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Nanovalves

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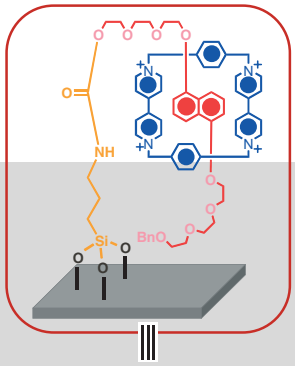

This article features both molecular and supramolecular chemistry involving: i) stimuli-induced nanoscale movements within mechanically interlocked molecules; ii) the fabrication of mesoporous silica substrates; and iii) the integration of the mechanically interlocked molecular/supramolecular actuators to act as gatekeepers at the entrances to the silica nanopores into which guest dye molecules can be uploaded and released on demand from the mesoporous silica substrates. The supramolecular actuators are based on two [2]pseudorotaxanes—that is, 1:1 complexes that can be dissociated by external inputs, such as acid/base cycles, electrons, and light. The molecular actuators are based on bistable [2]rotaxanes and can be operated mechanically by using either redox chemistry or electrochemistry. After these pseudorotaxanes and bistable rotaxanes have been attached covalently to the orifices of the silica nanopores, stimuli-controlled mechanical movements within these mechanically interlocked molecules can be harnessed to close and open the nanopores. Therefore, these mechanically interlocked molecules have been employed as nanovalves for controlled sequestering and release of guest dye molecules into and out of the mesoporous silica substrates. These actuators can be regarded as the prototypes of highly controllable drug-delivery systems.

1. Introduction

With the advent of nanotechnology, the fascination of achieving the miniaturization of macroscale machines, with the prospect of matching, if not eventually emulating, the performance of nanoscale biological machines, has acted as an incentive for chemists and engineers to develop artificial nanoscale machines[1,2] at the molecular and supramolecular levels. This Feature Article focuses on how nanoscale machines, capable of producing relatively large amplitude mechanical motions, have been employed to produce nanovalves, i.e., devices that can entrap and release guest molecules within nanopores on demand. For molecular-based systems to express machine-like functions, they should be able to execute stimuli-induced specific and directional mechanical movements that are otherwise restricted, by using only Brownian motion. Three types of external stimuli—chemical,[3] electrochemical,[4] and photochemical[5] inputs—have been employed to trigger large amplitude—indeed nanoscale—mechanical movements within molecular switches. Mechanically interlocked molecules, such as bistable [2]catenanes[4a,f,g,j] and bistable [2]rotaxanes,[4i] are amongst some of the most useful nanoscale switches whose molecular forms and functions rely on noncovalent bonding interactions, for example, π-donor–π-acceptor,[4a,f–i] hydrogen-bonding,[5c,e–j] metal–ligand,[4b,l,5d] and hydrophobic[5k] interactions. These mechanically interlocked molecules can be switched (Fig. 1) between two translational isomers—namely, a ground state co-conformation (GSCC) and a metastable state co-conformation (MSCC). A strong affinity allows the ring to encircle the templating site in the GSCC of the bistable molecule. An interaction, which can however be erased or reversed by external inputs—such as chemical, electrochemical, and photochemical stimuli—obliges the ring component to move to the alternative recognition site. After withdrawal of the external stimulus, the ring may still encircle the secondary recognition site for some time, generating the MSCC, which eventually relaxes back to the GSCC via thermally activated Brownian motion within the molecules. The physical properties, for example, conductivity, polarizability, hydrophobicity, and fluorescence, of the bistable, mechanically interlocked molecules are substantially different in the GSCC than in the MSCC. It follows that nanoelectromechanical systems (NEMS) can be developed,[1p,q] based on electrochemically switchable bistable [2]catenanes and [2]rotaxanes. Of all the external stimuli, light and electrons are the most efficient ones to power mechanical movements within mechanically interlocked molecules, considering that they are

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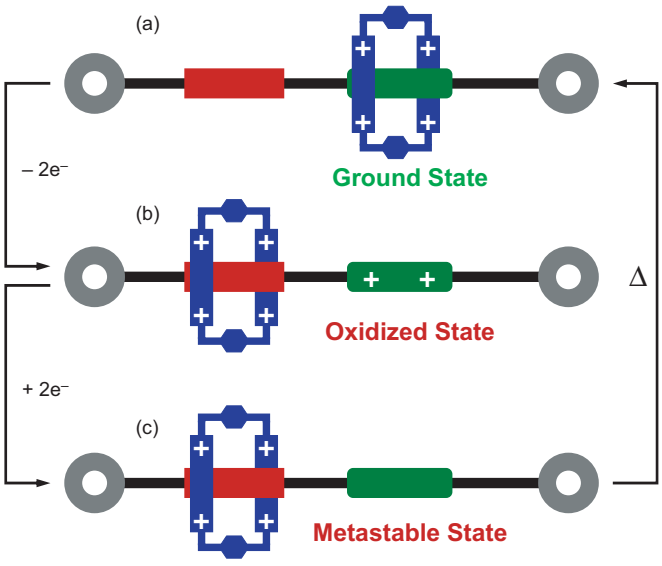
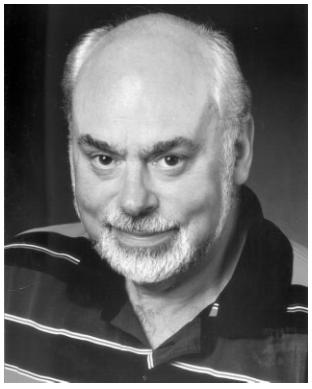


Figure 1. Graphical representations of a bistable [2]rotaxane in its a) ground state co-conformation (GSCC) with the interlocked ring component (blue) encircling the stronger recognition site (green), b) oxidation of the stronger recognition site induces ring's mechanical movement to the secondary recognition site (red), and c) isomeric metastable state co-conformation (MSCC), after reduction of the green unit back to its neutral state, but with the ring still encircling the red unit. The MSCC relaxes back to the GSCC, following a thermally activated return of the ring component to the original green unit.

waste-free and can be employed and withdrawn without leaving behind any impression—a phenomenon that allows for clean detection of the mechanical process. Some nanoscale devices, however, can be switched by controlling the pH of the medium—a process which could be utilized in the biological environment for drug-delivery purposes—at the inevitable expense of producing waste products.

In this Feature Article, we begin by introducing the threading/dethreading of supramolecular machines, namely [2]pseudorotaxanes,[5a,6] a process that can be powered either by means of direct photosensitization or by employing a light-harvesting molecular triad that produces photocurrent. Studies of these machines eventually led us to develop molecular nanovalves based on bistable [2]rotaxane molecules that are capable of functioning as gatekeepers for the controlled release of dye molecules from mesoporous silica substrates.[7]

A macroscopic valve is a machine assembled by combining a controllable component that regulates the flow of gases or liquids from a reservoir. The effectiveness of the valve in controlling flow is highly dependent on the fitting and matching of its components—the valve will leak when it is too loose and will not open when it is too tight. Miniaturization of a macroscopic valve to the nanoscale level requires the integration of stable and inert nanoreservoirs with appropriate functional molecules having movable components that can acts as gatekeepers at the entrances and exits to the nanoreservoirs, regulating the molec-



J. Fraser Stoddart was born in Edinburgh, Scotland, in 1942. He received all (B.Sc., Ph.D., and D.Sc.) of his degrees from the University of Edinburgh, UK. In 1967, he went to Queen's University (Canada) as a National Research Council Postdoctoral Fellow, and then in 1970, to Sheffield University as an Imperial Chemical Industries (ICI) Research Fellow, before joining the academic staff as a lecturer in Chemistry. After spending a sabbatical (1978–1981) at the ICI Corporate Laboratory in Runcorn, he returned to Sheffield where he was promoted to a readership in 1982. In 1990, he took up the Chair of Organic Chemistry at Birmingham University and was Head of the School of Chemistry there (1993–1997) before moving to UCLA as the Saul Winstein Professor of Chemistry in 1997. Presently, he holds the Fred Kavli Chair in NanoSystems Sciences at UCLA and is the Director of the California NanoSystems Institute. His current research interests are concerned with transporting well-established concepts in biology from the life sciences into materials and medicinal chemistry.

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ADVANCED FUNCTIONAL MATERIALS

ular transport in and out of these reservoirs. In the second part of this Feature Article, the construction of operational nanovalves based on mesoporous silica with supramolecular and molecular actuating components will be surveyed.

2. Supramolecular Machines Powered by a Photosensitizer

A [2]pseudorotaxane (Fig. 2) composed of a π-electron-accepting cyclobis(paraquat-*p*-phenylene) ($CBPQT^{4+}$) cyclophane that encircles a π-electron donating 1,5-bis[(2-hydroxyethoxy)ethoxy]naphthalene (BHEEN) stalk can be considered as a nanoscale machine.[5a,6] The absence of any bulky stoppers at the ends of the stalk component allows the cyclophane to slip on and off the stalk under equilibrium conditions—a process that can also be controlled by using light as the stimulus. A strong π–π charge transfer (CT) interaction, as well as [C–H···O] and [C–H···π] interactions between the BHEEN stalk and the $CBPQT^{4+}$ ring forms[8] a stable BHEEN ⊂ $CBPQT^{4+}$ pseudorotaxane in 80 % yield (acid dissociation constant, $K_a = 2.53 \times 10^4$ M^{-1} in acetonitrile, 298 K) at equilibrium. Photoinduced electron transfer to the $CBPQT^{4+}$ ring from an external photoactive electron donor or electrochemical reduction of the ring component destabilizes the CT interactions, inducing the dissociation of the [2]pseudorotaxane—a process that can be monitored by measuring the BHEEN-based fluorescence intensity, which is higher in the dissociated form than it is in the associated species, i.e., the [2]pseudorotaxane.

The first generation of this series of supramolecular machines was driven (Fig. 2a) photochemically by using 9-anthracenecarboxylic (ACA) acid as the photosensitizer (P), which donates an electron to the $CBPQT^{4+}$ ring in the presence of the sacrificial reagent triethanolamine (TEOA), thus preventing the back electron transfer (BET) process.[5a] In the absence of TEOA, BET is faster than the dissociation of the ring from the stalk. TEOA, however, quenches the photo-oxidized P^+ unit, allowing enough time for the photoreduced $CBPQT^{2\bullet/2+}$ to slip off the BHEEN stalk, thus increasing the BHEEN-based fluorescent intensity in the 320–370 nm region. Based on the change in fluorescent intensity, 35 % of the 4.8×10^{-5} M [2]pseudorotaxane could be dissociated after 25 min of irradiation in a deoxygenated solution in the presence of 5×10^{-6} M of P and 0.01 M TEOA.[5a] Introduction of air into the system regenerated the $CBPQT^{4+}$ ring, resulting in recomplexation, a process that reproduced the original fluorescence spectrum, albeit at lower intensity.

[2]Pseudorotaxane-based supramolecular machines are powered by photosensitizers,[9] not only in solution, but also when they are trapped physically in a rigid nanoporous sol–gel silica framework or when attached covalently to silica surfaces (Fig. 2b). Irradiation of a condensed silica sol–gel matrix containing i) the BHEEN ⊂ $CBPQT^{4+}$ pseudorotaxane, ii) ACA, and iii) a sacrificial donor, ethylenediaminetetraacetate (EDTA) with a 365 nm Hg lamp (100 W) bleaches the original pink color ($\lambda_{max} = 520$ nm) of the sample[9] arising from the CT interactions between the π-electron rich BHEEN stalk and the surrounding π-accepting $CBPQT^{4+}$ ring, and replaces it with the pale blue color ($\lambda_{max} = 650$ nm) of the

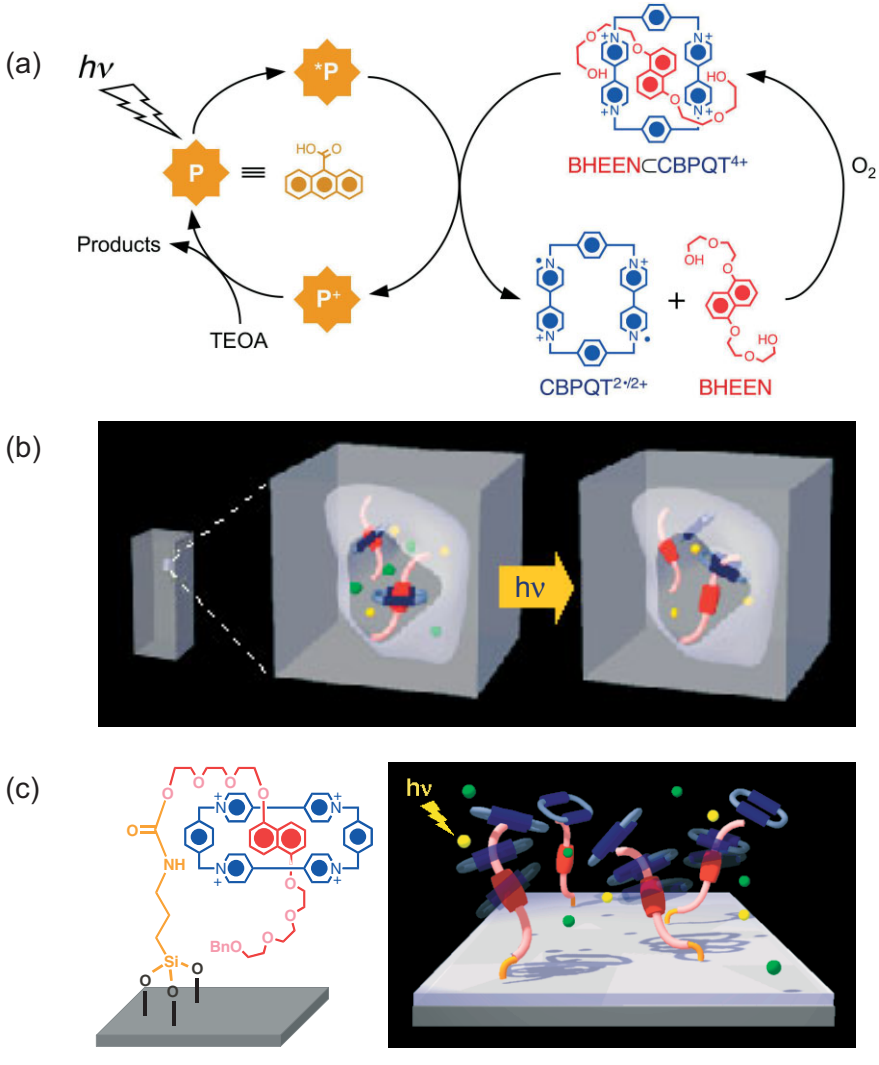

Figure 2. Light-induced dissociation of the BHEEN ⊂ $CBPQT^{4+}$ [2]pseudorotaxane in the presence of 9-anthracenecarboxylic acid as a photosensitizer, using triethanolamine (TEOA) as the sacrificial reductant and oxygen as the sacrificial oxidant: a) in solution phase; b) when confined in a rigid nanoporous silica sol–gel matrix; and c) when the BHEEN-analog, the BHEEEN-stalk, is grafted onto a silica thin film.

reduced bipyridinium units. This process occurs concomitantly with a rise in the BHEEN-based fluorescent intensity in the 320–370 nm region. Prolonged exposure of the sample to air in the dark reproduces the original spectrum, thus establishing the reversible character of the process. These spectroscopic changes indicate that photoinduced dissociation of the [2]pseudorotaxane occurs also in condensed phases, although the process is slower by at least an order of magnitude than it is in the solution phase on account of spatial confinement of the supramolecules within the nanopores.

In another device, the BHEEN homolog, BHEEEN, with an extra ethyleneoxy unit, was attached covalently to a silica surface (Fig. 2c).[9] Dipping of the BHEEEN-functionalized surface into an aqueous solution of the $CBPQT^{4+}$ ring led to the formation of the corresponding [2]pseudorotaxane, confined on a surface, as monitored by its reduced fluorescence intensity. A second immersion of the [2]pseudorotaxane-coated surface into an ACA and EDTA solution, followed by an irradiation at 365 nm, led to an increase in the naphthalene-based fluorescence intensity. Similar experiments also suggest that the [2]pseudorotaxanes, attached covalently to the silica surfaces,[9] undergo the same photoinduced dethreading in the presence of a photosensitizer and a sacrificial donor.

3. Supramolecular Machines Powered by a Light-Harvesting Molecular Triad

A molecular triad (Fig. 3a) composed of three unique electroactive components, namely, i) an electron-donating tetrathiafulvalene (TTF) unit, ii) a chromophoric porphyrin (P) unit, and iii) an electron-accepting C_{60} unit, was developed to harness light and convert it into electrical energy.[10] A disulfide-based anchoring group was tagged to the TTF end of the triad in order to promote its self-assembly onto gold surfaces. When irradiated near the absorption maximum (λ_{max}, Soret band) of the chromophore P at 413 nm (40 mW cm^{-2} Kr-ion laser), the triad undergoes a photoinduced electron transfer (PET) from the singlet excited state of porphyrin (*P) to the electron-accepting C_{60} unit, followed by a charge shift to the better electron-donating TTF unit to generate the final charge-separated state, $TTF^{\bullet+}$-P-$C_{60}^{\bullet-}$. This charge-separated state generates a photocurrent in a closed circuit in the form of a unidirectional electron flow from the working cathode through i) the photoactive triad and ii) the electrolyte solution, to iii) the counter electrode, and through iv) the outer circuit where the current is measured ($\Delta I \sim 1$ μA cm^{-2}, $\Phi_{photocurrent} \sim 1$ %).[10] The triad has been utilized as a nanoscale power supply to drive the dethreading of the BHEEN ⊂ $CBPQT^{4+}$ pseudorotaxane in the presence of 413 nm light at an applied potential ($V_{ap} = 0$ V) that is much lower than that required for direct electrochemical reduction ($E^{1/2} = -300$ mV) of the $CBPQT^{4+}$ ring.[10b] In accordance with the PET mechanism (Fig. 3), at $V_{ap} = 0$ V, the charge-separated state of the triad affords a $C_{60}^{\bullet-}$ unit on the triad-functionalized Au working electrode, resulting in an effective terminal potential of –550 mV, which is the reduction potential of the $C_{60}^{0/-\bullet}$ unit. This potential is high enough to reduce the $CBPQT^{4+}$ ring and induce its dissociation from the BHEEN stalk—a process which was monitored (Fig. 3b) by detecting the BHEEN-based fluorescence intensity.[10b] Based on the increase in the fluorescence intensity (320–370 nm), 6.7 % of the 0.37 mM [2]pseudorotaxane in acetonitrile underwent dissociation in the presence of triad excitation over 2900 s, an estimation that is commensurate with the triad's ability to photoreduce 7 % of the $CBPQT^{4+}$ ring by generating 1.1 μA cm^{-2} photocurrent during the period of irradiation.[10b]

4. Construction of Operational Nanovalves Based on Silica Supports

Since the idea of using [2]pseudorotaxanes as prototypes of artificial molecular machines first surfaced,[1,2,5a,6] operational supramolecular nanovalves employing these tethered complexes as the controllable (actuating) components have been constructed (Fig. 4) successfully.[11] The supramolecular nanovalves are based on mesoporous silica films and particles, which contain hexagonal arrays of cylindrical nanopores 2 nm in diameter, as the supporting materials. Moreover, they can be functionalized with [BHEEEN ⊂ CBPQT]$^{4+}$ pseudorotaxanes in which the tethered BHEEEN unit acts as a gatepost and the $CBPQT^{4+}$ ring serves as the gate that controls access of guest molecules into and out of the nanopores of the mesoporous silica films. In order to develop these particular nanovalves, mesoporous silica thin films were synthesized by using a sol–gel-based dip-coating method[12] prior to functionalization with isocyanatopropyltriethoxysilane (ICPES) at the openings to the nanopores. Subsequently, monobenzylated BHEEEN[9] molecules were immobilized on the silica film by reacting their free hydroxyl groups with the isocyanate functions at the openings to the nanopores, forming carbamate linkages. A luminescent probe molecule, tris(2,2′-phenylpyridyl)iridium(III) [$Ir(ppy)_3$, dimension: ca. 1.0 nm × 1.0 nm] was chosen as the substrate for controlled-release experiments on account of its intense luminescent properties. The loading of the $Ir(ppy)_3$ molecules into the nanopores was achieved by soaking the silica thin film in a solution (1.0 mM in toluene) of $Ir(ppy)_3$. Subsequently, the nanovalves can be closed by placing the film in an aqueous solution of CBPQT·4Cl (1.0 mM), allowing the self-assembly of the sterically bulky $CBPQT^{4+}$ rings (ca. 0.8 nm × 1.0 nm) onto the free BHEEEN stalks, thus forming tethered [2]pseudorotaxanes held together by donor–acceptor, [C–H···O], and [C–H···π] interactions. This self-assembly process seals the nanopores effectively, trapping the probe molecules inside the orifices of the nanopores and preventing them from leaking out. After extensive washing away of any surface-absorbed probe molecules, the nanovalves can be opened very efficiently on the addition of $NaCNBH_3$—a relatively mild reducing agent that causes the reduction of the $CBPQT^{4+}$ ring—switching off its weak noncovalent bonding interactions with BHEEEN and causing it subsequently to dissociate from

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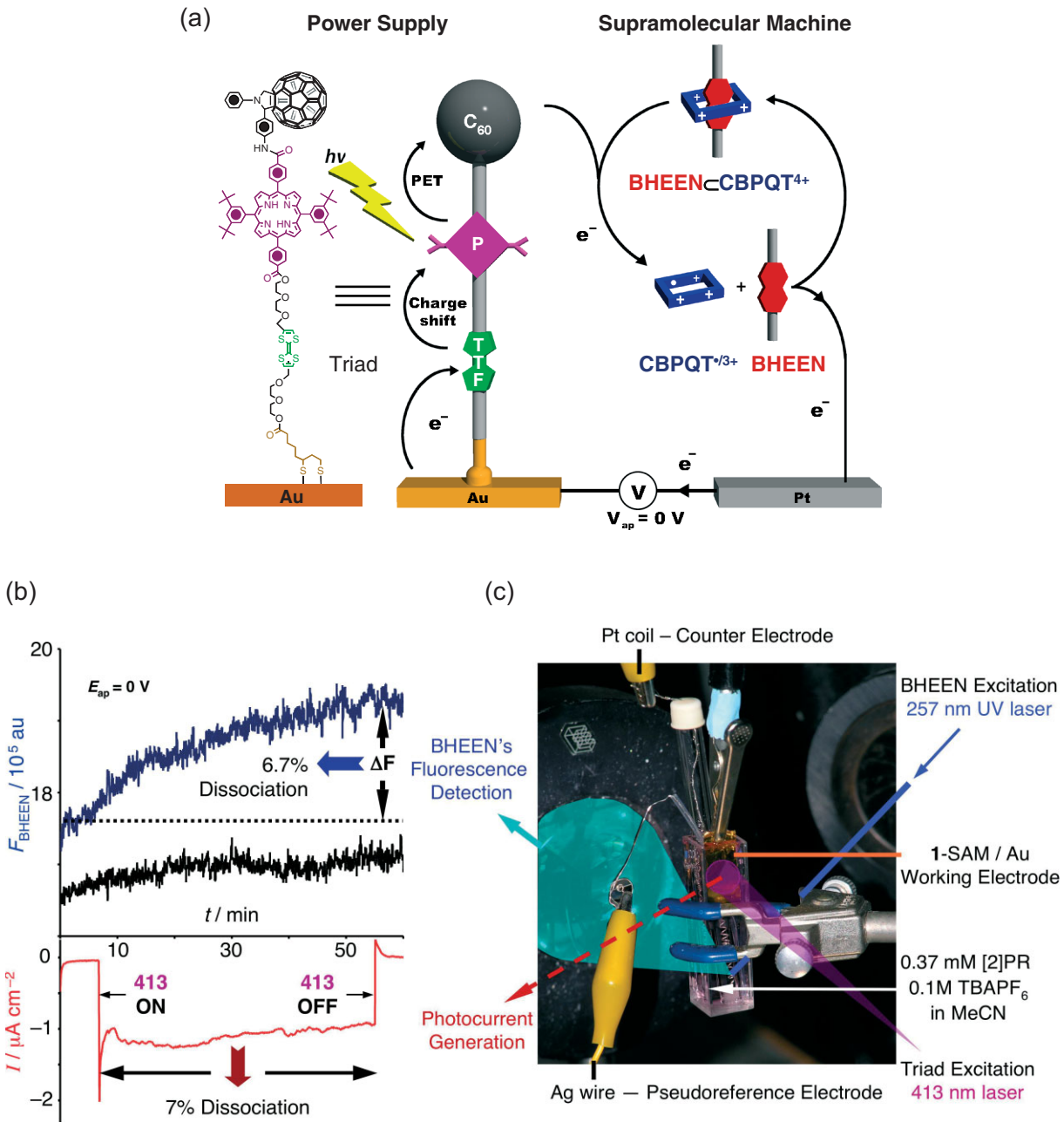

Figure 3. a) The light-harvesting molecular triad producing photocurrent, which powers the dissociation of the BHEEN ⊂ $CBPQT^{4+}$ pseudorotaxane-based supramolecular machine at a potential that is much lower than the threshold potential required for direct electrochemical dissociation of the pseudorotaxane. b) The BHEEN-based fluorescence intensity (blue trace) increasing gradually, concomitant with the photocurrent generation (red trace) by the triad in the presence of a 413 nm Kr-laser beam. Note that the fluorescence intensity of BHEEN does not change (black trace) in the absence of 413 nm light. c) Experimental setup for the triad-driven supramolecular machine. SAM: self-assembled monolayer; PR: pseudorotaxane; $TBAPF_6$: tetrabutylammonium hexafluorophosphate; MeCN: acetonitrile.

the BHEEEN stalk, leading to a controlled release of $Ir(ppy)_3$ from the nanopores into solution. The controlled release was monitored by time-dependent emission spectra. The emission spectrum of $Ir(ppy)_3$ increased gradually when the nanovalves were opened on the addition of $NaCNBH_3$ compared to the nanovalves that remain closed. Moreover, the emission spectrum of the 1,5-dioxynaphthalene (DNP) subunits on the BHEEEN stalks was monitored before and after the controlled release. The DNP emission before the controlled release is much lower than that after the release, an observation[13] that can be explained by the partial quenching effect associated with the complexation of the $CBPQT^{4+}$ ring with the DNP unit in [2]pseudorotaxane superstructure.

Although the use of the redox-controllable, donor–acceptor [2]pseudorotaxane is relatively straightforward in the construction of operational supramolecular nanovalves by taking

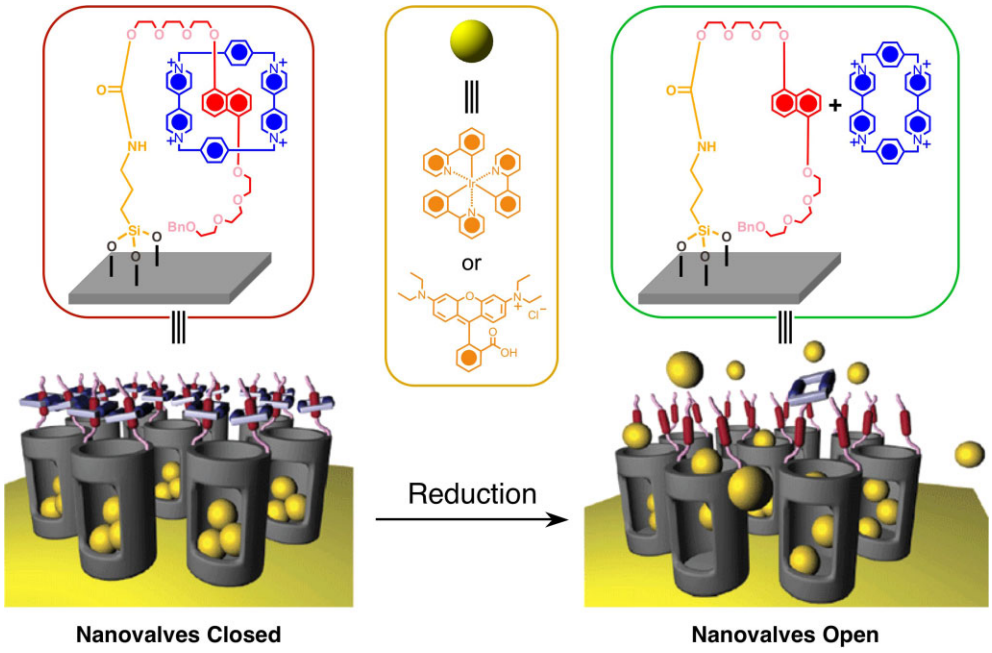

Figure 4. Graphical representation of redox-controllable supramolecular nanovalves attached to mesoporous silica films, using the BHEEEN ⊂ $CBPQT^{4+}$ [2]pseudorotaxane as gatekeepers. Reduction of the $CBPQT^{4+}$ ring induces the dissociation of the ring away from the covalently attached BHEEEN stalk on the silica surface—a process that allows luminescent probe molecules to release from the nanopores. Mesoporous silica substrates, pseudorotaxane-based gatekeepers, and probe molecules are not drawn to scale in the graphical representation. The numbers of the gatekeepers and guest molecules in each chamber are not constant.

advantage of the strong complexation (ca. 3.9 kcal mol^{-1}) of BHEEEN by the $CBPQT^{4+}$ ring, the approach lacks simplicity of operation as well as reusability and reversibility. Shortly after we communicated these results,[11] we reported the construction of redox-switchable and reversible molecular nanovalves (Fig. 5) employing bistable [2]rotaxanes as the controllable components.[7] The bistable [2]rotaxane described in this Feature Article was synthesized using a modular approach.[14] It consists of a DNP unit, a tetrathiafulvalene (TTF) unit, and two stoppers, as well as a $CBPQT^{4+}$ ring to act as the gate to control the passage of probe molecules into and out of nanopores. It was found that the $CBPQT^{4+}$ ring of the bistable [2]rotaxane predominantly encircles the TTF unit rather than the DNP unit.[7,14] Initially, roughly spherical (diameter, $d \sim 600$ nm) mesoporous silica particles, namely MCM-41, fabricated by a sol–gel method,[15] were employed as a supporting platform and reservoir for the construction of redox-controllable nanovalves. Firstly, mesoporous silica particles MCM-41 were treated with ICPES at the openings to the nanopores and then reacted with the bistable [2]rotaxane, thus forming molecular nanovalves (Fig. 5a). When the TTF units in the bistable [2]rotaxanes are in their neutral state and encircled with the $CBPQT^{4+}$ rings, the nanovalves are open. To evaluate the overall performance of the nanopores (Fig. 5b), they can be filled with different luminescent probe molecules such as $Ir(ppy)_3$, rhodamine B, and tetraethyl-3,6-diaminofluoran, as these probe molecules are known to be compatible with redox processes. Notably, the nanovalves can be closed by adding two equivalents of an oxidant, iron perchlorate hexahydrate, to oxidize the TTF unit on the rotaxane backbone. This process forces the $CBPQT^{4+}$ ring to shuttle mechanically from the oxidized TTF unit to the DNP unit, on account of the charge repulsion between the $CBPQT^{4+}$ ring and the oxidized TTF^{2+} dicationic unit, leading to closed nanovalves that completely block the entrance to the nanopores. After extensive washing to remove any surface-absorbed probe molecules, the controlled release of probe molecules can be demonstrated by adding an excess of ascorbic acid to open the nanovalves. This process reduces the oxidized TTF units back to their neutral state, so that the $CBPQT^{4+}$ rings will move away from the openings of the nanopores and once again complex with the neutral TTF unit, causing a subsequent release of the probe molecules.

Moreover, these redox-switchable molecular nanovalves have demonstrated their reversibility and reusability. It is possible to load a second batch of probe molecules into the nanopores from the previously discharged bistable [2]rotaxane-based nanovalves. The controlled release of the second loading of probe molecules exhibits a similar increase in emission intensity compared to the first release, affording them the status of being operational and reversible mechanical nanovalves.

One of the attractive features of nanovalve systems is their ability to induce controlled release using various external stimuli, for example redox processes, pH changes, and light sources. Recently, supramolecular nanovalves that are sensitive to pH changes were constructed (Fig. 6).[16] These nanovalves are based on the mutual recognition motif between secondary dialkylammonium ions and dibenzo[24]crown-8 (DB24C8).

ADVANCED FUNCTIONAL MATERIALS

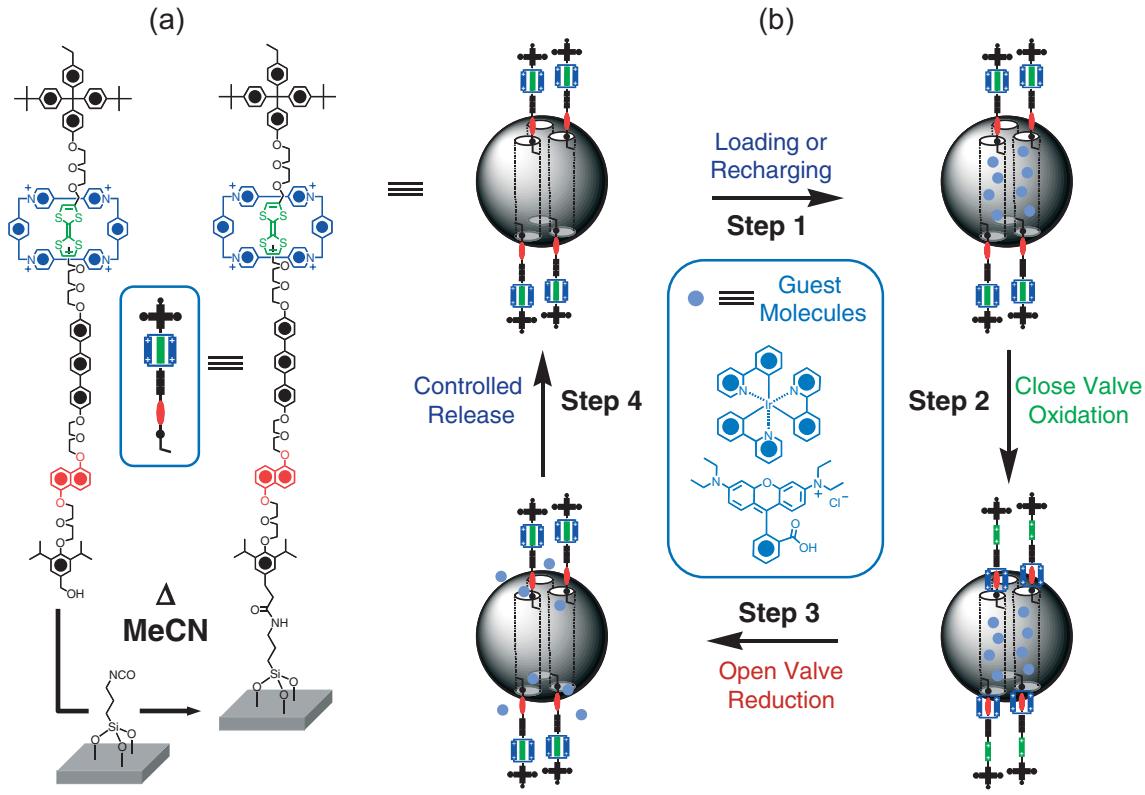

Figure 5. Graphical representation of the reversible, redox-controllable molecular nanovalves based on mesoporous silica particles, using a bistable [2]rotaxane that utilizes TTF and DNP units as the electron-rich recognition sites that serve as stations for the encircling $CBPQT^{4+}$ ring in the ground and oxidized states, respectively. When in the oxidized state the ring component encircles the DNP unit —which is closer to the silica nanopores—it holds the gate shut, confining the guest molecules inside the pores. Movement of the ring to the TTF unit—which is located away from the pore openings—opens the gate, releasing the guest molecules spontaneously. Mesoporous silica substrates, bistable [2]rotaxane-based gatekeepers, and probe molecules are not drawn to scale in the graphical representation. Numbers of the gatekeepers and guest molecules in each chamber are not constant.

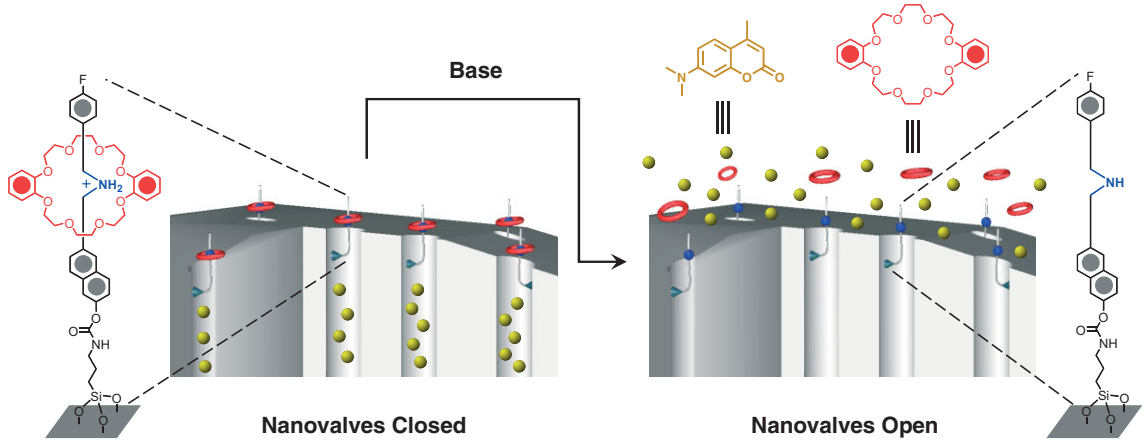

Figure 6. A graphical representation of the pH-driven supramolecular nanovalves based on mesoporous silica nanoparticles, using a DB24C8 crown ether and a dialkylammonium center-based pseudorotaxane as the gatekeeper. pH-controlled protonation/deprotonation closes or opens the gate, respectively, by virtue of 'complexation' and 'decomplexation'. This process allows the probe molecules—coumarin 460—to be confined or released from the nanopores. Mesoporous silica substrates, pseudorotaxane-based gatekeepers, and probe molecules are not drawn to scale in the graphical representation. The numbers of the gatekeepers and guest molecules in each chamber are not constant.

DB24C8 is a macrocyclic polyether,[17] which is able to encircle dialkylammonium centers ($-CH_2NH_2^+CH_2-$), thus forming [2]pseudorotaxanes held together by multiple hydrogen bonds. Neutralization of the acidic dialkylammonium centers with bases such as triethylamine switches off the hydrogen bonds and causes dissociation of the DB24C8 rings from the [2]pseudorotaxanes.[18] The pH-driven supramolecular nanovalves consist of numerous naphthalene-containing dialkyl-

ammonium stalks attached to mesoporous MCM-41 particles ($d \sim 600$ nm).[16] A base-compatible, luminescent amine probe molecule, coumarin 460, was chosen as the substrate for pH-driven controlled release. After the loading of the coumarin 460 molecules into the nanopores of MCM-41, the entrances of the nanopores were sealed by the addition of DB24C8. The DB24C8 rings recognize and self-assemble around the dialkylammonium ion stalks near the entrances of the nanopores to obtain closed nanovalves. After extensive washing to remove any surface-absorbed probe molecules, the nanovalves were subjected to controlled release using different bases—triethylamine (TEA), diisopropylethylamine (DIPEA) and hexamethylphosphorus triamide (HMPT). The rates of controlled release of probe molecules using the three bases separately differ according to the nature of the base used in the investigation. The least sterically bulky base—namely, TEA—gives the fastest rate of release, while the most sterically hindered base, HMPT, gives the slowest rate of release.

For future nanovalve applications, it is most desirable to develop molecular nanovalves with multiple activation mechanisms, such that they are responsive to the relatively benign stimuli that are applicable to biological systems. Photoactivation is obviously an attractive option. It would represent a significant step towards the use of less harsh forms of energy for the opening of nanovalves. Moreover, it is important that the nanovalves can release various types of molecules or nanoparticles with different sizes as well as having controllable rate of release. Metal salts can also be employed as activating agents for the DB24C8/dialkylammonium nanovalves, based on the fact that the DB24C8 rings can complex not only with dialkylammonium ions but also with metal cations, for example, Cs^+, K^+, and Ca^2. Cations, which have higher binding constants than dialkylammonium ions towards the crown ether, can be used as activating agents for the nanovalves by means of a competitive binding mechanism.

5. Conclusions

Operational nanovalves, with one mode of activation, constructed from donor–acceptor [2]pseudorotaxanes or bistable [2]rotaxanes, which act as gatekeepers, and mesoporous silica, which acts as both a supporting platform for the gatekeepers and a reservoir for the probe molecules, have been demonstrated to work in more ways than one. Moreover, the versatility of supramolecular nanovalves based on the controllable crown ether/dialkylammonium ion recognition motif has been demonstrated through the operation of nanovalves by using a wide range of stimuli. The ability to fine-tune different parts of nanoscale molecular machines—nanovalves—has been well demonstrated by means of rational design and the operation of nanovalves to achieve optimal functions. Reversibility is attainable for the molecular nanovalves operating under redox control. This ability to fine-tune the nanovalves' operational modes is fundamental and essential to the future design of bistable molecular switches, and will enhance the potential applicability of these nanovalves.

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