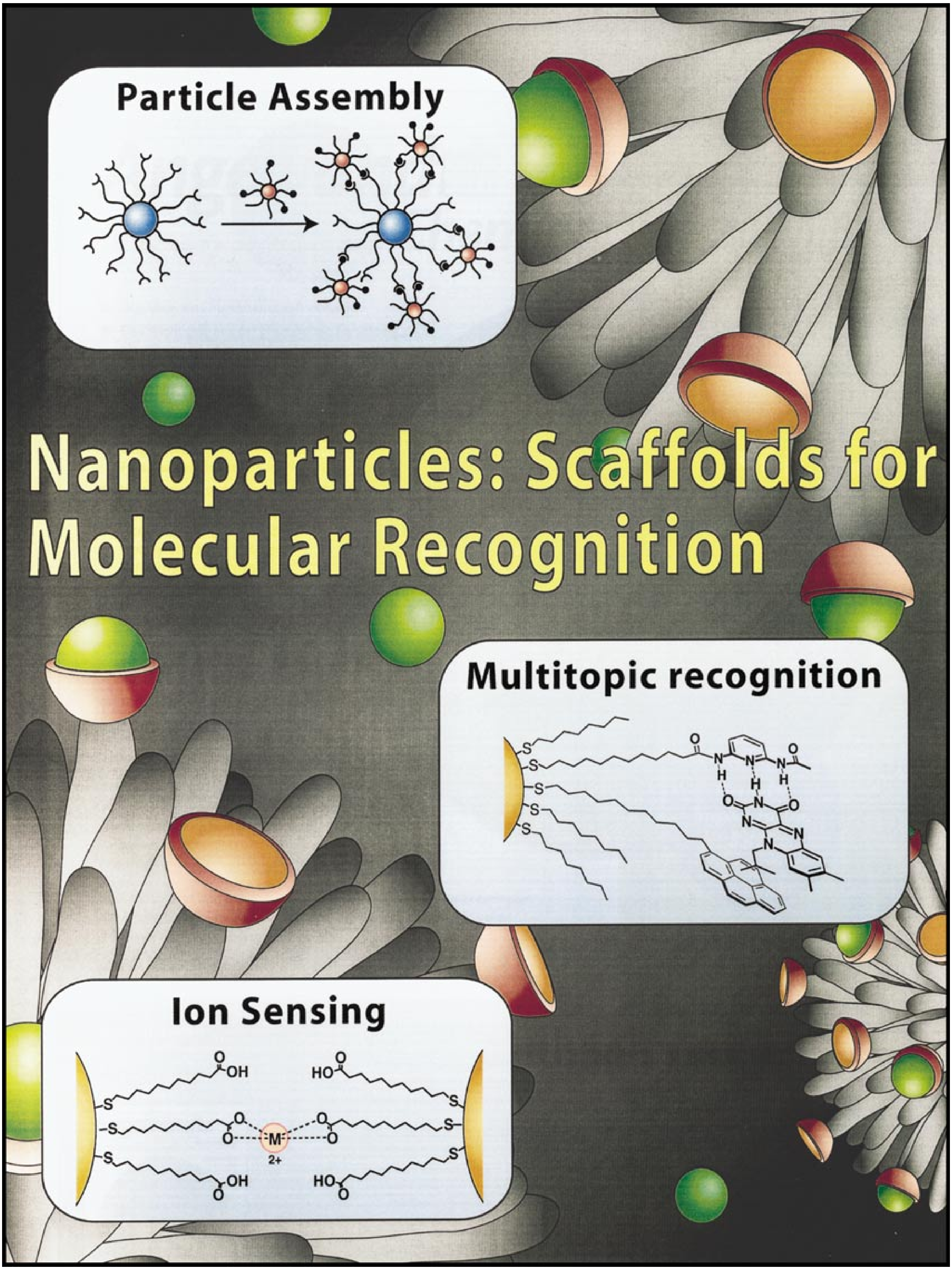

DOI: 10.1002/chem.200306076

Nanoparticles: Scaffolds for Molecular Recognition

Ulf Drechsler, Belma Erdogan, and Vincent M. Rotello*[a]

Abstract: Monolayer and mixed-monolayer protected clusters (MPCs and MMPCs) have great potential to combine molecular functionality with the intrinsic properties of nanometer-sized scaffolds. This synergy can be used to create complex functional devices, including redox-active, electronic, or magnetic storage devices, solution-based sensors, and highly efficient catalysts. This review outlines some of the recent developments in nanoscale receptors based on synthetic and nonbiological recognition elements. In these nanoparticle systems, molecular recognition is achieved by covalent attachment of receptors on the nanoparticles coupled with noncovalent interactions to target substrates. Synthetic host–guest systems, hydrogen bonding, change in redox states, π–π stacking, rotaxane formation, and ion recognition are the main topics covered in this review.

Keywords: molecular recognition · nanotechology · receptors · sensors

Introduction

The size (typically 1–100 nm) and unique physical properties of metal and semiconductor nanoparticles[1] play key roles in the emerging field of nanotechnology. Nanoparticles provide a means of bridging the gap between "top-down" lithographic techniques[2] and "bottom-up" synthetic strategies for the construction of functional devices,[3] by providing a building block for nanocomposite assemblies as well as a versatile scaffold for the introduction of chemical functionality.

Monolayer- and mixed-monolayer-protected clusters (MPCs and MMPCs) are of particular interest to chemists, since they combine a metallic or semiconductor core with a self-assembled organic shell.[4] In these systems a monolayer prevents agglomeration of the cores and serves as a well-organized scaffold for the attachment of functional molecular units. Mixed-monolayer systems greatly enhance the versatility of core-shell particles, allowing for multiple functionalities to be appended onto outer layer of the nanoparticle. These systems provide control over a variety of properties, from solubility in organic or aqueous solvents, to the introduction of redox active or specific molecular recognition elements.

The fabrication of MPC and MMPC systems has been greatly facilitated by the method developed by Brust and co-workers.[5] This technique utilizes the chemical reduction of metal salts (e.g., Ag, Au, Pt, Pd) in the presence of a capping ligand. The mild conditions used are compatible with a wide range of chemical functionalities and by varying the metal-to-ligand ratio, particles with core diameters ranging from 1.5 to 8 nm can be synthesized.[6] Ligand displacement reactions, developed by Murray and co-workers, have been successful in introducing multiple functionalities into these MPC systems in a stepwise fashion, relying on concentration equilibria.[7] This approach provides a potent and rapid means for rapidly obtaining a wide array of structurally diverse MMPC systems.

Molecular Recognition Using Nanoparticles

MMPCs exhibit characteristics similar to organic molecules, such as solubility in various solvents; this allows these systems to be characterized by using standard solution-phase spectroscopic techniques including NMR, IR, and UV-visible spectroscopy. This feature, combined with their ease of fabrication, makes MMPCs well-suited as starting materials for the creation of nanoscale receptors. These receptors rely on specific noncovalent interactions with complementary guests, utilizing, for example, ionic or hydrogen-bonding interactions. Recognition capability can be introduced through modification of nanoparticle systems with biomolecules,[8] including DNA[9] and specific proteins;[10] however, the focus of this Concepts article will be on nanoscale receptors based on synthetic and nonbiological molecular recognition groups.

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DOI: 10.1002/chem.200306076

Nanoparticle receptors featuring preformed binding sites: In an effort to incorporate molecular recognition elements into nanoparticle systems, Astruc and co-workers designed MMPCs featuring ferrocene units on the surface; these MMPCs utilized the interdependence between molecular recognition and redox events to selectively bind oxo anions.[11] In these studies the group has synthesized a series of gold nanoparticles displaying different concentrations of amidoferrocene units on variable chain lengths within a dodecanethiol monolayer through place-exchange reactions (Figure 1).

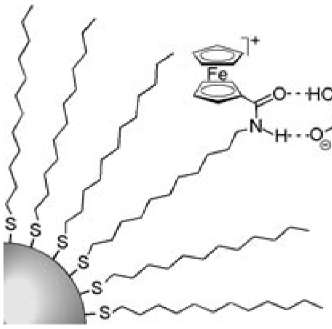

Figure 1. Complex formation between ferrocenyl gold MMPC and dihydrogen phosphate.

Through voltammetric experiments it was shown that the electrochemical oxidations of the attached ferrocene units lead to a single voltammetric wave, indicating near equivalency of all ferrocene moieties within the monolayer. Progressive addition of $[NBu_4][H_2PO_4]$ then caused the gradual appearance of a second voltammetric wave at less positive potential ($\Delta E_{1/2} = 220$ mV) at the expense of the first. Saturation of all of the ferrocene units with the phosphoanion finally led to complete disappearance of the original ferrocene oxidation. This behavior is indicative of a hydrogen-bonding-mediated association event between the $H_2PO_4^-$ ion and the amido groups adjacent to the ferrocene; binding of the guest is much stronger with the oxidized host. Evidence for selectivity in binding between dihydrogen phosphate and amide–ferrocene over other anions has been shown in binding studies with HSO_4^-; this leads to a significantly smaller shift in the half-wave potential of the ferrocene units ($\Delta E_{1/2} = 40$ mV vs $\Delta E_{1/2} = 220$ mV).

To introduce a positive dendritic effect, that is, enhanced recognition with increased generation number[12] into nanoparticle systems, Astruc and co-workers extended their studies to MMPCs featuring ferrocene units on dendritic tethers.[13] In these studies, a series of gold nanoparticles displaying different numbers of amidoferrocene or silylferrocene groups on AB_3 or AB_9 dendrons were synthesized through either place-exchange or Brust-type reactions (Figure 2).

Again, through voltammetric experiments, near equivalency of all ferrocene units is evidenced by the observation of a single redox couple. Addition of dihydrogen phosphate or the dianion of adenosine triphosphate (ATP^{2-}) led to the appearance of a second voltammetric wave at less positive potentials. The largest potential difference (200 mV) was observed with an MMPC that contained amidoferrocene dendrons; however, the redox process was not fully reversible. In contrast, all silylferrocenyl systems exhibited fully reversible redox characteristics with potential differences between 115 and 135 mV. All receptor systems under investigation displayed high selectivity for $H_2PO_4^-$ or ATP^{2-} even in the presence of other anions, such as HSO_4^- or Cl^-.

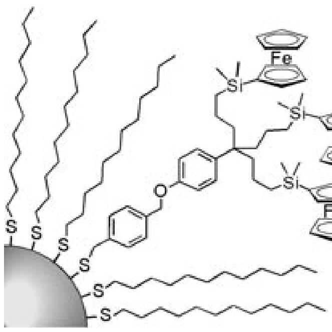

Figure 2. AB_3-dendronized gold MMPC.

Cyclodextrin-based host–guest chemistry can be incorporated into the monolayer of MPCs to provide a different motif for molecular recognition. Due to their ability to form inclusion complexes in aqueous media, cyclodextrins (CDs) have been studied extensively and have been utilized in multiple applications.[14] To integrate the inherent advantages of CD receptors into nanoparticle systems, Kaifer and co-workers developed a modified CD system that can readily be immobilized on the surface of platinum,[15a] palladium,[15a–c] silver,[15d] and gold[15e] colloids by converting the primary hydroxyl groups on the smaller rim of β-CD into thiol groups. The resulting perthiolated CDs were attached to metal core through multiple sulfur bonds, providing an orientation in which the wider opening is pointing away from the particle surface (Figure 3).

Since the CD-hydroxyl groups are located at the colloid–solvent interface, these nanoparticles were soluble in aqueous media, thus providing an optimized environment for specific guest recognition. A binding interaction between a dimeric ferrocene guest and β-CD-capped gold nanoparticles was established by the formation of slowly precipitating

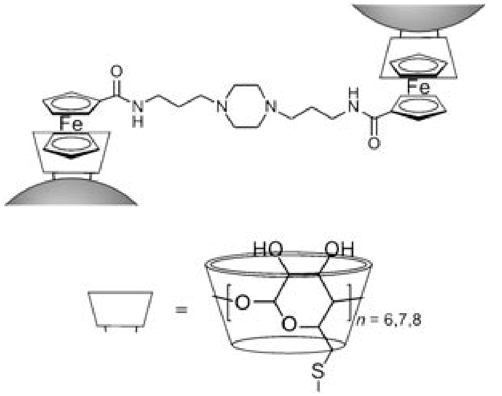

Figure 3. Aggregation of CD-functionalized gold MPCs with a dimeric ferrocene linker.

aggregates. Flocculation properties in this system were controlled through host–guest interactions, for example, competitive binding of a monomeric ferrocene guest resulted in partial redissolution of the precipitated aggregates. Similarly, addition of free β-CD at different concentrations provided control over the degree of flocculation through competitive binding.

In an extension of these studies, the same group has synthesized smaller (2–7 nm) gold MPCs featuring higher CD surface coverage[16] by employing a modification of Brust's protocol.[17] Specific recognition of ferrocenemethanol was confirmed through voltammetric experiments; binding of the guest to the receptor resulted in a lower overall current and a shift of the half-wave potential to more positive values, consistent with the formation of an inclusion complex. Furthermore, reversibility of the binding process has been confirmed by competitive binding studies with an electro-inactive guest. In these studies adamantol was found to replace bound ferrocenemethanol, leading to recovery of the voltammetric behavior of unbound ferrocenemethanol.

The high density of recognition elements on the surface of these MPCs also offers the possibility to reversibly alter the overall surface characteristics through saturation of all surface-bound CDs. To probe that possibility, Kaifer et al. studied the phase-transfer behavior of inherently hydrophilic CD-capped MPCs into chloroform through the binding of amphiphilic guests.[18] Using a series of cationic ferrocenes featuring different aliphatic chains, they showed that efficient water-to-chloroform phase-transfer occurred with guests that had chain lengths greater than 12 carbon atoms (Figure 4). Through a series of solubility experiments, it has also been concluded that the presence of water is necessary to stabilize these host–guest complexes; water is presumed to form a thin layer surrounding the surface-bound CD receptors and the counterions required to compensate for the cationic ferrocene guests.

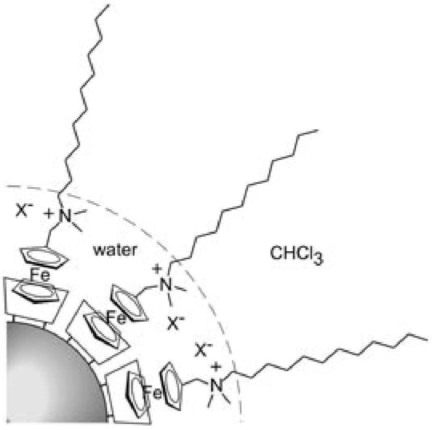

Figure 4. Possible structure of phase-transferred CD-MPC ferrocenyl complexes.

Another approach to incorporate inclusion-based host–guest recognition is through the use of pseudorotaxane assemblies. Crown ethers, for instance, have been shown to be excellent receptors for ammonium ions forming inclusion complexes.[19] To integrate this motif into nanoparticle systems, the groups of Fitzmaurice and Stoddart have synthesized gold MPCs featuring dibenzo[24]crown-8 ether moieties on the surface.[20] Through NMR experiments it has been shown that these MPCs in fact form pseudorotaxanes on the surface by binding dibenzylammonium ions to an 86% coverage (Figure 5). A more detailed analysis of the NMR data also revealed a positive cooperative binding effect, as a progressively more polar surface shows a higher affinity for the cationic guest.

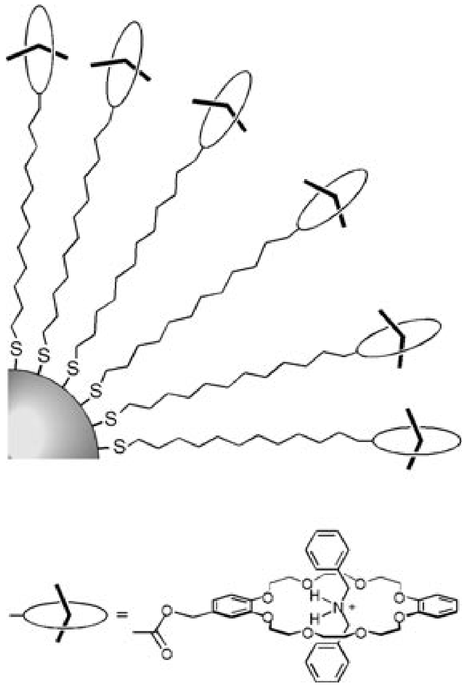

Figure 5. Pseudorotaxane complexes formed between crown ether MPCs and cationic guests.

In an extension to this work, the same groups explored the possibility to noncovalently link multiple MPCs by using ditopic guests.[21] In these studies silver nanoparticles featuring dilute (15%) dibenzo[24]crown-8 groups embedded in a dodecanethiol monolayer were synthesized through place-exchange reactions. Addition of stoichiometric amount of a ditopic bis-ammonium salt led, as expected, to a slow formation of a larger aggregates composed of individual MMPCs linked through [3]pseudorotaxane complexes (Figure 6).

By using dynamic light-scattering experiments monitoring the growing hydrodynamic radius, it was shown that a power-law model could describe the aggregate formation kinetics. These findings also suggest that the aggregation process is diffusion limited. Furthermore, control over the assembly process has been demonstrated through the addition of an excess of guest or a molecular crown ether host, both events leading to competitive binding and concurrent aggregation inhibition.

Pseudorotaxane recognition was taken one-step further and binary nanocrystal structures were assembled in solution from silver nanoparticles around silica nanospheres.[22]

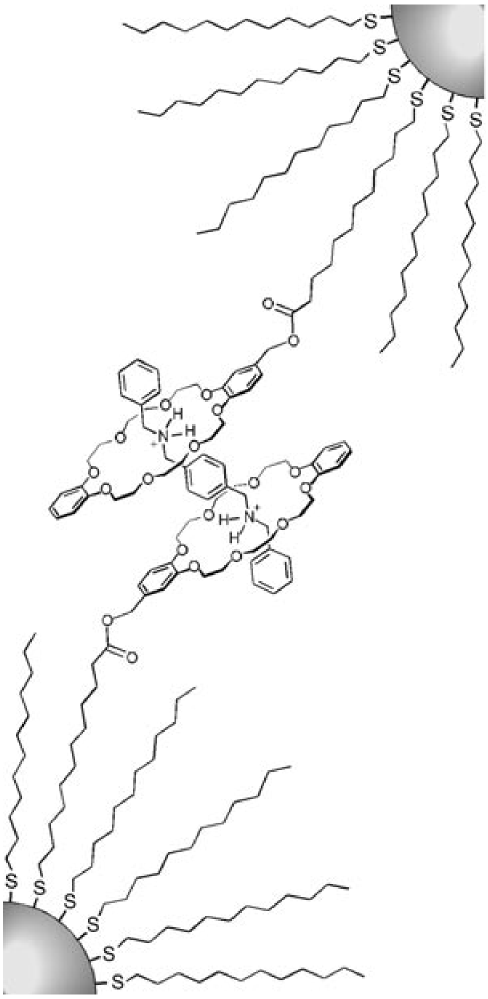

Figure 6. Aggregation of silver MMPCs through [3]pseudorotaxane formation.

As a result of the interaction between the covalently linked recognition units, [2]pseudorotaxane formation was achieved. The dibenzo[24]crown-8 units on silver nanoparticle surfaces were attached to the dibenzylammonium cations on silica surfaces though silane chemistry. The recognition of the silica nanospheres (180 nm in diameter) by silver nanoparticles (7 nm in diameter) led to the pseudorotaxane formation at the surface of the nanocrystals and subsequent aggregation (Figure 7).

Many control experiments were performed by excluding one or both recognition units. In these experiments, the same time period was used as employed for pseudorotaxane formation reaction between the silver nanocrystals and the silica nanosphere template, but no precipitation was observed in any control experiments. The nonspecific interactions between the control nanoparticles were confirmed by TEM images in which no size or density changes were observed after templation. UV-visible spectra showed no change in the surface plasmon band relative to free silver. Final proof of a binary nanostructure template was demonstrated by disassembly of the structure, indicating that the assembly process is indeed reversible. TEM and UV-visible spectroscopy experiments showed that addition of triethylamine, which effectively deprotonates the dibenzylammonium salts, prevents the interactions between the recognition units and causes complete dissociation of the silver particles from the surface of the silica nanospheres.

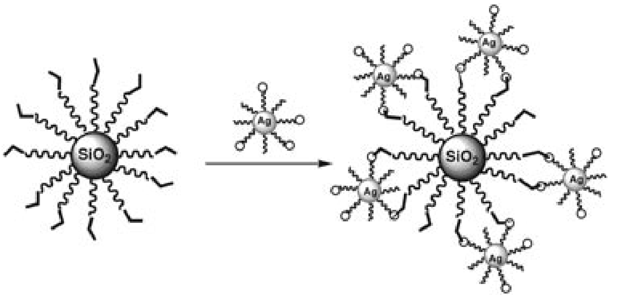

Figure 7. Silver nanocrystal assembly around the silica nanosphere.

Dynamic nanoparticle receptors using multitopic recognition: The previous examples have shown nanoparticles serving as carrier material for preformed binding pockets. However, many inherent properties of MMPCs, such as mobility of ligands within the monolayer, the ability to incorporate multiple functionalities, or the radial nature of these systems have not been fully exploited. The following section details how some of these features can be integrated into nanoparticle systems to construct multivalent dynamic receptors.

Based on their earlier work on TiO_2 colloids carrying hydrogen-bond receptors,[23] Fitzmaurice and co-workers developed a gold MMPC featuring uracil moieties on the surface.[24] These systems have been shown to recognize a complementary 2,6-diamidopyridine guest through a three-point hydrogen-bonding interaction.[25] Although the binding interaction was established by NMR and IR spectroscopy, the association constant had not been quantified. By using the same recognition units on either gold or silver nanoparticles, they also demonstrated that the nanocrystal aggregates can be formed in solution. In 1999, the Rotello group reported the development of an MMPC receptor carrying 2,6-diamidopyridine functionalities.[26] Again through three-point hydrogen bonding, this receptor system is capable of recognizing flavins (Figure 8a). Binding between receptor and guest was quantified in chloroform following the ^{1}H NMR shifts of the flavin imide proton at different concentrations. Since these shifts cleanly fit a 1:1 binding isotherm, an association constant of $196\,\text{M}^{-1}$ could easily be calculated from this data. This number is consistent with the 150 to $500\,\text{M}^{-1}$ typically observed with free diamidopyridines.[27] The redox activity of flavins presents a means to introduce extended functionality in these systems by providing electrochemically switchable recognition (Figure 8b). Through voltammetric experiments it was established that the bound, reduced radical anion of flavin is stabilized by 81 mV ($1.85\,\text{kcal}\,\text{mol}^{-1}$) and the association to the receptor is increased greater than 20-fold (4500 vs $196\,\text{M}^{-1}$) relative to the neutral oxidized species.

To extend this approach to a more specific multivalent recognition, the Rotello group developed MMPC receptors featuring both 2,6-diamidopyridine hydrogen-bonding moieties and pyrene groups capable of aromatic stacking.[28] In

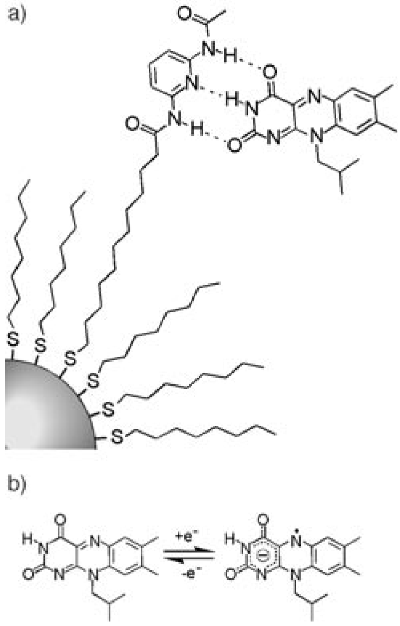

Figure 8. a) Three-point hydrogen bonding between diamidopyridine gold MMPC and flavin. b) Reduction of flavin to the radical anion.

addition to the three-point hydrogen bonding, the electron-deficient flavin can interact favorably with electron-rich pyrenes. As expected from this multitopic interaction, the binding constant is increased nearly twofold to $323\,\mathrm{M}^{-1}$ relative to the monovalent receptor.

Since the monolayer coatings on MMPCs are radial in nature, that is, order decreases with increased distance from the gold core, the distance between an array of functional groups on the outer surface and the center should have a marked effect on the multitopic binding to an external guest. To provide a means for quantifying this effect on mono- and ditopic recognition of flavin, the Rotello group synthesized a series of MMPC receptors featuring both mono- and divalent recognition elements, as well as different spacer lengths (Figure 9).[29] Receptors MMPC **1** and **2** are functionalized with only hydrogen-bonding elements, whereas receptors MMPC **3** and **4** additionally contain aromatic stacking units. Comparison of the first two with the last two MMPC receptors allows direct quantification of the effects on multitopic interactions. As expected, virtually no difference in affinity of the monotopic receptors to flavin was observed (196 vs. $185\,\mathrm{M}^{-1}$). In sharp contrast, the ditopic receptors exhibited a strong radial effect; the shorter, more pre-organized MMPC binds flavin three times more strongly than its longer chain equivalent (930 vs. $320\,\mathrm{M}^{-1}$).

To gain further insight into the radial control over multivalent binding, the redox behavior of flavin bound to these receptors was explored. Binding of flavin to the monotopic receptors generally resulted in a stabilization of the radical anion form and thus a stronger binding; the long-chain MMPC, however, binds the reduced flavin slightly more strongly than the short-chain receptor, possibly due to a somewhat greater degree of congestion on the short-chain system. In contrast, variation of the chain length in the ditopic system shows a striking effect on the redox chemistry of bound flavin. Again, reduction to the radical anion renders the flavin molecule electron rich, thus making interactions with the likewise electron-rich pyrene unfavorable. While the long-chain MMPC **3** still shows a binding preference for the reduced flavin, the short-chain system **4** preferentially binds the electron-deficient oxidized form. This behavior is a direct consequence of the alkane chain length. The 11-carbon spacer offers enough conformational flexibility to accommodate the electron-rich guest and to minimize repulsive stacking interactions, whereas the 6-carbon linker creates a much denser environment incapable of relieving the repulsive interactions (Figure 10).

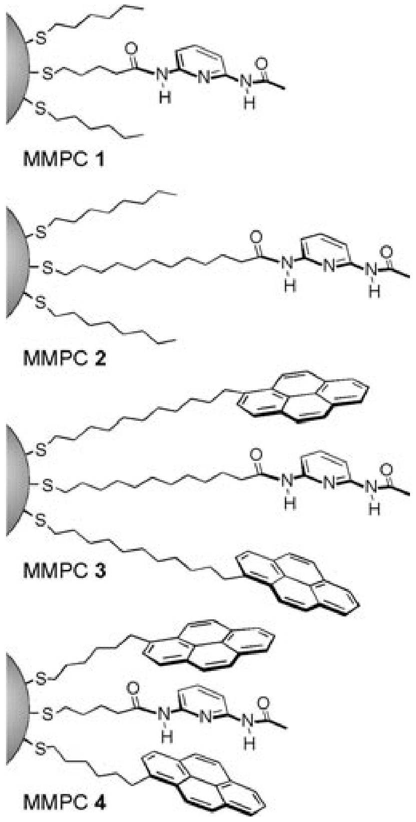

Figure 9. Monotopic diamidopyridine and ditopic diamidopyridine–pyrene gold MMPCs.

The mobility of thiols on the gold surface, an important feature of the surrounding monolayer in MMPCs, has led to another extension of the multitopic binding to create environmentally responsive receptors providing templated-guest recognition. To explore the possibility of a dynamic optimization of host–guest interactions, a trifunctional MMPC with dilute hydrogen bonding and aromatic stacking elements was employed (Figure 11).

The templation of binding sites on the receptor through flavin binding was demonstrated by time-course NMR experiments. Monitoring the gradual downfield shift of the flavin imide proton over the course of 70 h established gradually increasing receptor–flavin recognition. Concurrently, an upfield shift was observed for the aromatic protons of flavin, indicative of increased aromatic stacking with the pyrene units present on the surface. The association constant

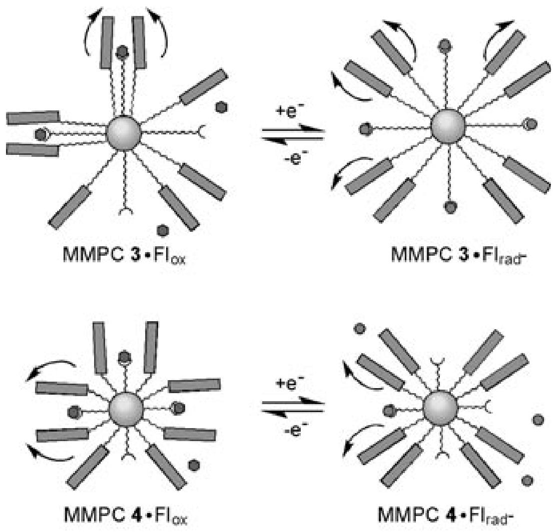

Figure 10. Schematic illustration of the chain length effect on redox-modulated binding.

calculated from these shifts increased from 168 to 235$\,\mathrm{M}^{-1}$, a 71 % enhancement. These findings clearly demonstrated a reorganization of the monolayer through the use of binding enthalpy.

Scrimin and Pasquato functionalized the gold nanoparticles with *N*-methylimidazole and showed that multivalent recognition of mono-, bis-, and tris(Zn-phorphyrin) can be obtained (Figure 12).[30] Due to steric hinderence, the binding constant of the model methylimidazole derivative **5** to monoporphyrin **6** is slightly larger than those measured for the bis- and trisporphyrins **7** and **8**. However, compared to monovalent systems, these multivalent ligands increased binding strength by up to three orders of magnitude independent of the methylimidazole concentration on the gold particles. Another important result of this experiment was that after certain point increasing the number of phorphyrin units on the gold surface does not improve the number of recognition sites.

Another focus in the Rotello group is the self-assembly of specific recognition units attached to polymers and gold

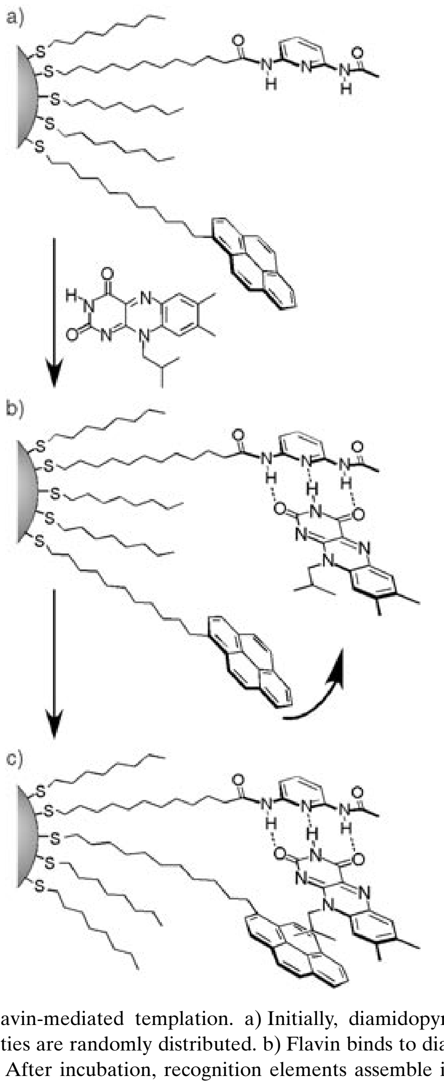

Figure 11. Flavin-mediated templation. a) Initially, diamidopyridine and pyrene moieties are randomly distributed. b) Flavin binds to diamidopyridine unit. c) After incubation, recognition elements assemble into multitopic binding pockets.

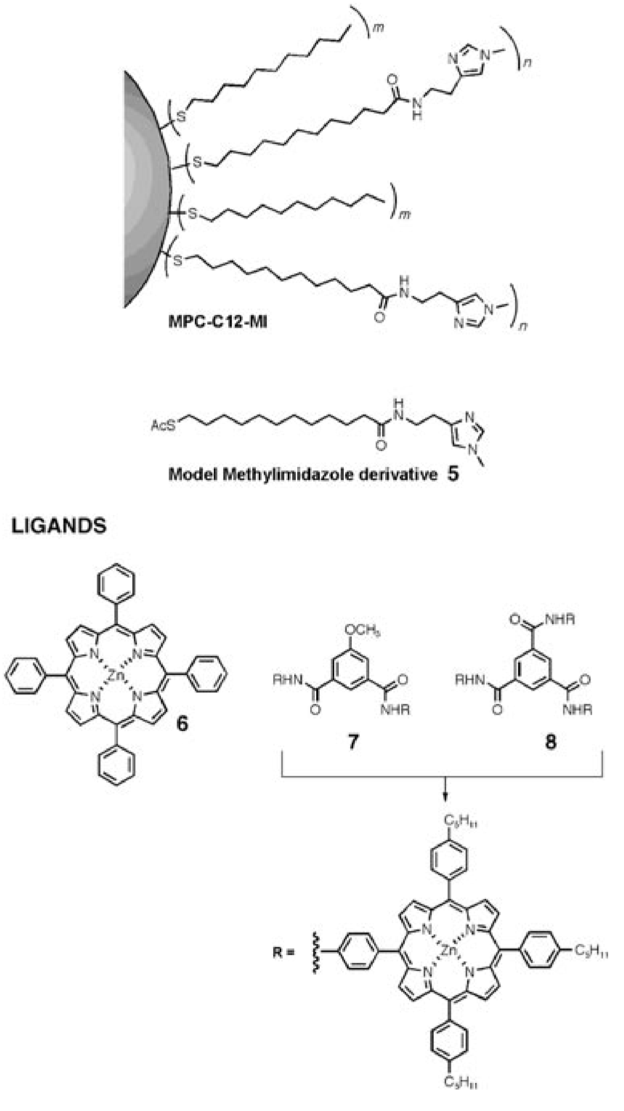

Figure 12. Zn–phorphyrins and *N*-methylimidazole functionalized gold nanoparticles.

nanoparticles. In one of their earlier works, polystyrene copolymers were functionalized with diaminotriazine and gold nanoparticles were functionalized with thymine to form a self-assembled network aggregates through specific three-point hydrogen-bonding interactions.[31] A black solid was formed after the addition of the polymer to the concentrated thymine–gold nanoparticles, because of the aggregation (Figure 13).

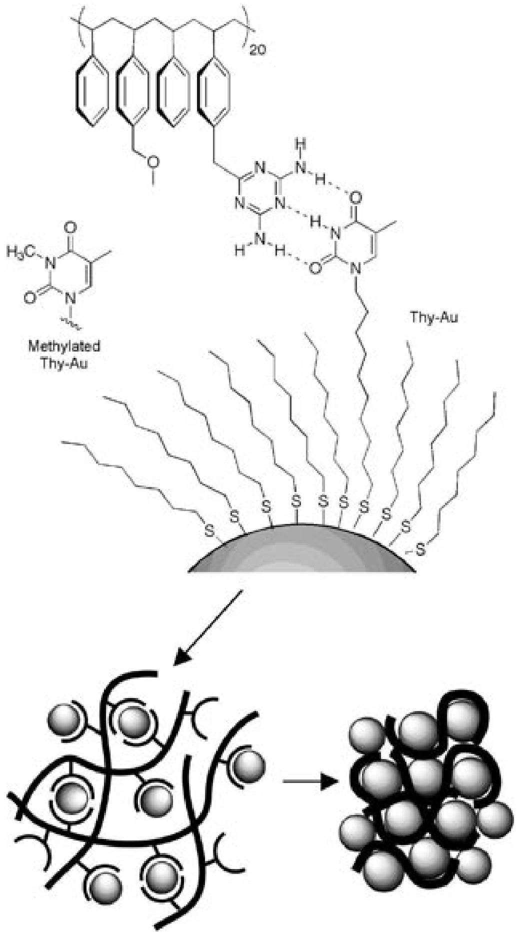

Figure 13. Polymer–Au aggregates formed through specific three-point hydrogen-bonding recognition between thymine-functionalized gold nanoparticles and a triazine-functionalized copolymer.

The control experiment with the *N*-methylthymine–gold nanoparticle showed no aggregation after polymer addition; this confirms that self-assembly did not take place and that specific three-point hydrogen-bonding is necessary for aggregate formation. Although these aggregates were controllable in size (100 to 1000 nm in diameter) by adjusting the temperature during the aggregate formation, the complex thermodynamics of the self-assembly process prevents the formation of structures of less than 100 nm.

To overcome the limitations of the size and structure of these aggregates, a series of diblock copolymers were prepared for the nanoparticle assembly. One block of the polystyrene backbone was functionalized with the diaminotriazine recognition group and the other block was left unfunctionalized to prevent extensive aggregation (Figure 14).[32]

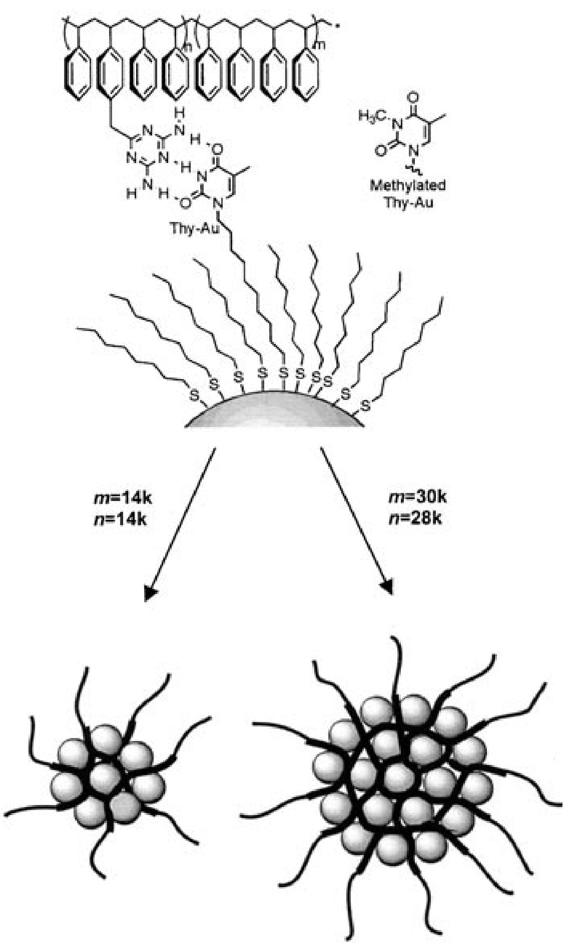

Figure 14. Schematic representation of polymer size affect on core diameter of the nanoparticle aggregates.

As proposed, the length of the functionalized block of the copolymer controls the size of the aggregates both in solution and in thin films. Further examination of the TEM and dynamic light scattering (DLS) results showed that the polymer length is also responsible in controlling the structure of the aggregates. Because of the lower number of recognition units on the shorter polymer, aggregates with smaller cores were formed, whereas aggregates with a more packed core were obtained with longer polymer.

Ion sensors: The advantage of the high extinction coefficient of the gold nanoparticles relative to the other organic dyes makes them very attractive as colorimetric reporters for particular metal ions. It has been shown in the literature that receptors can be covalently attached to gold nanoparticle surfaces, and molecular recognition based on calorimetric change of the solution can be easily observed when competitive analytes were introduced. Hupp and co-workers have prepared 11-mercaptoundecanoicacid-capped gold nanoparticles and monitored a red-to-blue color change in UV light when heavy metal ions like lead, cadmium, and mercury were added (Figure 15).[33]

The reason for the color change lies in the shift of the plasmon-energy band, which results from the aggregation of the particles through the salt addition. This was proven by

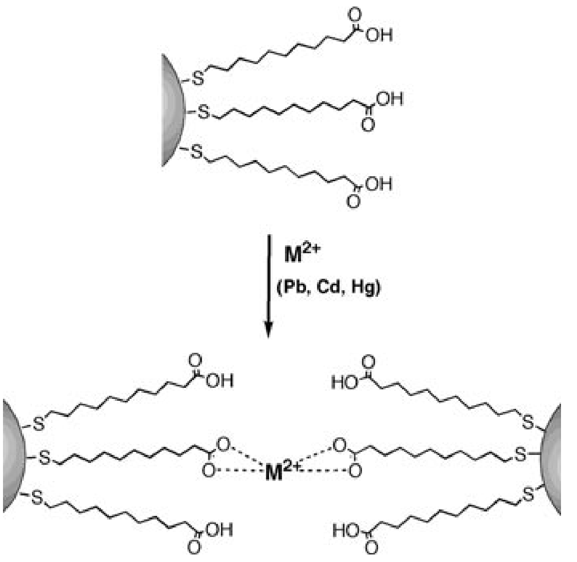

Figure 15. Simple colorimetric system for sensing heavy metal ions.

reversal of the band shift by addition of Pb^{2+}, which is a good EDTA extracting agent.

In contrast to Hupp's nonspecific method for metal-ion sensing with gold nanoparticles, Chen and co-workers have covalently attached crown ether receptors onto an Au surface in order to selectively detect the presence of potassium ions over Li^+, Cs^+, NH_4^+, Ca^{2+}, and Na^+ ions (Figure 16).[34]

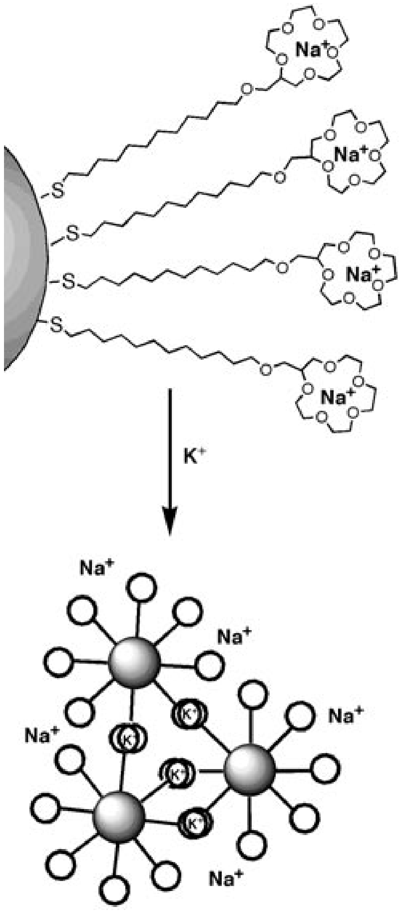

Figure 16. Schematic representation of specific K^+ sensors.

More favorable [15]crown-8 and Na^+ complexes were disrupted by the formation of a "sandwich complex" of 2:1 [15]crown-8 and K^+. Due to the aggregation of the particles, a red-to-blue plasmon shift was observed after addition of the metal ion, as the aggregation is dependent on the ion concentration.

Murphy and co-workers overcame the solubility problems of the lithium ion detection in aqueous solution by modifying their gold particles with 1,10-phenanthroline derivatives, which are particularly Li^+-selective organic chromophores (Figure 17).[35]

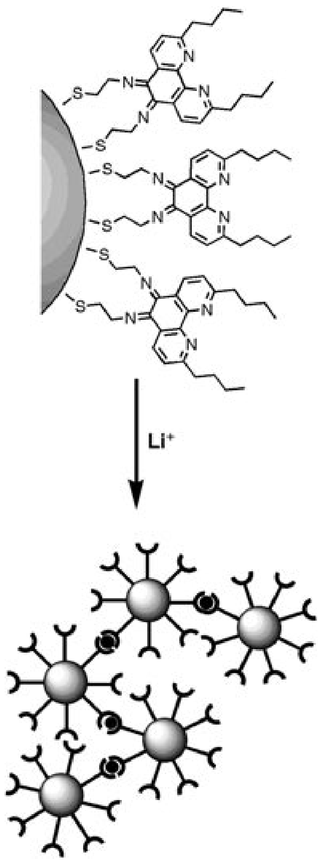

Figure 17. 1,10-Phenanthroline-functionalized gold nanoparticles and scheme for specific Li^+ sensing.

Aggregation of the particles after addition of the Li^+ ion results in a color change of the solution. This visible color changes from orange to gray, and the degree of aggregation mainly depends on the ion concentration. The distinctive red shift of the plasmon absorption band was observed upon addition of different concentrations of ions even for the bigger size of the nanoparticles from 4 to 32 nm. Because of the larger surface area, big particles were less aggregated relative to the small particles at the same concentration of the ion; this indicates that small particles are more sensitive toward analyte sensing.

Recently Davis' and Beer's work demonstrated that redox-active anion-receptor zinc metalloporphyrins show enhanced binding affinities toward anion sensing when placed onto gold nanoparticle surfaces relative to the free metallophorphyrins.[36] Free metallophorphyrins and zinc-metalloporphyrin-functionalized gold nanoparticles were placed in two different solvents and titrated with many different anions (e.g. Cl^-, Br^-, I^-, NO_3^-, $H_2PO_4^-$, ClO_4^-). The results showed that nanoparticles bind to anions more strongly than the free metallophorphyrin form, and that the basicity of the anions and the competitiveness of the chosen solvent play a great role in these systems.

Conclusions and Outlook

The control of nanoparticle properties provides opportunities for the design of unique systems. The ability to combine molecular functionality with the inherent properties of nanometer-sized entities makes nanoparticle scaffolds important tools for the creation of complex functional devices. Applying the concepts of supramolecular chemistry and molecular recognition to nanoparticles introduces a means of control over the assembly of these systems into extended morphologies, thereby enabling the design of elaborate nanocomposite structures. While many applications such as solution-based sensors, electrically stimulated devices, highly efficient catalysts, or nanometer-sized magnetic storage devices can be envisioned, this field of research is clearly still in its early stages of development. Further in-depth investigation integrating chemistry and nanotechnology will be required to fully achieve these important goals; knowing how to translate the rules of tailoring molecular-level functions into large-scale complex systems will be crucial to the fabrication of nanoparticle-based functional devices.

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[1] a) M. A. El-Sayed, *Acc. Chem. Res.* **2001**, *34*, 257–264; b) for a recent review on gold nanoparticles: M. C. Daniel, D. Astruc, *Chem. Rev.* **2004**, *104*, 293–346.

[2] a) E. W. H. Jager, E. Smela, O. Inganas, *Science* **2000**, *290*, 1540–1545; b) H. G. Craighead, *Science* **2000**, *290*, 1532–1535; c) G. M. Wallraff, W. D. Hinsberg, *Chem. Rev.* **1999**, *99*, 1801–1821.

[3] D. L. Feldheim, K. C. Grabar, M. J. Natan, T. E. Mallouk, *J. Am. Chem. Soc.* **1996**, *118*, 7640–7641.

[4] A. C. Templeton, M. P. Wuelfing, R. W. Murray, *Acc. Chem. Res.* **2000**, *33*, 27–36.

[5] M. Brust, M. Walker, D. Bethell, D. J. Schiffrin, R. Whyman, *J. Chem. Soc. Chem. Commun.* **1994**, 801–802.

[6] M. J. Hostetler, J. E. Wingate, C. J. Zhong, J. E. Harris, R. W. Vachet, M. R. Clark, J. D. Londono, S. J. Green, J. J. Stokes, G. D. Wignall, G. L. Glish, M. D. Porter, N. D. Evans, R. W. Murray, *Langmuir* **1998**, *14*, 17–30.

[7] A. C. Templeton, M. J. Hostetler, E. K. Warmoth, S. W. Chen, C. M. Hartshorn, V. M. Krishnamurthy, M. D. E. Forbes, R. W. Murray, *J. Am. Chem. Soc.* **1998**, *120*, 4845–4849.

[8] C. M. Niemeyer, *Angew. Chem.* **2001**, *113*, 4254–4287; *Angew. Chem. Int. Ed.* **2001**, *40*, 4128–4158.

[9] R. Elghanian, J. J. Storhoff, R. C. Mucic, R. L. Letsinger, C. A. Mirkin, *Science* **1997**, *277*, 1078–1081.

[10] a) W. Shenton, S. A. Davis, S. Mann, *Adv. Mater.* **1999**, *11*, 449–452; b) S. Mann, W. Shenton, M. Li, S. Connolly, D. Fitzmaurice, *Adv. Mater.* **2000**, *12*, 147–150.

[11] a) A. Labande, D. Astruc, *Chem. Commun.* **2000**, 1007–1008; b) A. Labande, J. Ruiz, D. Astruc, *J. Am. Chem. Soc.* **2002**, *124*, 1782–1789.

[12] a) C. Valerio, J. L. Fillaut, J. Ruiz, J. Guittard, J. C. Blais, D. Astruc, *J. Am. Chem. Soc.* **1997**, *119*, 2588–2589; b) A. Labanda, D. Astruc, *Chem. Commun.* **2001**, 2000–2001.

[13] a) M. C. Daniel, J. Ruiz, S. Nlate, J. C. Blais, D. Astruc, *J. Am. Chem. Soc.* **2003**, *125*, 2617–2628; b) M. C. Daniel, J. Ruiz, J. C. Blais, N. Doro, D. Astruc, *Chem. Eur. J.* **2003**, *9*, 4371–4379; c) D. Astruc, J. C. Blais, M. C. Daniel, V. Martinez, S. Nlate, J. Ruiz, *Macromol. Symp.* **2003**, *75*, 461–481.

[14] a) M. V. Rekharsky, Y. Inoue, *Chem. Rev.* **1998**, *98*, 1875–1917; b) K. A. Connors, *Chem. Rev.* **1997**, *97*, 1325–1357; c) W. Siliva, T. Girek, *Heterocycles* **2003**, 60, 2147–2183; d) A. E. Kaifer, *Acc. Chem. Res.* **1999**, *32*, 62–71; e) J. Liu, J. Alvarez, A. E. Kaifer, *Adv. Mater.* **2000**, *12*, 1381–1383.

[15] a) J. Alvarez, J. Liu, E. Roman, A. E. Kaifer, *Chem. Commun.* **2000**, 1151–1152; b) J. Liu, J. Alvarez, W. Ong, E. Roman, A. E. Kaifer, *Langmuir* **2001**, *17*, 6762–6764; c) L. Strimbu, J. Liu, A. E. Kaifer, *Langmuir* **2003**, *19*, 483–485; d) J. Liu, W. Ong, A. E. Kaifer, *Langmuir* **2002**, *18*, 5981–5983; e) J. Liu, S. Mendoza, E. Roman, M. J. Lynn, R. L. Xu, A. E. Kaifer, *J. Am. Chem. Soc.* **1999**, *121*, 4304–4305.

[16] J. Liu, W. Ong, E. Roman, M. J. Lynn, A. E. Kaifer, *Langmuir* **2000**, *16*, 3000–3002.

[17] M. Brust, J. Fink, D. Bethell, D. J. Schiffrin, C. Kiely, *J. Chem. Soc. Chem. Commun.* **1995**, 1655–1656.

[18] J. Liu, J. Alvarez, W. Ong, E. Roman, A. E. Kaifer, *J. Am. Chem. Soc.* **2001**, *123*, 11148–11154.

[19] a) P. R. Ashton, E. J. T. Chrystal, P. T. Glink, S. Menzer, C. Schiavo, N. Spencer, J. F. Stoddart, P. A. Tasker, A. J. P. White, D. J. Williams, *Chem. Eur. J.* **1996**, *2*, 709–728; b) P. R. Ashton, P. J. Campbell, E. J. T. Chrystal, P. T. Glink, S. Menzer, D. Philp, N. Spencer, J. F. Stoddart, P. A. Tasker, D. J. Williams, *Angew. Chem.* **1995**, *107*, 1997–2001; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1865–1869; c) P. R. Ashton, E. J. T. Chrystal, P. T. Glink, S. Menzer, C. Schiavo, J. F. Stoddart, P. A. Tasker, D. J. Williams, *Angew. Chem.* **1995**, *107*, 2001–2004; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1869–1871.

[20] D. Fitzmaurice, S. N. Rao, J. A. Preece, J. F. Stoddart, S. Wenger, N. Zaccheroni, *Angew. Chem.* **1999**, *111*, 1220–1224; *Angew. Chem. Int. Ed.* **1999**, *38*, 1147–1150.

[21] a) D. Ryan, S. N. Rao, H. Rensmo, D. Fitzmaurice, J. A. Preece, S. Wenger, J. F. Stoddart, N. Zaccheroni, *J. Am. Chem. Soc.* **2000**, *122*, 6252–6257; b) P. M. Mendes, Y. Chen, R. E. palmer, K. Nikitin, D. Fitzmaurice, J. A. Preece, *J. Phys. Condens. Matter* **2003**, *15*, S3047–S3063.

[22] a) D. Ryan, L. Nagle, H. Rensmo, D. Fitzmaurice, *J. Phys. Chem. B* **2002**, *106*, 5371–5377; b) D. Ryan, L. Nagle, D. Fitzmaurice, *Nano Lett.* **2004**, *4*, 573–575.

[23] L. Cusack, S. N. Rao, J. Wenger, D. Fitzmaurice, *Chem. Mater.* **1997**, *9*, 624–631.

[24] D. Aherne, S. N. Rao, D. Fitzmaurice, *J. Phys. Chem. B* **1999**, *103*, 1821–1825.

[25] a) S. Fullam, H. Rensmo, S. N. Rao, D. Fitzmaurice, *Chem. Mater.* **2002**, *14*, 3643–3650; b) S. Fullam, S. N. Rao, D. Fitzmaurice, *J. Phys. Chem. B* **2000**, *104*, 6164 –6173.

[26] A. K. Boal, V. M. Rotello, *J. Am. Chem. Soc.* **1999**, *121*, 4914–4915.

[27] A. Niemz, V. M. Rotello, *Acc. Chem. Res.* **1999**, *32*, 44–52.

[28] A. K. Boal, V. M. Rotello, *J. Am. Chem. Soc.* **2000**, *122*, 734–735.

[29] A. K. Boal, V. M. Rotello, *J. Am. Chem. Soc.* **2002**, *124*, 5019–5024.

[30] G. Fantuzzi, P. Pengo, R. Gomila, P. Ballester, C. A. Hunter, L. Pasquato, P. Scrimin, *Chem. Commun.* **2003**, 1004–1005.

[31] A. K. Boal, F. Ilhan, J. E. DeRouchey, T. T. Albrecht, T. P. Russell, V. M. Rotello, *Nature* **2000**, *404*, 746–748.

[32] a) B. L. Frankamp, O. Uzun, F. Ilhan, A. K. Boal, V. M. Rotello, *J. Am. Chem. Soc.* **2002**, *124*, 892–893; b) R. J. Thibault, T. H. Galow, E. J. Turnberg, M. Gray, P. J. Hotchkiss, V. M. Rotello, *J. Am. Chem. Soc.* **2002**, *124*, 15249–15254.

[33] Y. Kim, R. C. Johnson, J. T. Hupp, *Nano Lett.* **2001**, *1*, 165–167.

[34] S. Y. Lin, S. W. Liu, C. M. Lin, C. H. Chen, *Anal. Chem.* **2002**, *74*, 330–335.

[35] S. O. Obare, R. E. Hollowell, C. J. Muphy, *Langmuir* **2002**, *18*, 10407–10410.

[36] P. D. Beer, D. P. Cormode, J. J. Davis, *Chem. Commun.* **2004**, 414–415.