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# Switchable Host–Guest Systems on Surfaces

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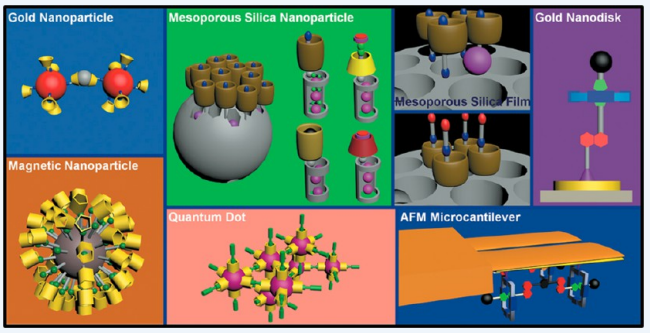
**CONSPECTUS:** For device miniaturization, nanotechnology follows either the "top-down" approach scaling down existing larger-scale devices or the "bottom-up' approach assembling the smallest possible building blocks to functional nanoscale entities. For synthetic nanodevices, self-assembly on surfaces is a superb method to achieve useful functions and enable their interactions with the surrounding world. Consequently, adaptability and responsiveness to external stimuli are other prerequisites for their successful operation. Mechanically interlocked molecules such as rotaxanes and catenanes, and their precursors, that is, molecular switches and supramolecular switches including pseudorotaxanes, are molecular machines or prototypes of machines capable of mechanical motion induced by chemical signals, biological inputs, light or redox processes as the external stimuli. Switching of these functional host–guest systems on surfaces becomes a fundamental requirement for artificial molecular machines to work, mimicking the molecular machines in nature, such as proteins and their assemblies operating at dynamic interfaces such as the surfaces of cell membranes. Current research endeavors in material science and technology are focused on developing either a new class of materials or materials with novel/multiple functionalities by shifting host–guest chemistry from solution phase to surfaces.




In this Account, we present our most recent attempts of building monolayers of rotaxanes/pseudorotaxanes on surfaces, providing stimuli-induced macroscopic effects and further understanding on the switchable host–guest systems at interfaces. Biocompatible versions of molecular machines based on synthetic macrocycles, such as cucurbiturils, pillararenes, calixarenes, and cyclodextrins, have been employed to form self-assembled monolayers of gates on the surfaces of mesoporous silica nanoparticles to regulate the controlled release of cargo/drug molecules under a range of external stimuli, such as light, pH variations, competitive binding, and enzyme. Rotaxanes have also been assembled onto the surfaces of gold nanodisks and microcantilevers to realize active molecular plasmonics and synthetic molecular actuators for device fabrication and function. Pillararenes have been successfully used to control and aid the synthesis of gold nanoparticles, semiconducting quantum dots, and magnetic nanoparticles. The resulting organic–inorganic hydrid nanomaterials have been successfully used for controlled self-assembly, herbicide sensing and detection, pesticide removal, and so forth, taking advantage of the selective binding of pillarenes toward target molecules. Cyclodextrins have also been successfully functionalized onto the surface of gold nanoparticles to serve as recycling extractors for $C_{60}$. Many interesting prototypes of nanodevices based on synthetic macrocycles and their host–guest chemistry have been constructed and served for different potential applications. This Account will be a summary of the efforts made mainly by us, and others, on the host–guest chemistry of synthetic macrocyclic compounds on the surfaces of different solid supports.

## 1. INTRODUCTION

Since the 1987 Nobel Prize in chemistry shared by Pedersen,[1] Cram,[2] and Lehn,[3] supramolecular chemistry based on molecular recognition and self-assembly has been paid much attention and has been under intensive and extensive investigation in scientific and technological fields. Host–guest systems based on synthetic macrocycles, being the traditional focus of supramolecular chemistry and encompassing an innovative concept to deal with reversible noncovalent interactions between macrocyclic hosts and suitable guests, have been highly evaluated and well established in solution.[4−6] Among them, we have shown the advancement of the basic science of receptor design, selective molecular recognition, self-assembly, and molecular machinery of pillarenes,[7−11] cyclodextrins (CDs),[12−18] crown ethers,[12,19] and cyclophanes,[20,21] in solution phases.

For the development of host–guest systems toward practical applications, changing the surrounding medium of operation from solution to solid surface fulfills several urgent demands for host–guest systems to switch and function including direct observation, connection with functional devices and enablement of sequential actions.[22−24] Nature has already given us a direction in terms of the evolution of living creatures from in solution (ocean) to on surface (earth) over billions of

Special Issue: Responsive Host–Guest Systems

Received: January 16, 2014
Published: March 17, 2014

   dx.doi.org/10.1021/ar500022f | Acc. Chem. Res. 2014, 47, 1950−1960

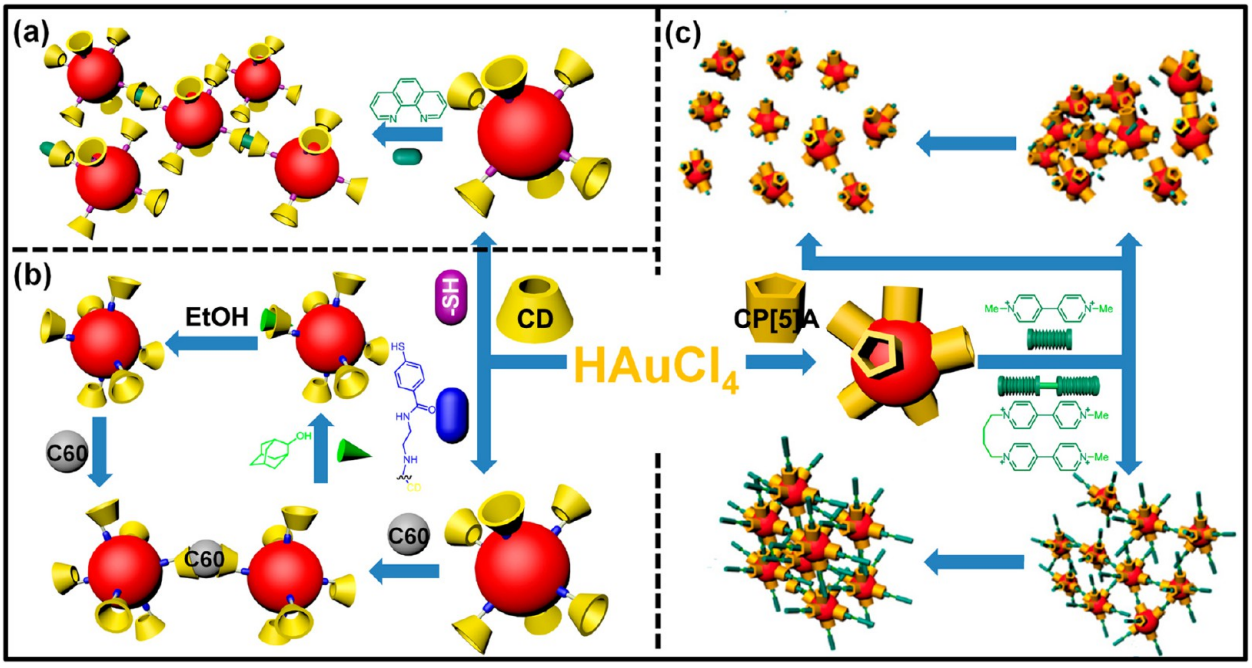



**Figure 1.** (a) Aggregation of monothiolated-$\beta$-CD-modified AuNPs induced by 1,10-phenanthroline. (b) Recycling extraction of $C_{60}$ by thio[2-(benzoylamino)ethylamino]-$\beta$-CD-modified AuNPs. (c) Viologen-mediated assembly of and sensing with CP[5]A-modified AuNPs.

evolutional processes. However, the field of switchable host–guest systems on solid supports or at dynamic interfaces is still immature as compared with the sophisticated molecular mechanical systems observed in nature.

Mechanically interlocked molecules (MIMs)[25] such as rotaxanes and catenanes are molecular machines capable of mechanical motion induced by chemical signals, biological inputs, light, or redox processes. Their precursors, that is, molecular switches and supramolecular switches including pseudorotaxanes being unique types of host–guest systems, have been used for controlled guest uptake and release.[26] Most of these molecular machines were investigated isotropically distributed in solution, so that unidirectional motion or concerted switching is difficult to achieve.[20] Switching of these functional compounds on surfaces becomes a fundamental requirement for these machines to work, which relies largely on the host–guest chemistry in confined spaces.[26,27] Meanwhile, host compounds immobilized on nanomaterials with no matter curved or planar surfaces are envisaged to show excellent capture or sensing abilities toward many different analytes to realize their applications in nanotechnology, biology, environmental and energy technologies, via specific host–guest interactions. Interests have grown significantly on moving host–guest chemistry from solution phase to surfaces. In this Account, we will show our recent endeavors on the construction of hybrid functional systems utilizing host–guest systems in conjunction with solid nanoparticles (NPs), porous NPs, films, microcantilevers, and gold nanodisks, for different potential applications.[28−46]

## 2. Host–Guest Systems on Solid NPs

### 2.1. Gold NPs (AuNPs)

The introduction of supramolecular concepts to AuNPs has provided compelling demonstrations of the structural control and selectivity afforded by noncovalent interactions,[47−49] paving a new avenue for the fabrication of novel hybrid nanomaterials with improved functionalities. The marriage of AuNPs and host–guest systems based on supramolecular macrocycles is leading to the birth of novel hybrid materials, combining and enhancing the characteristics of the two entities, such as the electronic, thermal, and catalytic properties of AuNPs and switchable molecular recognition and selectivity of synthetic macrocylic compounds.[28] We have successfully shown that supramolecular host compounds, such as mono-CD (Figure 1a),[29] bridged CD dimer (Figure 1b),[30] and carboxylatopillarene (Figure 1c),[31] could be used as stabilizing ligands for the preparation and morphology/array control of AuNPs and enhance their recognition and sensing abilities on Au surfaces, which is promising for the ultimate miniature device.

In 2005, we synthesized thio[2-(benzoylamino)ethylamino]-$\beta$-CD fragment modified AuNPs (Figure 1b) through the association of bis($\beta$-CD)s possessing disulfide bond with AuNPs to serve as recycling extractors for $C_{60}$ for potential applications in the separation techniques of fullerenes.[30] This hybrid nanomaterial can selectively capture $C_{60}$ to form large supramolecular assemblies by forming 2:1 host–guest systems of $\beta$-CDs and $C_{60}$, and then release the captured $C_{60}$ upon using competitive binding agent to switch off the inclusion complexation of $C_{60}$ and $\beta$-CD-modified AuNPs.

This molecular recognition strategy was explored in our further work[31] on "herbicide sensing and detection" (Figure 1c) where water-soluble carboxylatopillar[5]arenes (CP[5]As) were used as the stabilizing ligand for in situ AuNP synthesis to result in a hybrid nanomaterial as optical probes for the detection of 1,1′-dimethyl-4,4′-bipyridinium salt, that is, paraquat (PQ), one of the world's most widely used herbicides. A small amount of PQ can cause the aggregation of CP[5]A-functionalized AuNPs in a short time, accompanying with a spectral change that was proportional to the PQ amount. We envision that pillarenes can induce AuNP aggregation thus form hot spots between two or more AuNPs from rigid macrocyclic structures. Surface-enhanced Raman spectroscopy-based nanosensors employing pillarene-modified AuNPs, with enhanced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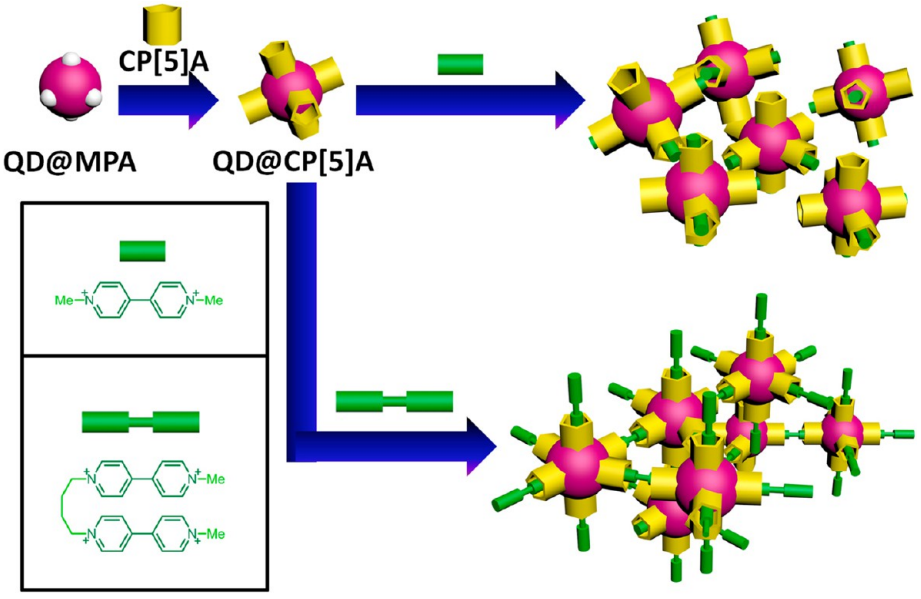


**Figure 2.** Schematic representation of the preparation of CP[5]A@QD and its self-assembly mediated by host–guest interactions. 3-Mercaptopropionic acid (MPA) was exchanged and replaced with CP[5]As on QD surfaces.

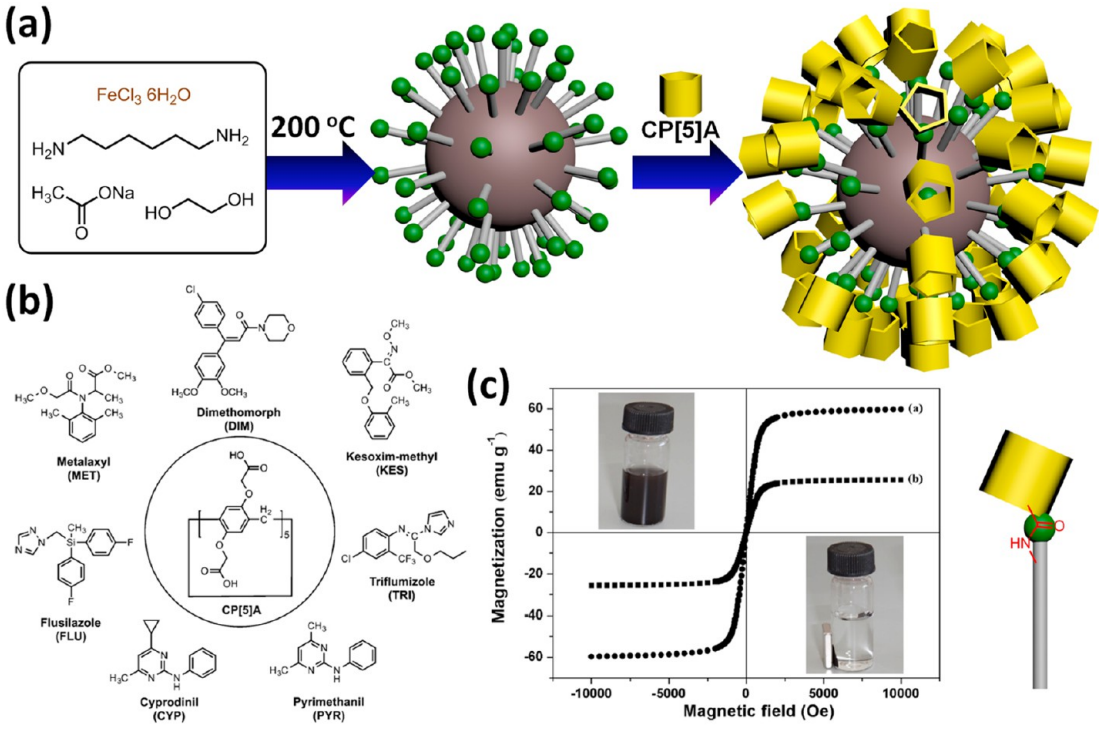


**Figure 3.** (a) Synthetic route to CP[5]A-functionalized MNPs. (b) Chemical structures of the target pesticides and CP[5]A. (c) Magnetic hysteresis loops of $Fe_3O_4$–$NH_2$ (inset a) and $Fe_3O_4$/CP[5]A (inset b). Insets show the images of CP[5]A-functionalized MNP dispersions before and after exposing to an external magnet.

selectivity and sensitivity, are currently underway in our laboratory.

### 2.2. Quantum Dots (QDs)

In general, water-soluble colloidal semiconductor nanocrystals or QDs, as one of the fastest and attractive developing research topics in biological sensing and imaging, are synthesized in the presence of various thiol-ligands. Recently, we have demonstrated[32] that CP[5]A, containing five carboxylate anions on each rim of the cavity, can be functionalized onto the surfaces of CdTe QDs via a ligand-exchange approach, utilizing the strong interactions of the preorganized multicarboxylated groups of CP[5]A with CdTe (Figure 2). This organic–inorganic nanocomposite is stable in aqueous media at room temperature, and showed significantly improved photophysical and photochemical properties as potential candidate for herbicide detection. Furthermore, upon addition of bridged bis(methyl viologen)s guest, the QD@CP[5]A hybrid nanocomposite could form an aggregated supramolecular network via host–guest interactions.


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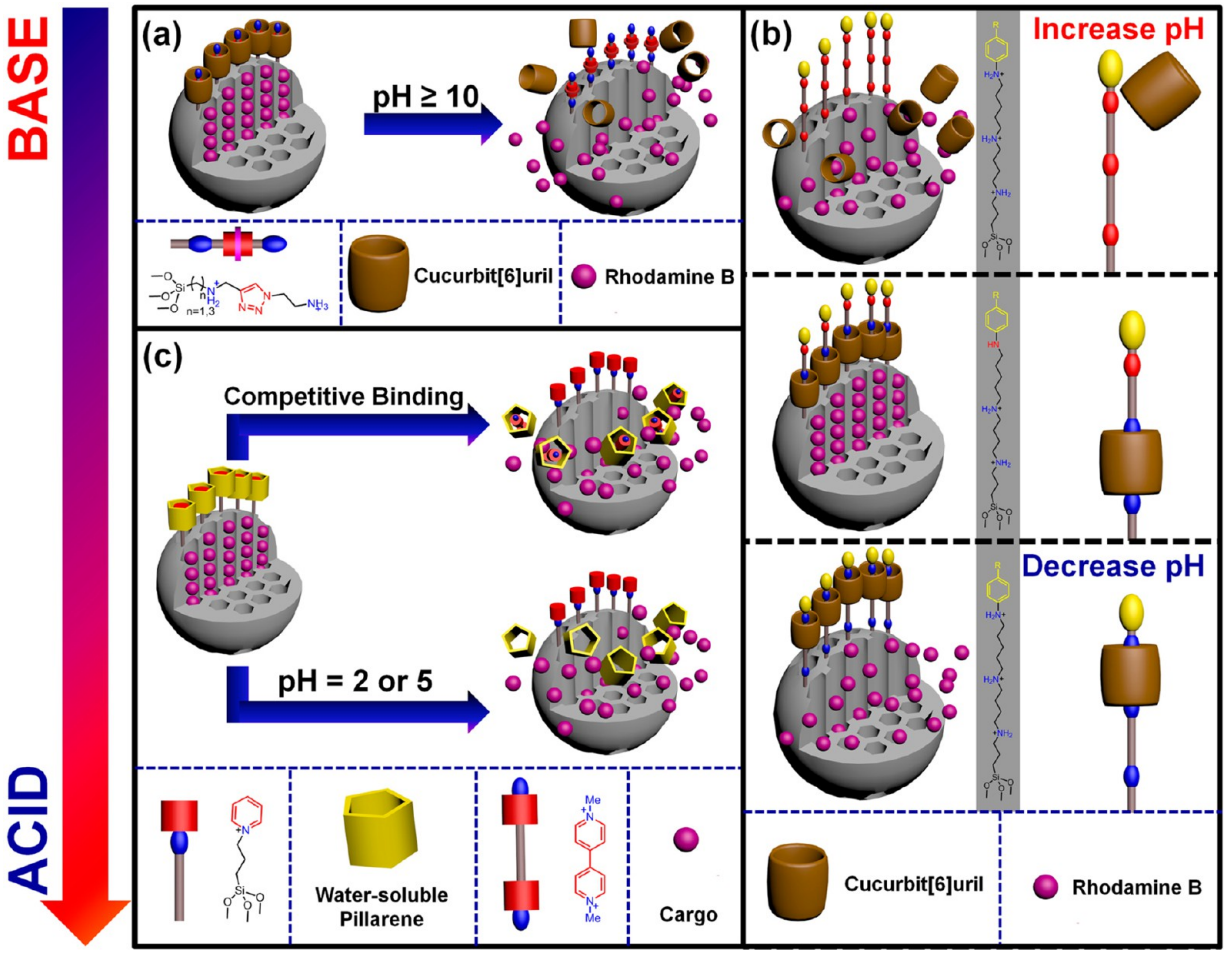


**Figure 4.** Schematic representations of (a) the base-triggered cargo release from the mechanized MSNs comprising CB[6]-based [2]pseudorotaxanes, (b) cargo being released from the bistable CB[6]/trisammonium pseudorotaxane-based mechanized MSNs in response to both acid and base, and (c) CP[5]A-[2]pseudorotaxane-based mechanized MSNs operated by either pH variations or competitive binding.

### 2.3. Magnetic NPs (MNPs)

Another important aspect of the marriage of synthetic macrocycles with NPs is their abilities to absorb and remove herbicides/pesticide residues affecting the environment and human health. Magnetic solid-phase extraction (MSPE) with MNPs as sorbents provided a new and efficient methodology in sample pretreatment and separation. We constructed[33] hybrid adsorbents with good adsorption ability and strong superparamagneticity, consisting of $Fe_3O_4$ MNPs covalently functionalized with CP[5]As, and investigated their application for the preconcentration of pesticide residues in beverage samples (Figure 3). Seven target pesticides (Figure 3b) in commercial beverage samples, that is, orange juice and wines, have been extracted, with high selectivity and adsorption capacity and good recovery, by the employment of this magnetic hybrid nanomaterials as MSPE sorbents, exhibiting a new direction in food safety control.

## 3. HOST–GUEST SYSTEMS ON MESOPOROUS SILICAS

A significant step of developing host–guest systems from in solution to on solid supports is building responsive switches, that is, (supra)molecular nanovalves,[34] on the surfaces of mesoporous silica NPs (MSNs) or films, as gating components, in particular for drug controlled release. The seminal investigation[50] by Stoddart, Zink, and co-workers in 2001 demonstrated that supramolecular machines can be either trapped within a silica monolith or mounted on a silica film and yet continue to function as if they were in solution but with more ordered manner. Mechanized MSNs, that is, MSNs surface-functionalized with (supra)molecular nanovalves, provide a robust reservoir on the nanoscale level for the storage of cargos which can then be released by activating the nanovalves with a range of stimuli, including pH variations, light, redox, enzymes, competitive binding agents, and ultrasound.[34,35] Owing to their inertness, large pore volumes, high surface areas, tunable pore sizes, low cytotoxicity, and ease of functionalization and endocytosis by cells, MSNs are ideal vehicles for incorporating nanovalves on to their surfaces.[34] Inspired by the early studies based on sophisticated machines consisted of cyclophanes or crown ethers that carried out in organic solvents,[51] we set out to develop novel nanovalve systems for use in biological systems. Series of MSNs coated with nanovalves by installing stalk components on their surfaces that can be encircled by synthetic macrocyclic hosts,[36−44] that is, cucurbiturils (CB[*n*]s), carboxylatopillarenes, CDs, and sulfonatocalixarenes, have been designed, in our laboratory, some of which in collaboration with the Stoddart group and the Zink group, and were demonstrated to operate in biological media, showing great potentials in cancer therapy. We believe that these nanovalve systems could be fine-tuned to increase


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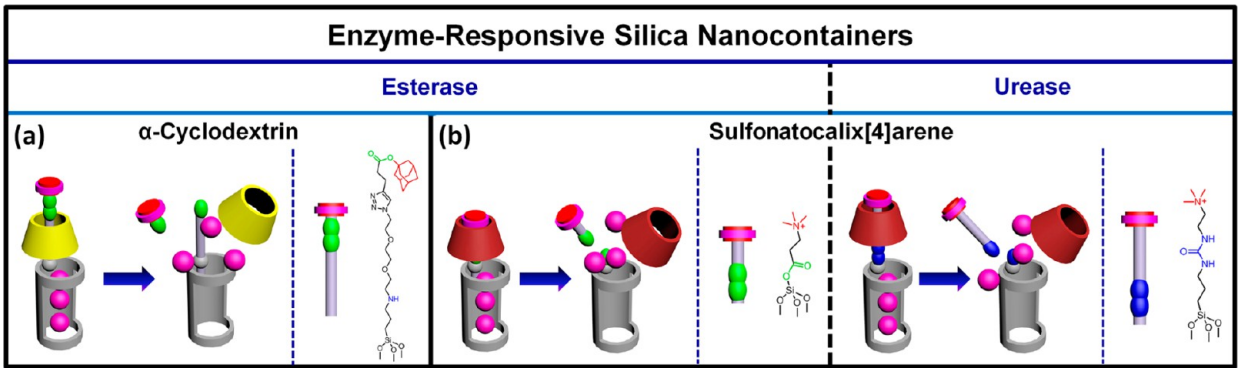


**Figure 5.** Enzyme-responsive mechanized MSNs based on (a) $\alpha$-CD-[2]rotaxanes with ester-linked stalks operable by esterase, and (b) SC[4]A-[2]pseudorotaxanes with ester-linked stalks (left) or urea-linked stalks (right) operable by either esterase or urease.

the therapeutic effect of a drug by delivering them to target specific areas of the body, with a concurrent minimization of drug side effects or concerns over toxicity, and finally help transform medical treatment in the future.

### 3.1. pH Activation

In 2008, as the first nanovalve system functioning in aqueous solution and the earliest proof-of-principle study (Figure 4a), a biocompatible integrated system was constructed that consists of [2]pseudorotaxanes stalks with bisammonium binding sites, which have a high binding affinity for cucurbit[6]uril (CB[6]) by dint of ion-dipole interactions.[36] Taking advantage of the capability of CB[6] to catalyze 1,3-dipolar cycloadditions, a pH-responsive [2]pseudorotaxane-based nanovalve system was fabricated on MSN by the reaction of an azide-containing ammonium and an alkyne-substituted ammonium, affording a disubstituted 1,2,3-trazole-linked bisammonium stalk encircled by CB[6]. The pH-dependent complexation/decomplexation of CB[6] with diaminoalkanes enables the formation of host–guest complexes whose dynamic behavior can be controlled by pH to regulate the cargo release from MSNs. At neutral and acidic pH values, the CB[6] rings encircle the bisammonium stalks tightly, thereby encasing cargos inside the mesopores of MSNs efficiently. Upon increasing the basicity (pH > 10) to deprotonate the ammonium centers of stalks, a spontaneous dethreading of the CB[6] rings, unblocking of the mesopores, and release of the cargos are realized, as evidenced by fluorescence spectroscopy using the emission of the cargo, rhodamine B (RhB).

A promising stimulus for successful incorporation into anticancer drug delivery vehicles is one that depends on decreasing the pH value below 7, instead of raising it, considering the fact that cancerous cells are known to thrive in more acidic environments in comparison with healthy cells. In 2009, we fabricated tunable pH-regulated nanovalves by incorporating a more sophisticated host–guest system consisting of bistable CB[6]/trisammonium pseudorotaxanes covalently linked onto MSN surfaces (Figure 4b),[37] which enables the transition of CB[6]-based nanovalves for potential in vivo applications using the natural variations in pH that exist within healthy and diseased cells in living organisms. In a proof-of-concept design, this system could trap propidium iodide (PI) cargos within the mesopores at neutral pH (i.e., in the bloodstream) but open under mildly acidic conditions (i.e., in lysosomes of cancerous cells), thus releasing their payloads autonomously upon cell uptake. This design relies on the translocation of the CB[6] rings on the trisammonium stalks that contain one anilinium and two $-CH_2NH_2^+CH_2-$ centers upon lowering the pH. At neutral pH, CB[6]s reside on the $-NH_2^+(CH_2)_4NH_2^+-$ recognition sites, allowing both portals of CB[6] to engage in ion–dipole interactions, thus blocking the mesopore orifices and encapsulating PI dyes inside the MSNs. Thus, when the pH is lowered and the anilinium nitrogen becomes protonated, the CB[6] ring translocates to the distal $-NH_2^+(CH_2)_6NH_2^+-$ recognition site due to an order of magnitude stronger binding, resulting in the unblocking of the mesopores and the cargo release. Significantly, the release rate of cargos can be fine-tuned by the modification of the anilinium nitrogen p*K*a by changing the aniline groups with *p*-anisidines. This demonstrates that these newly designed nanovalve systems exhibit an excellent opportunity to deliver therapeutic compounds into various types of human cancer cells with varying lysosomal pH levels.

In 2013, we introduced a new category of mechanized MSNs (Figure 4c) consisting of MSNs capped by supramolecular switches based on a new class of synthetic macrocycles, namely, pillarenes.[38] In this study, pH-responsive mechanized MSNs have been fabricated, based on organic stalk components containing positively charged pyridinium termini grafted onto the surfaces of MSNs, which form [2]pseudorotaxanes with negatively charged, electron-rich CP[5]A rings under neutral and basic conditions where they could trap cargo molecules irrespective of their charge and size. Release of the cargos, either dyes or drugs, can be achieved by lowering the pH or adding a competitive binding agent for CP[5]A.

### 3.2. Enzymatic Activation

In all the above-mentioned mechanized NPs based on responsive host–guest systems, the macrocyclic rings were movable and the stalks of the nanovalves were immobilized on MSN surfaces. A conceptually fresh approach is one that uses external stimuli such as enzymes to either cleave the stalks off MSN surfaces together with the rings, or cleave the end groups/stoppers of the stalks leading the ring-dethreading off the stalk residues on MSN surfaces, both of which realize the pore unblocking and the cargo release. Also in 2008, we designed and constructed a "snap-top" version of $\alpha$-CD-based [2]rotaxane-gated MSNs (Figure 5a) capable of operation in water.[39] This biocompatible, enzyme-responsive motif consists of [2]rotaxanes, in which $\alpha$-CD tori encircle polyethylene glycol stalks and are seized in place by cleavable ester-linked adamantly stoppers tethered to the MSN surfaces. When in the closed state, the snap-tops hold the cargo entrapped within the mesopores, but, upon enzymatic cleavage of the stalks to


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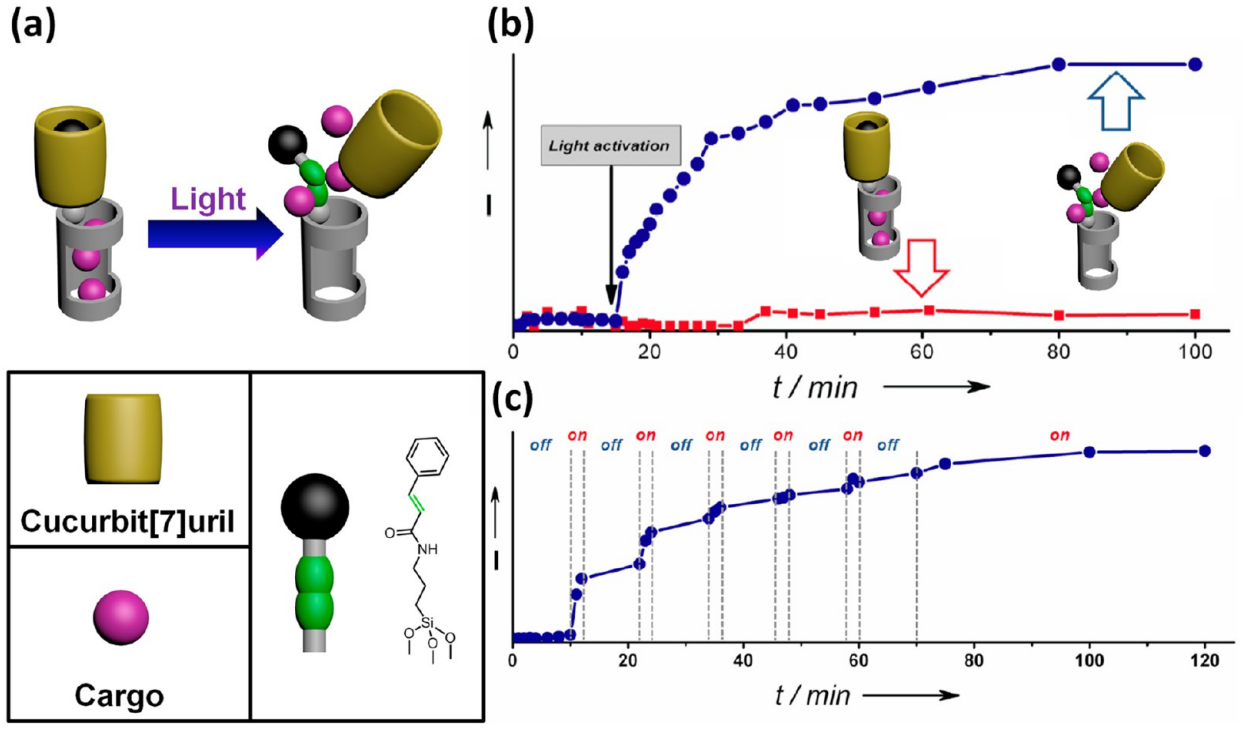


**Figure 6.** (a) CB[7]-based light-switchable mechanized MSNs and their release profiles upon (b) continuous light and (c) pulsed light irradiation.

remove stoppers, $\alpha$-CD rings fell off to release the cargos. We employed porcine liver esterase to catalyze the hydrolysis of adamantyl ester stoppers, leading to dethreading of $\alpha$-CD and release of the luminescent dyes.

Our latest design[40] also demonstrated the feasibility of the enzyme-responsive nanovalve motif, but instead using two different enzymes and supramolecular nanovalves to further prove orthogonality (Figure 5b). Here, calixarenes, which are made up of phenol units linked by methylene bridges, were introduced to this field of nanovalves, for the first time, employing the effective host–guest complexation of sulfonatocalix[4]arene (SC4A) and choline derivatives. MSNs have been surface-functionalized with choline derivatives with different structures and lengths, followed by cargo loading via diffusion and SC4A capping via host–guest complexation. Two enzyme cleavable sites, that is, ester linkage and urea bond, are incorporated into the stalks for specific enzymes, that is, esterase and urease, to regulate the release of loaded cargos from MSNs, showing a clear enzymatic response and proven orthogonality. Using UV–vis spectroscopy, we have validated the ability of esterase to selectively activate the ester-linked nanovalves, and urease to selectively activate the urea-linked nanovalves, while the unmatched tether-linked system is left intact. These researches feature biocompatible nanovalves, which exploit enzymatic specificity and efficiency, and prove the snap-top and supramolecular switch design concepts are feasible for drug release applications.

### 3.3. Light Activation

We employed light[41] and pulsed light as "remote control" stimuli for the controlled release of cargos from mechanized MSNs (Figure 6), showing rapid and directional processes and low invasiveness in biological systems.[42] Cucurbit[7]uril (CB[7]) has a suitable cavity and reasonable water solubility, and can form stable host–guest complexes with *trans*-cinnamamide derivatives, which undergoes a *trans*- to *cis*-conformational change upon UV light irradiation (300 nm), leading to complex dissociation due to steric hindrance effect. Therefore, we functionalized the surfaces of MSNs with cinnamamide-containing stalks surrounded by CB[7] rings to act as a photoresponsive gating system. In biological relevant media, that is, pure water, phosphate buffer solution (PBS), and fetal bovine serum (FBS), CB[7] can be threaded onto the stalks and bind to *trans*-cinnamamide units, thus sealing the nanopores to prevent premature release of the preloaded cargos. Upon irradiation with 300 nm of light, the isomerization of *trans*-to-*cis*-cinnamamide units results in the dissociation of CB[7] rings from the stalks, thus opening the gates and releasing the cargos. Significantly, by the operation of CB[7]-based light-switchable nanovalves, a "ladder" pulsatible drug release has been achieved in an "initial-burst-then-sustained-release" manner to overcome the drawback of UV light in real biological systems and potentially serve the need of accurately controlling drug release dose in targeted disease areas. The hydrophilic nature of these CB[7]/cinnamamide-containing mechanized MSNs and their capability of cargo release in response to an external light source make them potentially useful for remote-controlled intracellular drug delivery and the treatment of degenerative diseases such as skin cancer. Meanwhile, we are currently working on building a system responsive to near-infrared (NIR) light stimulus enabling deeper penetration and less risk of damage to body tissues, which is also desirable for real biological applications.

### 3.4. Dual Activation

For applications in drug-delivery and molecular electronics, we recently developed dual-controlled systems (Figure 7),[43] presenting a new method for attaining more sophisticated levels of precise controlled release regulated by two different types of switches, that is, azobenzene molecular switch and CB[2]pseudorotaxanes supramolecular switch. Besides (supra)-molecular nanovalves that are anchored on the outer rims of


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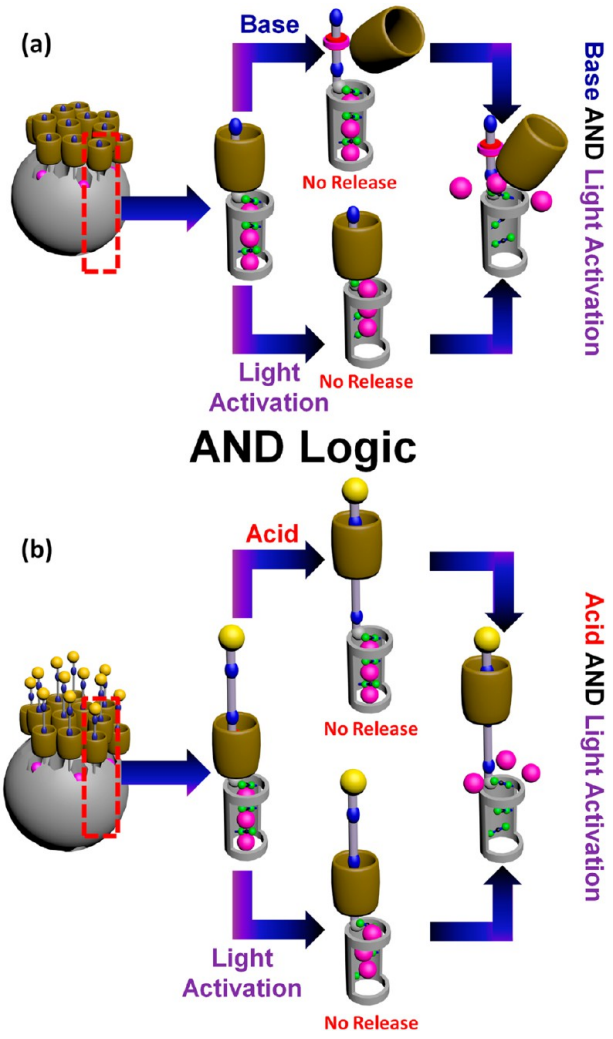


**Figure 7.** Schematic representations of dual-controlled systems consisting of (a) base-responsive nanovalves (raising pH) and azobenzene nanoimpellers, and (b) acid-responsive nanovalves (lowing pH) and azobenzene nanoimpellers.

MSN mesopores, azobenzene-based photoresponsive nanoimpellers have been tethered to the inner pore walls. The azobenzene molecules exist in the *trans*-configuration in their ground state, but change to *cis*-configuration via photoisomerization upon irradiation with UV light and convert back to the *trans* configuration upon exposure to visible light. Both the *trans*- and *cis*- conformers of the azobenzene units absorb light at ca. 457 nm, continuous excitation at this wavelength produces constant isomerization reactions between *trans*−*cis*, resulting in a continual dynamic wagging motion of the untethered terminus that expels cargos from the mesopores of the MSNs into solution. Thereafter, we incorporated the azobenzene-based nanoimpeller switches at the pore interiors and CB-based pH-responsive nanovalves around the mesopores of MSNs to regulate the transport of cargos and achieve AND logic types of systems. Positive output is obtained only when the dynamic wagging motion of the azobenzene nanoimpellers is activated by a 448 nm photoexcitation followed by a pH variation to achieve the dethreading of CB[6] rings from the bis- or trisammonium stalks. By having one release mechanism operate in the presence of a specific biological trigger and having another release mechanism remotely controlled in a noninvasive fashion, it is expected to manually regulate the dosage delivered to a targeted specific region in cancer therapy.

### 3.5. Functional Micropatterned Mesoporous Silica Films

Besides spherical shaped NPs prepared by sol−gel methods, mesostructured silica thin films on macroscopic substrates have also gained great attention owing to their potential macroscopic applications in smart coatings and biomedical implants. Many efforts were made to control the orientation of mesopores' openings, with most of them toward the upper surface of the films. We are devoted to controlling the orientation of mesopores in the plane of the film, forcing them to run perpendicular to the film surface to increase significantly the accessibility of the pore openings for supporting mechanized gatekeepers (Figure 8).[44] This type of functional micropatterned framework derived from mesoporous silica films permanently attached to a substrate was created by an unusual vapor-phase deposition method, through etching away selectively narrow regions of the material that are perpendicular to the pore orientation, and demonstrated its use for creating new gated nanosystems for storage and controlled release of cargo molecules by installing responsive host−guest systems on the pore openings. The robust silica films were 300 nm in thickness with an ordered two-dimensional hexagonal mesostructures, and 2.4 nm of tubular nanopores in diameter were aligned in the pulling direction. The gated nanosystems employed in these studies utilize the previously described nanovalve motifs such as acid/base-triggered ones and ester triggered one based on CB[6] and $\alpha$-CD. This novel type of gated materials may find applications in biomedical implantation for sustained drug release to cure bone fractures, intelligent anticorrosion coatings, and so forth.

## 4. TOWARD FUNCTIONAL DEVICES

### 4.1. Mechanical Actuator Based on Artificial Molecular Muscles

An urgent need and immediate challenge have been to use surface-bound molecular shuttles to manipulate and position other materials, providing direct evidence of machine operations of an individual shuttle and the transduction of molecular-level movements to output to external artificial devices. Inspired by simple, biological molecular machines in nature, we have developed an artificial molecular muscle-based mechanical actuator[45] by utilizing a hybrid top-down/bottom-up manufacturing approach (Figure 9), where motions of molecular shuttles were converted to macroscopic mechanical output of a solid object. We immobilized numerous doubly bistable palindromic [3]rotaxane molecules covalently to a silicon cantilever (500 $\mu$m × 100 $\mu$m × 1 $\mu$m) of an atomic force microscope (AFM) coated on its topside with a 20 nm layer of Au. This palindromic bistable [3]rotaxane is composed of a symmetrical semirigid dumbbell containing two tetrathiafulvalene (TTF) and two $\pi$-electron-rich 1,5-dioxynaphthalene (DNP) units, encircled by two macrocyclic $\pi$-electron-deficient cyclobis(paraquat-*p*-phenylene) ($CBPQT^{4+}$) rings, where each ring carries a disulfide tether to allow the self-assembly of the rotaxane onto Au surface. The distance between two rings contracts and extends upon electrooxidation and reduction. Therefore, the switching of surface-bound molecular muscles in response to chemical or electrochemical stimulation resulted in molecular-level torsions, and the cumulative nanoscale movements of molecular muscles accumulated tension on the AFM cantilever surface, leading to


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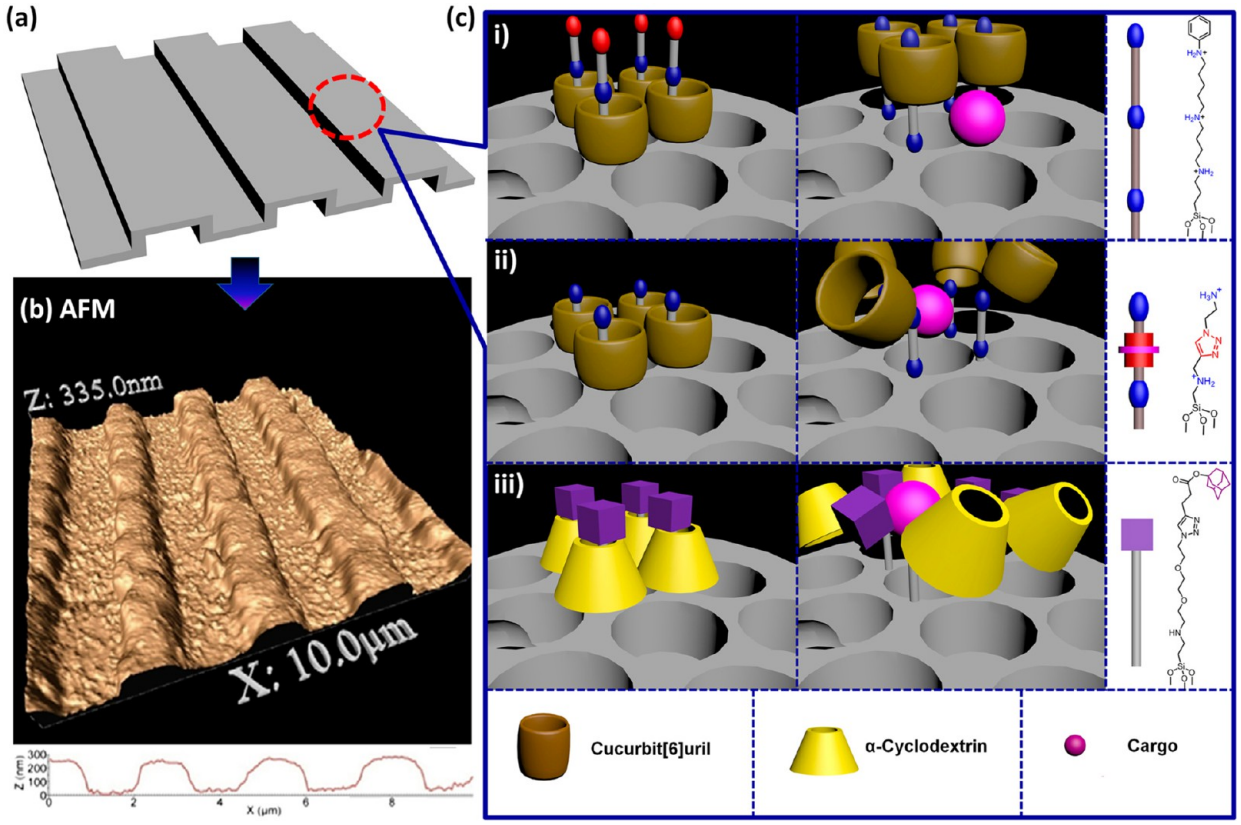


**Figure 8.** (a) Schematic diagram of mesoporous silica film. (b) AFM image of the film. (c) Incorporation of the film with (i) acid-activated nanovalves, (ii) base-activated nanovalves, and (iii) enzyme-responsive snap-top system.

the reversible bending and stretching of the microcantilever to perform larger-scale mechanical work. A mean molecular force of 14−21 pN caused a cantilever deformation of 34−50 nm.

### 4.2. Active Molecular Plasmonics Based on Molecular Switches

In 2009, we created a plasmonic switch from switchable bistable rotaxanes (Figure 10), collaborating with Huang, Stoddart, Weiss, and colleagues.[46] In this system, Au nanodisk arrays fabricated on glass substrates were coated with bistable-rotaxane-based molecular switches via disulfide tethers to exhibit reversible plasmon-based switching when exposing to chemical reductants and oxidants. Upon oxidation and reduction of the TTF entities of the switchable [2]rotaxanes, the encircled $CBPQT^{4+}$ rings could reversibly translocate between TTF and DNP stations of the dumbbell, leading to a change in the refractive index of the surface bound molecules, inducing the dielectric environment change of the gold nanodisks, thus changing the localized surface plasmon resonance (LSPR). Consequently, this molecular plasmonic device can be operated by switching the extinction properties of the bistable rotaxanes and the reversible switching correlates with the chemically driven mechanical motions witnessed for surface-bound bistable rotaxanes. This correlation, also supported by controlled experiments and a time-dependent density functional theory (TDDFT) microscopic model, indicates that the nanoscale movement of surface-bound molecular switches can be employed as the active components of plasmonic devices, guiding light at subwavelength scales by plasmons and sending signals on a circuit in future potential applications. We envision that this chemically driven redox process can be replaced with direct electrical or optical simulation, which would logically establish a technological basis for the production of a new class of active plasmonic components based on molecular switches for solid-state nanophotonic integrated circuits with the great potential for low-energy, ultrasmall operations.

## 5. CONCLUSIONS AND OUTLOOK

We have presented an overview of the hybrid materials and functional devices utilizing switchable host−guest systems on surfaces of different types, sizes, and curvatures. One of the important themes shown here is the stimuli-responsive property of the integrated molecular or supramolecular switches/machines on solid supports instead of in solution. Switching phenomena of the surface-bounded host−guest systems underlie biological function and machines in nature; however, there is still a large gap between the in-laboratory synthesized (supra)molecular switches/machines and those found in nature through billions of natural evolution processes. Changing the medium of switchable host−guest systems from solution to a solid surface is the first step that we learned from nature, which satisfies many demands of machine function shown in this Account. However, no matter Au/CdTe/silica NPs or films/disks/cantilevers could only provide a platform for basic demonstration and characterization but are far from allowing practical applications partially because they lack versatility in materials selection. Necessary developments of switchable host−guest systems mimicking nature include greater dynamic functionality similar to that in many complex cell-membrane-bound systems. We envision that research on molecular switches/machines function at dynamic interfaces,[22,23,52] such as polymer membranes, gels, carbon materi-


dx.doi.org/10.1021/ar500022f | Acc. Chem. Res. 2014, 47, 1950−1960

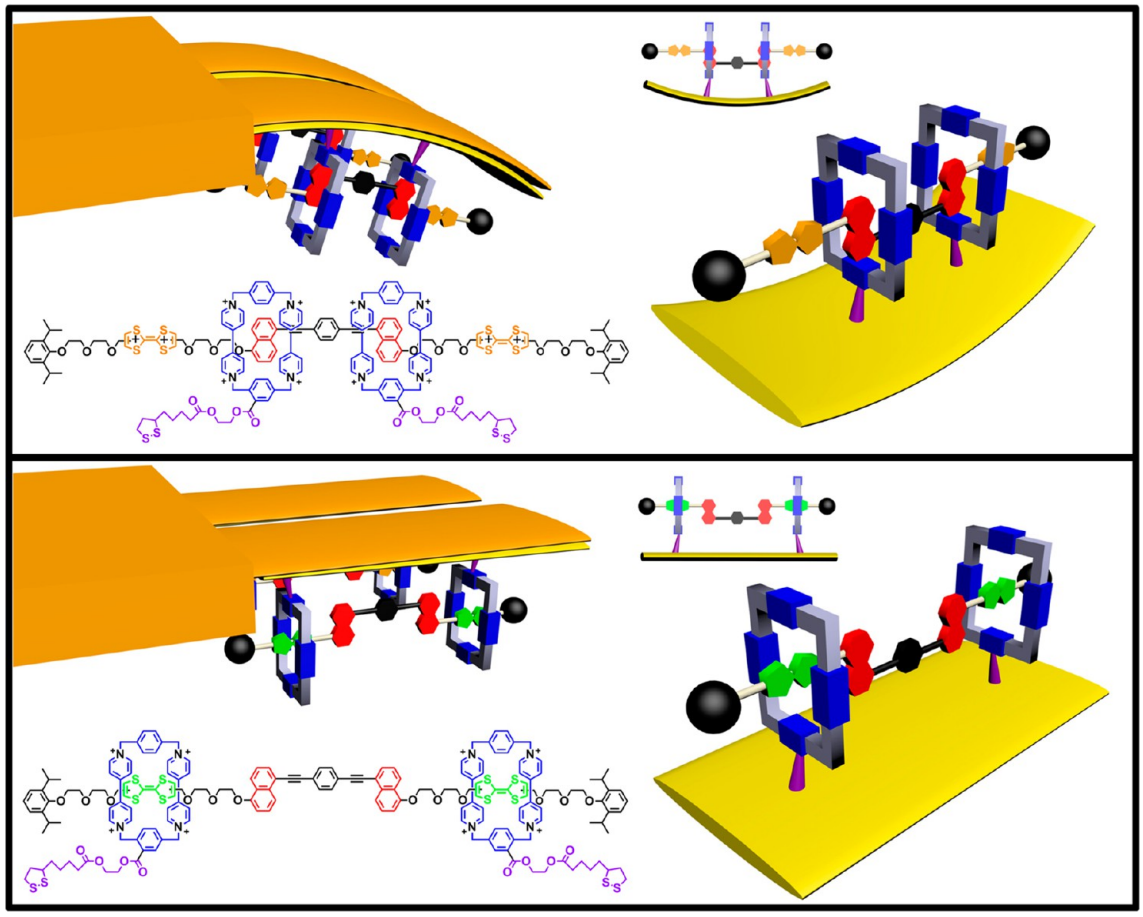

**Figure 9.** Schematic representation of the in situ electrochemical activation of the palindromic bistable [3]rotaxanes on AFM microcantilever. The reversible electrochemical oxidation and reduction of the [3]rotaxanes led to the bending and stretching of the microcantilever.

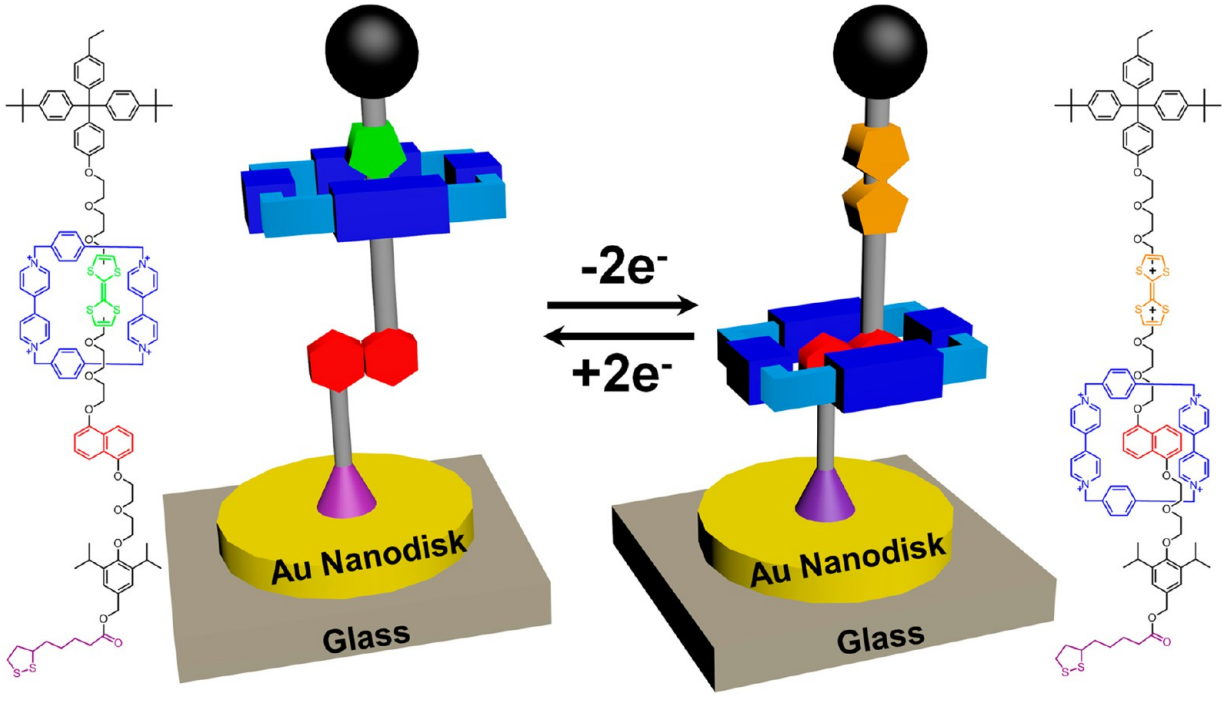


**Figure 10.** Schematic representation of the working principle of active molecular plasmonics based on the bistable rotaxanes self-assembled onto Au nanodisks.


dx.doi.org/10.1021/ar500022f | *Acc. Chem. Res.* 2014, 47, 1950−1960

als,[53] thin films,[54] or biomacromolecules, will become a hot topic because such soft interfaces both fulfill conditions of surface confinement and promote dynamic motions. Although much progress has been made in switchable host−guest systems, surface-tethered host−guest systems for real applications are still in their infancy, and learning from nature followed by human discovery, the development of wholly synthetic host−guest systems hybridized with interfaces may find applications in many different settings of science and technology.

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### Notes

The authors declare no competing financial interest.

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**Nan Song** was born in 1991 in Henan, China and grew up in Lanzhou, China. She attended Jilin University for her undergraduate studies and completed her B.Sc. in Chemistry in 2013, where she performed research under the direction of Professor Ying-Wei Yang. She is currently a M.S. student in the same research group.

## ACKNOWLEDGMENTS

We acknowledge the National Natural Science Foundation of China (21272093), the Innovation Program of the State Key Laboratory of Supramolecular Structure and Materials, and the SRFDP (20120061120117) for financial support.

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