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Leading Opinion

Self-assembled molecular magnets on patterned silicon substrates: Bridging bio-molecules with nanoelectronics ☆

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Abstract

The paper reports the methods of preparing molecular magnets and patterning of the molecules on a semiconductor surface. A highly magnetically aligned metallothionein containing Mn and Cd (Mn,Cd-MT-2) is first synthesized, and the molecules are then placed into nanopores prepared on silicon (0 0 1) surfaces using electron beam lithography and reactive ion-etching techniques. We have observed the self-assemble growth of the MT molecules on the patterned Si surface such that the MT molecules have grown into rod or ring type three-dimensional nanostructures, depending on the patterned nanostructures on the surface. We also provide scanning electron microscopy, atomic force microscopy, and magnetic force microscope studies of the molecular nanostructures. This engineered molecule shows molecular magnetization and is biocompatible with conventional semiconductors. These features make Mn,Cd-MT-2 a good candidate for biological applications and sensing sources of new nanodevices. Using molecular self-assembly and topographical patterning of the semiconductor substrate, we can close the gap between bio-molecules and nanoelectronics built into the semiconductor chip.

Keywords: Silicon; Surface modification; Electron beam lithography; Molecular magnet

1. Introduction

Molecular magnets, also known as organic or biological molecules bearing magnetic moments, offer new opportunities in the creation of novel, low dimensional, and nanostructured materials. Molecular magnetic clusters have attracted interest for their potential applications such as single molecule memory units and spin sensors. There have been emphases on those molecular magnets that operate at room temperatures or above [1], and improving the magnitude of the critical temperature is in fact a necessary condition for any potential application with single molecule magnets. Another major problem for their use in applications is how to address a single molecule. The attempt to deposit clusters on substrates (metallic [2], insulating or semiconductor [3]) is a necessary step toward the utilization of these molecular clusters.

Surface modification and patterning at the nanoscale are new frontiers in science as they have potentially significant applications in biomedical technology and nanoelectronics [4–6]. Recently, chemomechanical surface functionalization has been developed as a means toward the simultaneous chemical-patterning and direct covalent-bonding of molecules to silicon surfaces [7,8]. By mechanically breaking the Si–Si or Si–H bonds on the silicon surface, a chemically active surface is created. This surface then reacts with

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a variety of molecules, covalently binding them directly to a crystalline silicon substrate. In contrast to the traditional top–down lithography approach, the bottom–up approach, in which materials are assembled molecule-by-molecule to produce novel supramolecular architectures, offers numerous advantages such as inexpensive mass fabrication and attainment of nanoscale feature sizes [9]. The technique of self-assembly is one of the few practical strategies available in order to arrive at one to three-dimensional (3D) ensembles of nanostructures. There are many different mechanisms by which the self-assembly of molecules and nanoclusters can be accomplished, such as chemical reactions, electrostatic and surface forces, as well as hydrophobic and hydrophilic interactions. More recently, in the epitaxial assembly of block-copolymer films, molecular level control over the precise size, shape, and spacing of the order domains was achieved with advanced lithographic techniques [10]. Combining nanoimprint lithography (NIL) and molecular assembly patterning by lift-off (MAPL), Falconnet et al. [11] have produced streptavidin patterns with feature sizes in the order of 100 nm. Modification of a surface to anchor protein molecules is an important strategy toward the construction of new biocompatible materials with smart bioactive properties. In fact, surfaces patterned by protein molecules can act as active agents in a large number of important applications including biosensors capable of multifunctional biological recognition.

It has been predicated that the current very large-scale integrated circuit paradigm based on complementary metal oxide semiconductor (CMOS) technology cannot be extended into a region with features smaller than 10 nm [12]. With a gate length well below 10 nm, the sensitivity of silicon field-effect transistor parameters may grow exponentially due to the inevitable random variations in device size. Therefore, an alternative nanodevice concept was proposed—molecular circuits—which was a radical paradigm shift from pure CMOS technology to hybrid semiconductor [13]. The concept combines the advantages of nanoscale components, such as the reliability of CMOS circuits, and the advantages of patterning techniques, which include the flexibility of traditional photolithography and the potentially low cost of nanoimprinting and chemically directed self-assembly. The major attraction of this concept is the incorporation of the richness of organic chemistry with the versatilities of semiconductor science and technology. However, before this, one needs to bring directed self-assembly from the present level of single-layer growth on smooth substrates to the reliable placement of three-terminal molecules on patterned semiconductor structures.

In this report, we demonstrated methods of synthesizing and patterning of 3D magnetic molecular self-assembly produced from metallothionein (MT-2) on nanostructured semiconductor surfaces, and investigated their magnetic properties and possible applications in nanodevices.

2. Preparation of molecular magnets

Pertinent details on the structures and preparation of Mn,Cd-MT-2 magnetic proteins can be found elsewhere [14,15]. Atomic absorption (AA) spectroscopy was used to confirm that the two Mn and five Cd atoms have replaced all seven original Zn atoms in a single MT-2 molecule to form Mn,Cd-MT-2. Meanwhile, there are no Fe ions detected by AA measurement. The effective diameter of Mn,Cd-MT-2, measured by dynamic light scattering (DLS) spectrophotometer is 2.86 ± 0.29 nm which is identical to the effective size of the native MT-2. The UV absorption and circular dichroism (CD) spectra from Mn,Cd-MT-2 are both similar to the native MT-2, but with red shift (data not shown), which indicates that the Mn,Cd-MT-2 has been refolded into its native conformation.

The magnetic moment of a cluster is equal to $Ng_e\mu_B$, where N and n are the total number and the effective number of unpaired electrons of magnetic atoms in the cluster, respectively, and g_e is the g factor of electrons ($g_e = 2$). In the case of perfect alignment, the $l = 0$, $s = 5/2$, $j = l + s = 2.5$, the cluster $(Mn_2CdS_3)^{3-}$, conforming a Zinc Blende structure, may have a magnetic moment of $11.8\,\mu_B$. The magnetic moment of Mn,Cd-MT-2 was measured on a lyophilized powder sample, weighing 1.8 mg, $M_W =$ 6.8 KD, by a commercial SQUID magnetometer in a sealed capsule from 10 to 330 K. By applying a cyclic external magnetic field between 3 and -3 T, a clear magnetic hysteresis cycle can be observed the throughout the whole temperature range (as shown by the curve with squares in Fig. 1). In contrast to the Mn,Cd-MT-2 molecules, the native MT-2 molecules did not reveal any magnetic property (as shown by the curve with black dots in Fig. 1). However, measurements on Mn-MT-2 molecules in which all the Zn ions have been replaced by Mn ions, only show weak paramagnetic properties (as shown by the curve with triangles in Fig. 1).

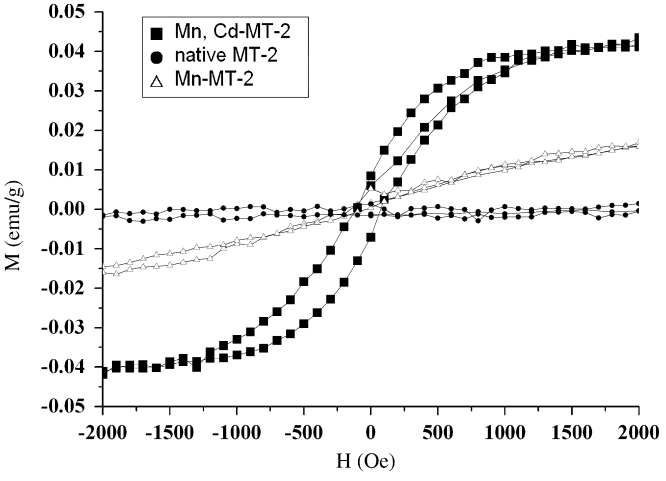

Fig. 1. Magnetization measurements at 10 K for Mn,Cd-MT-2 (squares), native MT-2 (dots) and Mn-MT-2 (triangles).

The magnetic moment of Mn,Cd-MT-2 is saturated at ± 0.2 T, and the value of the magnetic moment is about 0.046 emu/g (emu, electron magnetic unit) at 300 K; the coercive field was around 40 Oe (Oersteds). Although the Bohr Magneton of this protein is as small as $0.056\,\mu_B$, the observed hysteresis behavior of the magnetic moments indicates that Mn,Cd-MT-2 is a room-temperature magnetic protein. In the following sections, we demonstrate how to pattern magnetic proteins on a semiconductor surface.

3. Nanostructured semiconductor templates

The nanostructured templates were prepared using electron-beam (e-beam) lithography techniques on Si (0 0 1) substrates. The flow chart of the lithography and etching processes is shown in Fig. 2. A Si wafer was first diced into 1 cm^2 substrates, which were then cleaned with a modified RCA cleaner to remove organic contaminants before drying at 150 °C for 1 h to remove excess moisture. The fabrication process commenced by spinning a thin layer of ZEP-520 photoresist onto the Si wafer using LAURELL coater and then pre-baking the layer at 180 °C for 2 min. Nanopore patterns were directly written with the e-beam in a square area of about $200 \times 200\,\mu m$, and the exposed sample was developed at 25 °C in a ZED-N50 solution for 5 min, followed by residue ZEP-520 descumming through the ULVAC Ozone system. After developing, the exposed Si areas were then etched into the substrates with a depth of approximately 120 nm below the Si surface via the reactive ion etching (RIE) technique for 80 s. The schematic of a completed nanostrucured template is shown in Fig. 2(b). Si templates with pore sizes ranging from 40 to 150 nm and pitch sizes from 100 to 1200 nm were fabricated.

In Fig. 3(a) and (b), we show the scanning electron microscope (SEM) images of the nanopores before and after the RIE processes on one of the templates we have made. From the images, we can see that the size of the nanopore only increased by one to two nanometers after the etching process. The results indicate that we were successful in the preparation of periodically distributed nanopores on Si substrates as their sizes and distributions are highly uniform and can be controlled with high precision.

4. Self-assemble growth of molecules

The self-assemble growth of the MT-2 proteins is demonstrated as follows. One mg/ml magnetic MT in Tris–HCL buffer solution was placed onto the patterned surface, and an electric field with an intensity of 100 V/cm was then applied for 5 min to drive the MT molecules into the nanopores. The sample was then washed with DI water twice to remove the unbounded MT molecules and salts on the surface (the schematic of the process is also shown in Fig. 1(a)). Fig. 4 shows the atomic force microscopy

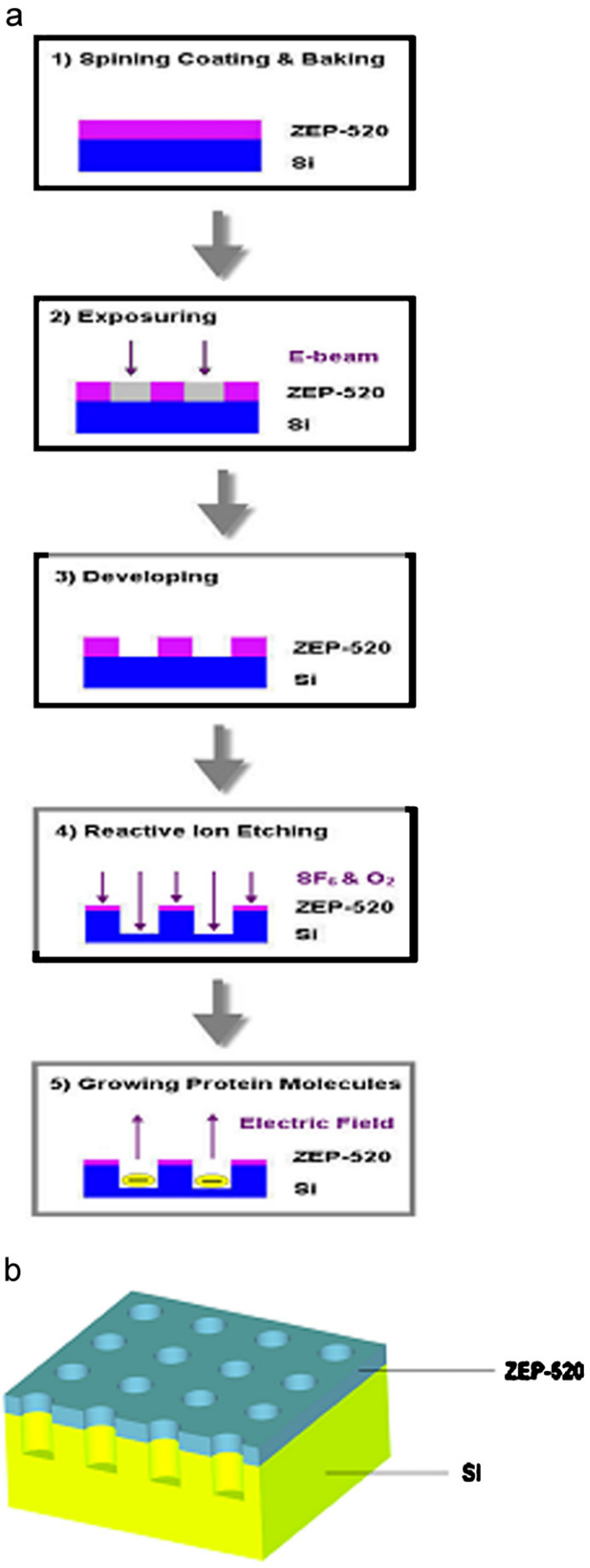

Fig. 2. (a) Flow chart of the lithography, etching processes and growth of protein molecules; (b) schematics of the patterned templates with nanopores.

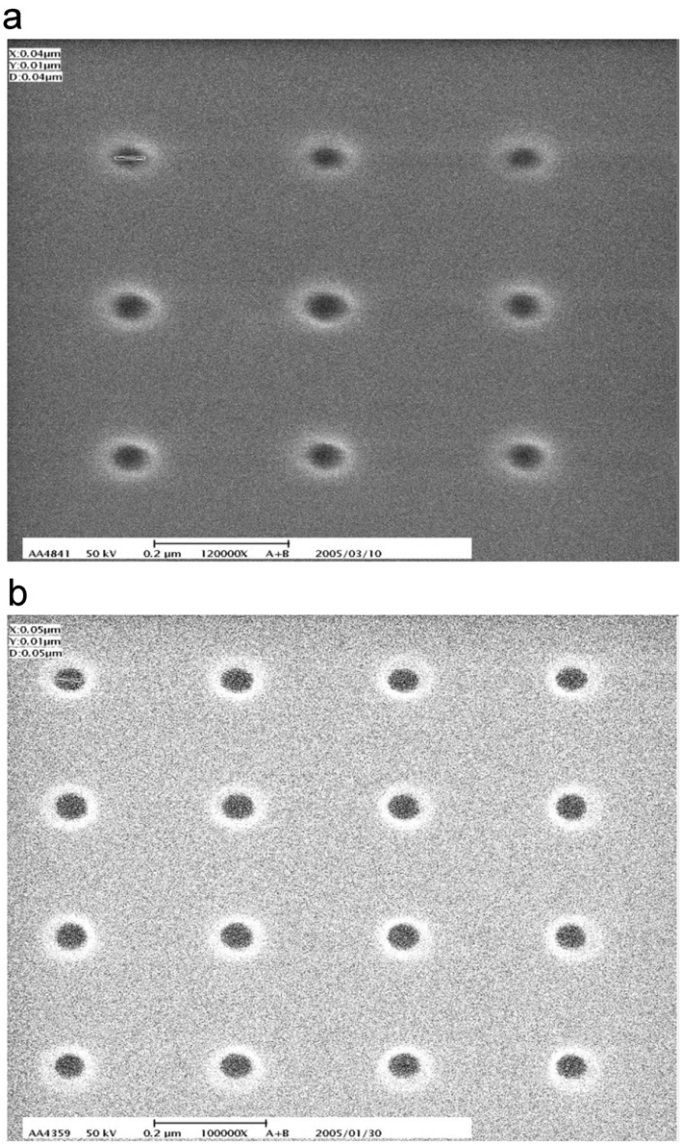

Fig. 3. SEM image of the nanopores on a Si (0 0 1) substrate: (a) after e-beam lithography process; (b) after reactive ion etching process. The nanopore show uniform size of 40 nm and pitch size of 300 nm.

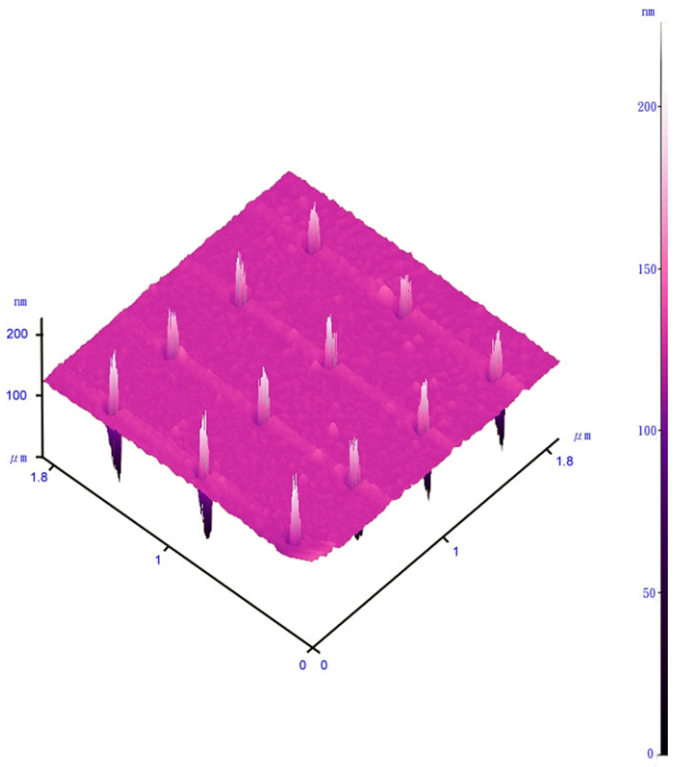

Fig. 4. Three-dimensional (3D) AFM image of the patterned magnetic molecules. The molecules have self-assembly grown into a rod shape.

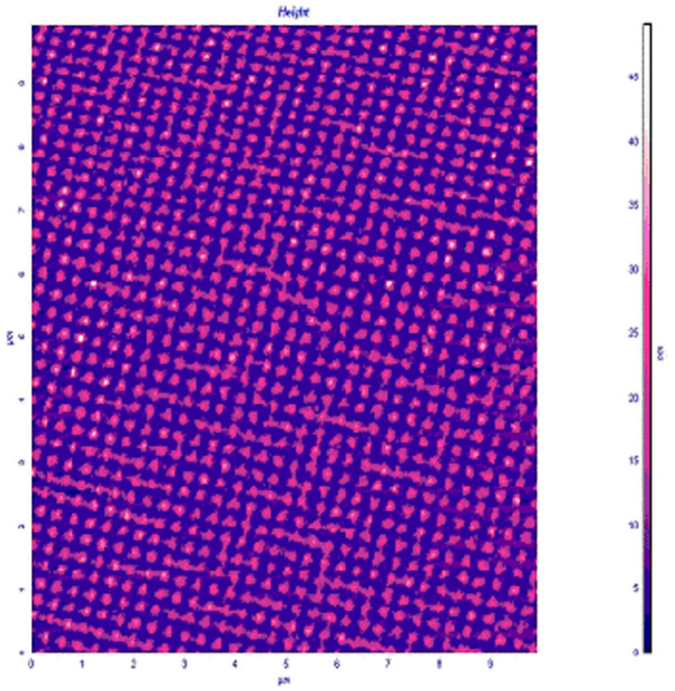

Fig. 5. Two-dimensional (2D) AFM images of the patterned MT-molecules on the template with pore size of 130 nm and pitch size of 300 nm.

(AFM) image of the template surface with 40 nm nanopores after they were filled by the MT-molecules. Keep in mind that most of the Si surface was still protected by photoresist after the etching processes, which has prevented the MT-molecules from forming strong OH bonds with the Si surface underneath. Therefore, the electrical field-driven MT molecules were all anchored on those areas that were not covered with photoresist. The molecules landing in each pore were then self-assembly grown vertically from the bottom of the pore into the shape of a rod (as shown in Fig. 4). These molecular nanorods have an average height of ~120 nm above the template surface and with a diameter equal to the size of the nanopore.

However, experiments on the templates with pore sizes larger than 100 nm gave quite different results. Fig. 5 shows the two-dimensional (2D) AFM image of the template surface with larger pores where we can see that the molecules did not grow vertically above the template surface. Therefore, we were not able to generate 3D images

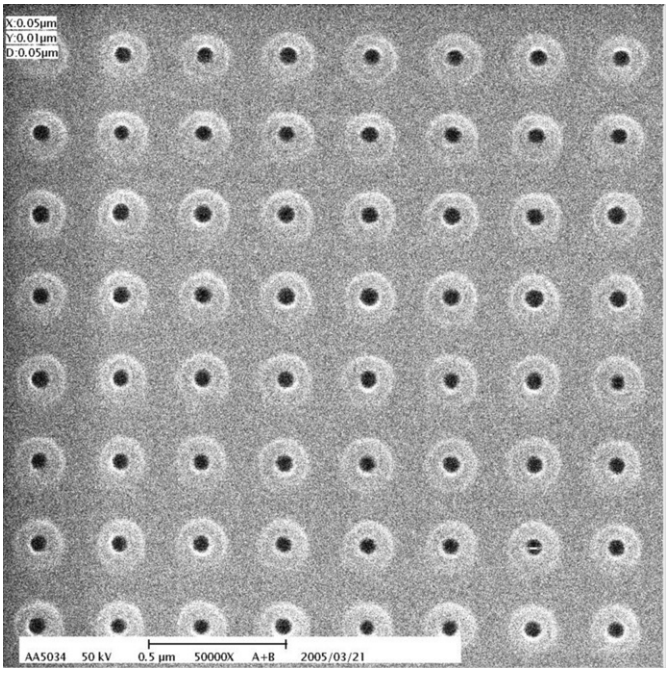

Fig. 6. SEM image of the Si template shows a ring shape Si exposed area around the circumference of nanopores.

on this type of template. However, judging from the AFM phase images, the MT molecules did form a more dense structure in the larger pores compared with the case of the smaller pores. On templates with thinner photoresist and smaller pitch sizes (less than 600 nm), we also found that the molecules anchored in the pore can grow laterally toward the neighboring pores (data not shown).

By increasing both the e-beam exposure and dry etching time on the Si surface covered with a thin photoresist layer with a thickness less than 150 nm, we were able to create a ring-type area with exposed Si surface along the periphery of the nanopores. The SEM image of this type of template is shown in Fig. 6. On this particular template, the molecules not only independently grew inside the pores, but they also grew along the circumference of pores to form molecular rings on the template. Fig. 7 shows the 2D and 3D AFM images of such molecular rings.

In order to gain better control of the formation of molecular nanostructures, it is important to uncover the underlying self-assembled growth mechanism. Molecular self-assembly can be mediated by weak, noncovalent bonds—notably hydrogen bonds, ionic bonds (electrostatic interactions), hydrophobic interactions, van der Waals interactions and water-mediated hydrogen bonds. Although these bonds are relatively insignificant in isolation, when combined together as a whole, they govern the structural conformation of all biological macromolecules and influence their interaction with other molecules. The water-mediated hydrogen bond is especially important for living systems, as all biological materials interact with water. We believe that the first layer of proteins anchored inside the nanopores was bonded with the Si surface

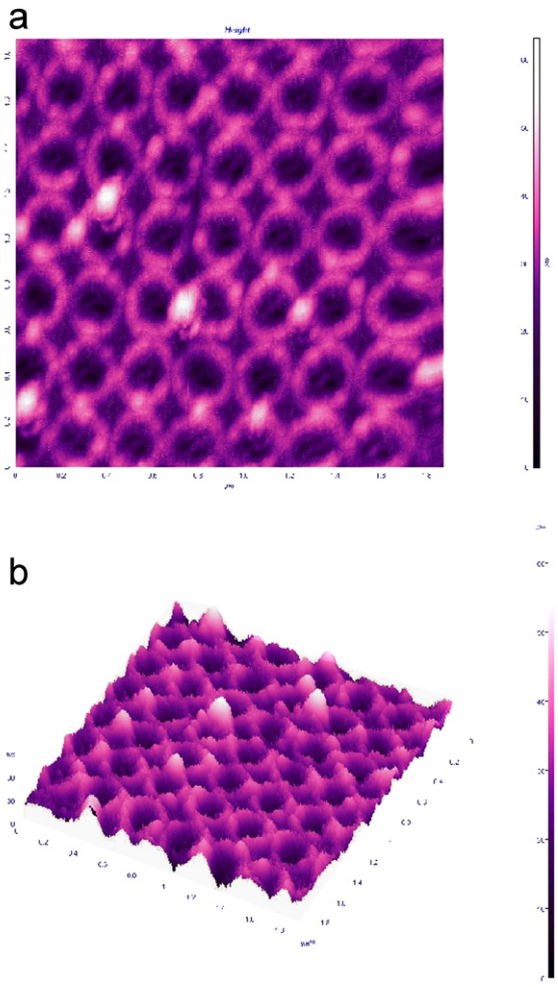

Fig. 7. (a) 2D and (b) 3D AFM images of the patterned MT-molecules.

dangling bonds. They have provided building blocks for proteins which arrived at a later time. With the assistance of spatial confinement from the patterned nanostructures, the rest of the proteins are able to self-assemble via the van der Waals interactions and perform molecular self-assembly.

5. Magnetic properties of molecular nanostructures

The magnetic properties of the self-assembled molecular nanorods were investigated with the magnetic force microscope (MFM). We monitored the change of contour of a particular nanorod on the template when an external magnetic field was applied. Fig. 8(a) shows the MFM image of the nanorod without the external magnetic field. In Fig. 8(b), a magnetic field of 500 Oe was applied during the measurement with a field direction from the right to left. The strength of the field was kept at a minimum so as not to perturb the magnetic tip on the instrument. In Fig. 8(b), we can see clearly that the contour of the nanorod has changed in shape as compared to the case with no applied field. It indicates that the molecular

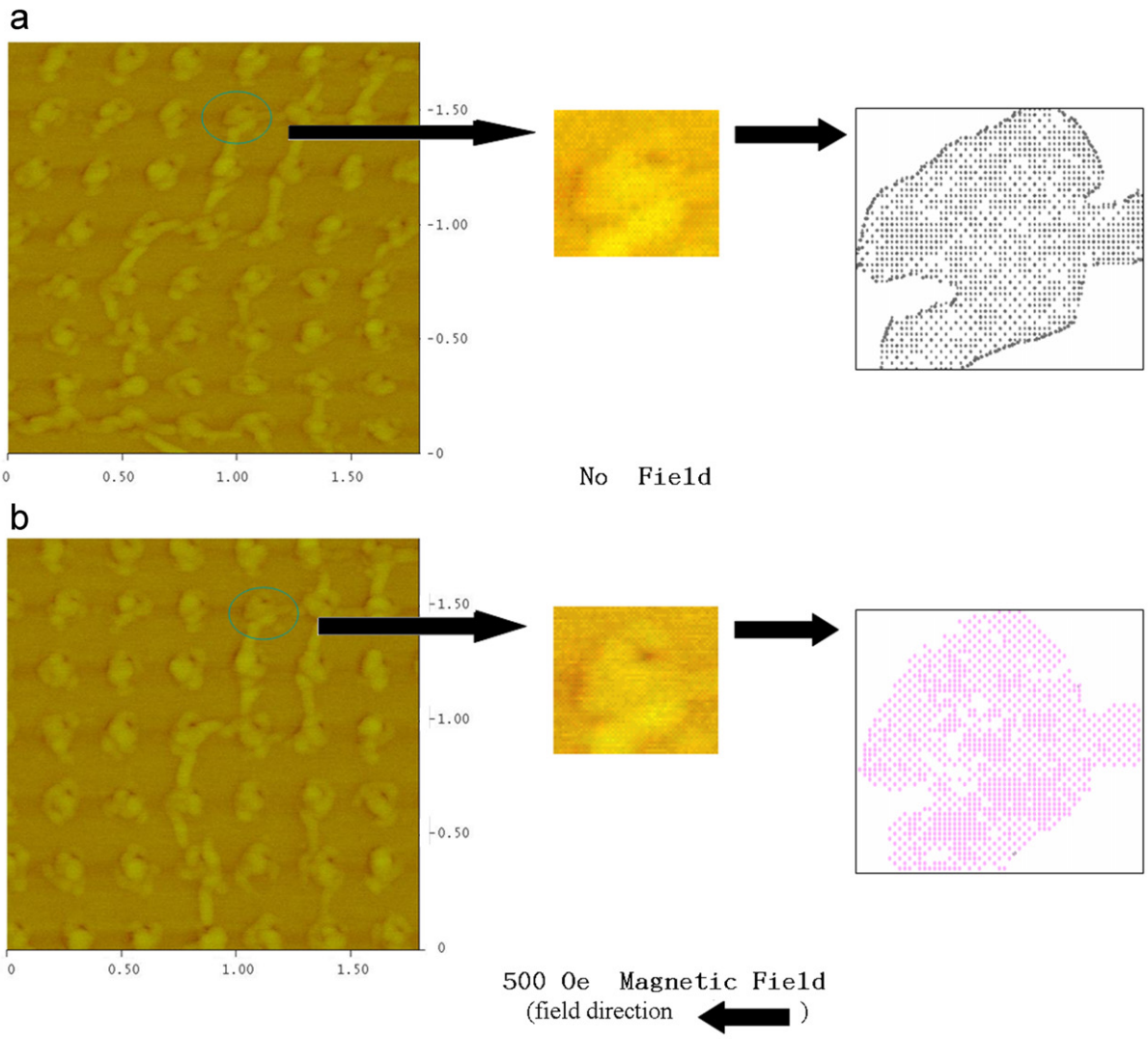

Fig. 8. MFM images of nonorods: (a) without the magnetic field; (b) with a 500 Oe magnetic field applied with a field direction from right to left.

self-assembly carry a magnetic dipole moment which interacts with the external magnetic field.

6. Conclusion and future perspectives

We have synthesized the magnetic molecules produced from metallothionein (MT-2) by replacing the Zn atoms with Mn and Cd. Hysteresis behavior in the magnetic dipole momentum measurements was observed over a wide range of temperature when an external magnetic field was scanned. These magnetic MT molecules were also found to self-assemble into nanostructures with various shapes, depending on the nanostructures patterned on the Si templates. Data from the MFM measurements indicate that these molecular self-assemblies also carry magnetic dipole momentum. Since the pore size, spacing and shape can easily and precisely be controlled by lithography and etching techniques, this work should open up a new path toward an entire class of new biomaterials that can be easily designed and prepared. The techniques we have developed in this work promise to facilitate the creation of many bio-related nanodevices and spintronics. Magnetic molecular self-assembly may find its use in data storage or magnetic recording systems, as an example. They can also act as spin bio-sensors and be placed at the gate of the semiconductor spin valve to control the spin current from source to drain. More importantly, this work should not be limited to MT-2 molecules and should be extended to other type of molecules and proteins as well.

As mentioned in the beginning of this article, the various surface patterning techniques developed over the years to interface organic or biological materials with semiconductors have not only provided new tools for controlled 2D and 3D self-organized assemblies, but have also been essential to the creation and emergence of new semiconductor-molecular nanoelectronics as recently discussed by Likharev [12].

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References

[1] Sessoli R, Gatteschi D, Caneschi A, Novak MA. Magnetic bistability in a metal-ion cluster. Nature (London) 1993;365:141–3.
[2] Fonticelli M, Azzaroni O, Benitez G, Martins ME, Carro P, Salvarezza RC. Molecular self-assembly on ultrathin metallic surfaces: alkanethiolate monolayers on Ag(1 × 1)–Au(1 1 1). J Phys Chem B 2004;108:1898.
[3] Wacaser BA, Maughan MJ, Mowat IA, Niederhauser TL, Linford MR, Davis RC. Chemomechanical surface patterning and functionalization of silicon surfaces using an atomic force microscope. Appl Phys Lett 2003;82:808–10.
[4] Demers LM, Ginger DS, Park SJ, Li Z, Chung SW, Mirkin CA. Direct patterning of modified oligonucleotides on metals and insulators by dip-pen nanolithography. Science (Washington, DC) 2002;296:1836–8.
[5] Hodneland CD, Lee YS, Min DH, Mrksich M. Supramolecular chemistry and self-assembly special feature: selective immobilization of proteins to self-assembled monolayers presenting active site-directed capture ligands. Proc Natl Acad Sci 2002;99:5048–52.
[6] Houseman BT, Mrksich M. Carbohydrate arrays for the evaluation of protein binding and enzymatic modification. Chem Biol 2002; 4:443–54.
[7] Niederhauser TL, Lua YY, Jiang G, Davis SD, Hess DA, Linford MR. Arrays of chemomechanically patterned patches of homogeneous and mixed monolayers of 1-alkenes and alcohols on single silicon surfaces. Angew Chem Int Ed Engl 2002; 41:2353–6.
[8] Lua YY, Niederhauser TL, Wacaser BA, Mowat I, Woolley AT, Davis RC, et al. Static time-of-flight secondary ion mass spectrometry of monolayers on scribed silicon derived from 1-alkenes, 1-alkynes and 1-haloalkanes. Langmuir 2002;18:4840–6.
[9] Brust M, Kiely CJ. Some recent advances in nanostructure preparation from gold and silver particles: a short topical review. Colloids Surf A 2002;202:175.
[10] Kim SO, Solak HH, Stoykovich MP, Ferrier NJ, de Pablo JJ, Nealey PF. Epitaxial self-assembly of block copolymers on lithographically defined nanopatterned substrates. Nature 2003;424:411–4.
[11] Falconnet D, Pasqui D, Park S, Eckert R, Schift H, Gobrecht J, et al. A novel approach to produce protein nanopatterns by combining nanoimprint lithography and molecular self-assembly. Nano Lett 2004;4(10):1909–14.
[12] Likharev KK. Hybrid semiconductor—molecular nanoelectronics. The Industrial Physicist, Forum, June/July 2003. p. 20–3.
[13] Likharev KK, Mayr A, Türel Ö, Muckra I. CrossNets: high-performance neuromorphic architectures for CMOL circuits. In: Proceedings of the sixth molecular—scale electronics conference, Key West, FL, December 2002.
[14] Chang CC, Lee SF, Sun KW, Ho CC, Chen YT, Chang CH, et al. Md,Cd-metallothionein-2: a room temperature magnetic protein. BBRC 2006;340:1134–8.
[15] Chang CC, Lee SF, Sun KW, Kan LS. Mn,Cd-metallothionein-2: a room temperature ferromagnetic protein. In: Proceedings of 50th magnetism and magnetic materials conference (MMM2005), San Jose, CA, October 30–November 3, 2005.