzyme systems and the well known example in molecular assembly, the tetrameric strepavidin interaction with biotin. Multiple interactions provide a far stronger association than the affinity (K_A) of single ligand for its target substrate. This point has been extensively explored[7] and in fact, discussed in terms of stability of alkane thiol monolayers, which spontaneously desorbed in solvent under ambient conditions from gold, silver, platinum, or copper. Both desorption and self-exchange were observed although residual thiols that could not be desorbed were observed[8]. The resulting patchy surface, however, left significant areas of metal exposed. The desorption-resorption phenomenon has been proposed as a mechanism for stochastic switching in wired molecules that are part of an alkanemonothiol self-assembled monolayer[9]. It is clear that stability of the monolayer could be improved significantly by the simple construction of divalent or polyvalent thiols. The reasoning is as follows: for uncorrelated desorption of widely spaced adsorbing groups such as those on a dithiolalkane phenyl ring, the adsorption can be treated statistically. The probability of a polyvalent molecule, for example, a Nanotether™, having all thiols off the gold surface simultaneously (total desorption) is a power series. That is, if the association constant $k_a = x$ for a monothiol, then $k_a = x^2$ for a dithiolalkane phenyl group. Imagine a group of monkeys hanging by only one hand from a tree branch, reaching for a banana in a wind flow. Any monkey who lets go will be blown away without the banana. If the monkeys were hanging by both hands while reaching for a banana with their tails, then they would be exponentially more stable and much less likely to be blown off the branch. Monkeys hanging by both hands and their tails would, of course, be k_a^3 more stable.

Monothiol vs Dithiol Monolayers

Figure 1 shows that aromatic dithiol tethers (Aldrich Prod. No. **674338**) do in fact adsorb more quickly and provide more surface coverage than aromatic monothiols (Aldrich Prod. No. **673560**). The data were recorded on a Reichert 7000 Surface Plasmon Resonance (SPR) instrument by flowing the nanotethers™ (1 mM in 100% ethanol) over a clean gold SPR slide then washing with 100% ethanol at a preset time.



Aldrich Prod. No. **674338** Aldrich Prod. No. **673560**

Figure 1. Monolayer formation by dithiol aromatic Nanotether™ (red) vs monothiol aromatic Nanotether™ (blue) followed by solvent wash. Arrow indicates introduction of 100% ethanol wash.

The dithiol adsorption is significantly faster and after washing, the resulting dithiol monolayer has a higher refractive index (higher pixel number) than the monothiol dendron monolayer suggesting better coverage. We believe the sharp drop upon initiation of ethanol wash is due to

loss of unadsorbed dendrons accumulated on the saturated monolayer surface. Non-specifically adsorbed films have been previously observed when slides are pulled from solutions containing thiols after set-up of the self-assembled monolayer. Desorption and loss of the non-specifically adsorbed material can be directly observed on a quartz crystal microbalance or a surface plasmon resonance slide during washing of the freshly prepared slide mounted in the appropriate instrument. For 1:10 molar ratio of mixed self assembled monolayers consisting of carboxyl-terminated and hydroxyl-terminated thiol or dithiol nanotethers™ (see **Figure 2**), unpublished AFM data (Suo, Z. Montana State University, Bozeman, personal communication) indicated that monothiol alkane PEG mixed self-assembled monolayers showed patches of bare gold while dithiol aromatic PEG mixed monolayers appeared to be homogeneous. XPS data for the same slides indicated significantly more sulfur-gold interaction for the dithiol over the monothiol mixed self-assembled monolayers.

The apparent stability of the dithiol mixed self-assembled monolayer may account for the observation that the detection ratio of *Staphylococcus aureus* binding compared to *E. coli* binding for a dithiol surface ratio was 2.3, while for the monothiol surface was 1.29, indicating greater selectivity for the pathogen on the dithiol surface. In the same study, nonspecific binding response was 133.3 for the monothiol surface and 39 for the dithiol surface[10].

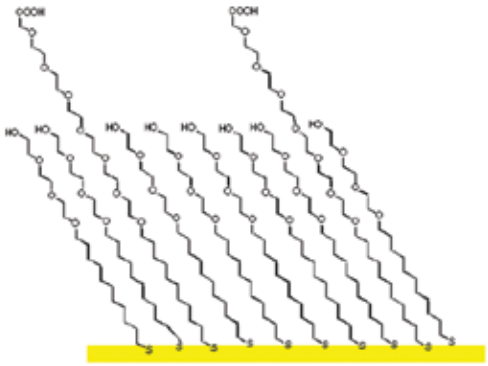


Figure 2. Monothiol and dithiol mixed self-assembled monolayers with PEGolated spacers.

Immobilization Strategies

Self-assembled monolayers provide the opportunity for a variety of chemical strategies to be employed for immobilization of specific ligands, for construction of a non-fouling surface or for electrochemical applications. The hydroxyl terminated dithiolalkane aromatic rigid-rod tether (Nanotether BPA, Aldrich Prod. No. **674346**) can be used as a non-fouling SAM or for further functionalization. The carboxyl-terminated Nanotether BPA-HA (Aldrich Prod. No. **674354**) in **Figure 3** can be coupled to proteins, amino-terminated DNA oligomers or any other amine-containing molecule using standard EDC/NHS coupling chemistry[11]. It could be used to provide a hydrophilic, negatively charged surface, or further functionalized chemically. Hydrazide-terminated tethers (Nanotether™ BPA-HH, Aldrich Prod. No. **674370**) in **Figure 4** couple easily with any aldehyde, including aldehydes generated from glycosylated antibodies by sodium periodate[11,12] resulting in specific orientation of the antibody without impairing antibody activity, rather than the random orientation that results from EDC/NHS coupling to carboxyl-terminated tethers.

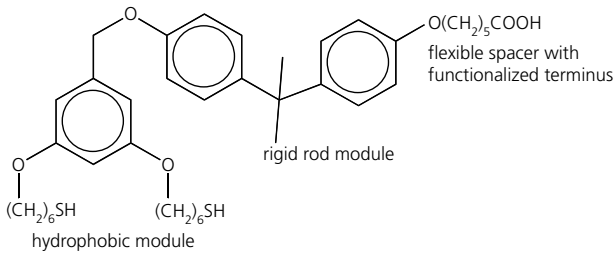


Figure 3. A typical rigid-rod dithiol tether (Nanotether™ BPA-HA Aldrich Prod. No. **674354**).

Future Outlook

Monodisperse macromolecules including flexible linear, rigid-rod and dendritic segments offer unique design capabilities that allow positioning of a variety of ligands through multivalent attachment functionalities while controlling the ultimate flexibility of the tether. These types of constructs can be functionalized for attachment to various surfaces and, on their other terminus, functionalized for covalent coupling of proteins, peptides, and small organic ligands, all of which can be varied independent of one another and be connected to each other through spacers with varying degrees of rigidity. A hydroxyl terminus, for example Nanotether BPA (Aldrich Prod. No. **674346**) either alone or as part of a poly(ethylene glycol) module, provides an excellent antifouling surface.

The rigid-rod (bisphenolA) modular construct shown in Figure 3 contains a flexible alkane spacer with functional terminus for attachment of ligand. In effect, it becomes a "nano fishing rod" for many different assay applications in which the ligand may be presented as if it were on a cell membrane. A typical application is shown in Figure 4 in which antibody capture ligand (the "bait") has been covalently coupled to immobilized hydrazide-terminated Nanotether BPA-HH (Aldrich Prod. No. **674370**). With a PEGolated spacer module, the "line" would swing free in aqueous solvent, to mimic solution-phase binding.

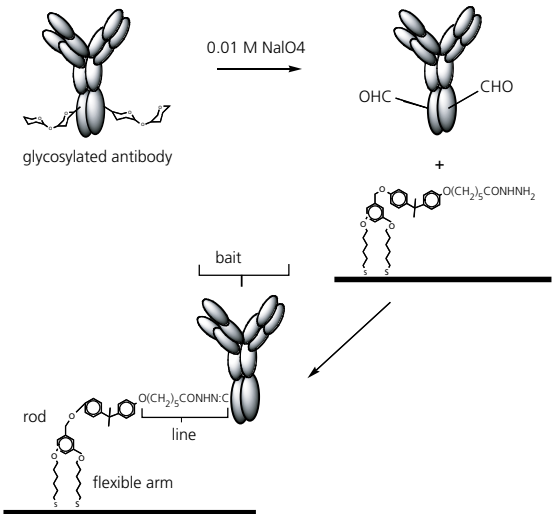


Figure 4. Tethering an oxidized antibody to a hydrazide-terminated tether

The rigidity of the bisphenol A module on the tether makes it an interesting choice for use with a quartz crystal microbalance where it could be used to probe viscoelastic effects in a flow cell configuration. Atomic force microscopy applications are another potential use for rigid-rod tethers, to prevent the coupled (or "bait") ligand from swinging back onto the AFM tip where it may become ensnared. Considering other modular approaches, it is possible to modify the thiol terminus by substituting orthopyridinium disulfide or other coupling reagents, linking the Nanotether™ to carbon nanotubes through the carboxyl terminus, or through a triethoxysilane terminus to provide a 3-point attachment for coupling to glass. Applications are limited only by a researcher's imagination.

References

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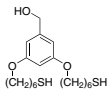
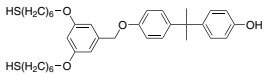
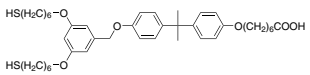
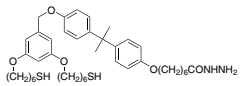
Polyvalent Alkane Thiols – Nanotethers™

Product Description	Structure	Purity,%	Product No.	
Nanotether OH		96.5	674338-50MG	150.00
Nanotether BPA		96.5	674346-50MG	250.00
Nanotether BPA-HA		96.5	674354-50MG	350.00
Nanotether BPA-HH		96.5	674370-50MG	367.00

Nanotethers™ is a trademark of Sigma-Aldrich Biotechnology, L.P.

Research Biotechnology Biosensor Program

Sigma-Aldrich Research Biotechnology has recently signed a series of agreements that expands its position in the areas of RNA Interference (RNAi), gene expression and cell-based assays. Sigma-Aldrich and Panomics (formerly Genospectra), a leading developer of products to support systems biology, have signed several agreements in which Sigma-Aldrich has acquired a minority equity stake in Panomics and has been granted access to various Panomics technologies.

Under the agreed upon terms Sigma-Aldrich gained access to Panomics's unique nano-particle system for delivery of siRNA and other biomolecules to cells. The companies will participate in a joint program to develop new technologies and products in the area of cell-based assays, particularly to supply novel live cell biosensor assay reagents. These reagents provide real-time data on protein activity and location in living cells, and will make an impact in the High Content Screening and Cell-Based Assay fields. David Lawrence, Ph.D. from Albert Einstein College of Medicine and Klaus Hahn, Ph.D. from University of North Carolina, Chapel Hill, are two noteworthy scientists who are collaborating with Panomics and Sigma-Aldrich in this endeavor.

As Sigma-Aldrich expands its involvement in the area of cell-based assays, a focused business development approach is being undertaken. Sigma-Aldrich welcomes the opportunity to license and/or acquire novel biosensors and biosensor technologies to provide to the research community.

If you are interested in collaborating with us,
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For questions, product data, or new product suggestions,
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A Step-by-Step Guide for Solution Based Self-Assembly

Dr. Dan Graham, Assemblon;
Dr. Sean Dingman,
Sigma-Aldrich

Self-assembled monolayers of thiols are prepared by immersion of a clean gold substrate into a dilute solution of the desired thiol. Although self-assembly takes place very quickly, good experimental procedures are needed to produce highly ordered films. A recommended protocol for preparing SAMs is outlined in this article.

Equipment and Materials

Equipment Checklist and Considerations

1. Gold coated substrates (See pg 10 for our substrates)
2. Thiol compound(s)
3. Fresh 200 proof ethanol (or appropriate solvent)
4. Calibrated micropipettes
5. Container for mixing thiol solution (solution container)
6. Tweezers for sample handling
7. A dedicated ethanol solvent bottle
8. Parafilm for sealing containers
9. Containers for sample preparation (sample containers)
10. Petri dishes for transporting and storing SAMs
11. Dry nitrogen
12. Analytical Balance
13. Sonicator
14. pH paper

Environment: A clean environment is key to preparing quality SAMs. Low levels of contaminants can affect monolayer quality. Avoid rooms or hoods in which silanes or poly(dimethyl siloxane) (PDMS) have been used. These compounds easily cross contaminate a variety of surfaces. Iodine adsorbs readily onto gold and should be avoided.

Handle all thiols in a fume hood. Most thiols have an obnoxious odor and are toxic (check MSDS before using).

Containers: Appropriate containers include glass or polypropylene (e.g., scintillation vials, polypropylene test tubes and centrifuge tubes). Glass containers must be cleaned thoroughly to avoid solution contamination[1].

Containers that can be easily sealed are recommended. For the highest quality films, oxygen exposure should be minimized during the assembly process. This is achieved by reducing the headspace above the thiol solution and backfilling with an inert gas. Each substrate is placed in its own container to avoid interactions that would be detrimental to film quality.

[1]One option for glass cleaning is the use of piranha solution (30:70 v/v solution of 30% hydrogen peroxide (H_2O_2) and concentrated sulfuric acid (H_2SO_4)). Extreme caution has to be taken when using piranha solution. It is a very strong oxidant and reacts violently with organic matter.

Containers can be reused, as long as they are rinsed well with solvent after each use and dedicated to the same thiol to avoid cross-contamination.

Solvent: For most thiols, pure ethanol (200 proof) is required for successful assembly. Alternately, denatured alcohol, containing up to 5% isopropanol and/or methanol, is a suitable substitute. Solvent purity should be verified due to potential contamination by copper. Copper disrupts the assembly of the thiols and may affect the performance of the resulting SAM.

Sample Slides: Gold slides must have an adhesion layer of chromium (Cr) or titanium (Ti) under the gold layer. If this layer is missing the gold will delaminate and ruin the monolayer during sonication.

Dedicated wash bottle: It is best to have a dedicated solvent wash bottle used for rinsing containers, substrates and SAMs. Store the bottle empty and only fill it with fresh ethanol when needed.

Step-by-Step Procedure

This general protocol is appropriate for most thiols. Thiols containing amine, carboxy groups require modifications to the protocol as noted in green below. The properties of PEG thiol monolayers depend on the method of self-assembly. Researchers should review references 5–7 before using these materials.

1. Determine necessary amounts and concentration of thiol solution.

a. Calculate the total volume of thiol solution needed to make the number of samples desired.

[Total volume of solution (mL)] = [total number of samples] x [Sample solution volume (mL)]

b. Calculate the total amount of thiol needed to prepare desired amount of solution. (where C = 1-5 mM solutions)

[Mass of thiol (g)] = [Total Volume (mL)] x [C x 10^{-6} mol/ml] x [MW(g/mol)]

If the thiol is a liquid, you can convert the mass to a volume using the density of the thiol. Use a calibrated micropipette for measuring and dispensing liquid thiols.

2. Preparing the thiol solution. Prepare enough solution for all samples to ensure the solution concentration is constant across the sample set. When preparing mixed thiol solutions, prepare a stock solution of each thiol separately, then mix them at the proper proportions for the final stock solution.

a. Rinse all assembly containers with solvent by squirting ~3 to 5 mL around the inside of the containers. Repeat 2–3 times and re-cap each container. Rinse all beakers, tweezers, etc., to be used in the experiment with solvent. Label all containers.

b. Measure the appropriate volume of solvent into the clean solution container.

c. Dispense the mass (or volume) of thiol, to the solvent.
d. Sonicate the container 5–10 min to dissolve.
e. Once dissolved, dispense the planned volume of solution into each sample container.

- Carboxy terminated thiols: Adjust the solution pH to ~2 with a few drops of concentrated HCl. Then sonicate stock solution.
- Amine terminated thiols: Adjust the solution pH to ~12 with concentrated NH_4Cl or triethylamine. Then sonicate stock solution.

3. Sample Self-Assembly.

a. Immerse gold substrate in container containing the thiol solution. Handle gold substrates with tweezers and minimize expose to air, to reduce surface contaminants.

b. Backfill each container with dry nitrogen and seal the cap and wrap the cap with Parafilm.

c. Store the sample for at least 24 to 48 hours. In general, longer assembly times tend to result in better packing of the monolayers.

4. Terminating self-assembly: Functional groups on the thiols affect self-assembly termination.

For simple alkanethiols:

a. Hold the sample with clean tweezers and rinse with solvent for 10 to 15 seconds from a clean solvent bottle.

b. Dry sample with a stream of dry nitrogen.

For thiols with hydrogen-bonding, polar or bulky head groups:

c. Hold the sample with clean tweezers and rinse with solvent for 10 to 15 seconds from a clean solvent bottle. (Solvent should be pH adjusted for carboxy and amine terminated SAMs)

d. Place each sample in a container with fresh solvent and close the cap. (Again solvent should be pH adjusted if needed)

e. Sonicate the samples for 1–3 minutes.

f. Remove the samples individually and rinse again for 10–15 seconds under a steady stream of ethanol. (At this stage no pH adjustment is necessary. Use pure solvent)

g. Dry sample with a stream of dry nitrogen.

5. Sample Storage

a. Place in clean Petri dish.

b. Backfill Petri dish with dry nitrogen.

c. For long-term storage: Place the Petri dishes in a jar backfilled with dry N_2 and sealed with Parafilm.

If you are going to use the monolayers for further experimentation, plan your experiments so you can rinse the samples right before use. Minimize time between preparation and use since SAMs can oxidize over time.

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