Self-Assembly of Soft Hybrid Materials Directed by Light and a Magnetic Field

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Self-assembly is a most efficient way to prepare functional nanomaterials.[1] If nanoscale building blocks are equipped with molecular recognition units, the self-assembly of a nanomaterial can be directed by noncovalent interactions. As a consequence, such self-assembled materials are inherently dynamic, self-healing and adaptive and – depending on the type of noncovalent interaction – can also be stimulus-responsive. In this respect, self-assembled materials that respond to external stimuli such as light or magnetic field are particularly attractive, since these stimuli can be delivered with high spatial and temporal resolution so that superstructures may arise that are not accessible in the absence of the stimulus. Nanomaterials that respond to either light[2] or magnetic field[3] are by now rather well-established. However, nanomaterials that respond to light *and* magnetic field are still very rare.[4]

In this article we report a soft hybrid material composed of magnetic nanoparticles and vesicles which self-assemble in microscale linear aggregates under the influence of a magnetic field. The linear aggregates can be stabilized by a noncovalent and photoresponsive cross-linker, which can be photoisomerized between an adhesive and a nonadhesive configuration. Thus, the hybrid material responds to light and to magnetic field, and a stable self-assembled structure can only be obtained in a magnetic field in the presence of the photoresponsive cross-linker. The self-assembled structure is metastable in the absence of the cross-linker and it cannot form if the magnetic field is off or if the cross-linker is photo-inactivated.

Nanoscale magnetic materials have recently attracted considerable attention because of their innumerable applications in biomedicine. Amongst others, magnetic nanoparticles are used in drug and gene delivery,[5] magnetic hyperthermia,[6] and contrast agents in magnetic resonance imaging.[7] Significant progress has also been made in the preparation of magnetic hybrid materials containing both inorganic nanoparticles and organic compounds, such as magnetic micelles,[3b],[8] magnetic polymer spheres[9] and dendrimer-functionalized magnetic nanoparticles.[10] The use of vesicles or liposomes to design magnetic hybrid materials is attractive because they are water soluble, biocompatible and biodegradable. Several groups also reported liposomes with magnetic nanoparticles embedded in the bilayer membrane.[11]

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In this study, we report a hybrid material that is composed of iron oxide (magnetite) nanoparticles and vesicles composed of amphiphilic cyclodextrins (CDs). Cyclodextrin vesicles (**CDV**) with an average diameter of 150-200 nm are obtained by dispersing amphiphilic β-CD in aqueous solution.[12] A crucial advantage of **CDV** in comparison with conventional liposomes is the fact that **CDV** can selectively form inclusion complex with hydrophobic guest molecules (such as adamantanes, *t*-butylbenzenes, and azobenzenes) and hence can be decorated with functional guest molecules such as carbohydrates, peptides and proteins simply by mixing the host vesicles with the desired mixture of guest-appended biomolecules.[13] Azobenzenes constitute a well-known class of photoresponsive guest molecules for CDs since they can reversibly isomerize from *trans* to *cis* by irradiation at 350 nm and from *cis* to *trans* by irradiation by 455 nm. *trans*-Azobenzene is apolar and rod-like and forms stable inclusion complex with α-CD and β-CD, whereas *cis*-azobenzene is polar and bent and does not fit into either CD. In recent years, the photoreversible molecular recognition of CDs with azobenzenes has been used to develop light-responsive materials such as hydrogels,[14] vesicles,[15] and mesoporous nanoparticles.[16] Our group has reported a photoresponsive ternary system which can selectively capture and release biomolecules (such as DNA or proteins) on the basis of supramolecular interaction of **CDV** and azobenzene modified guest molecules.[17] We have also shown that a divalent azobenzene cross-linker acts as a photoreversible supramolecular glue in the adhesion of **CDV**.[18]

Here we demonstrate that "magnetic" **CDV** can be prepared by incorporating oleic acid stabilized magnetic iron oxide nanoparticles (**MNP**) in the bilayer of the **CDV**. These hybrid materials composed of magnetic nanoparticles absorbed in the membrane of cyclodextrin vesicles (**MNP-CDV**) align in an external magnetic field due to the dipolar interaction of the superparamagnetic **MNP**. Moreover, these magnetic vesicles can form photoactive inclusion complexes with a divalent azobenzene cross-linker. Thus, the self-assembly of **MNP-CDV** is controlled by magnetic field as well as light.

Amphiphilic β-CD (see **Figure 1**) was synthesized as described in the literature.[12] This macrocyclic amphiphile forms unilamellar bilayer vesicles in aqueous solution at physiological pH. Multilamellar **CDV** are readily obtained by dispersing a film of amphiphilic CD in aqueous solution by gentle stirring at room temperature.[12] The diameter of these multilamellar **CDV** is around 400 nm according to dynamic light scattering (DLS). The **CDV** form inclusion complexes with guest molecules since many CD cavities are exposed outside on the surface of vesicles. Photoresponsive cross-linker **G1** (see Figure 1) was synthesized as reported in the Supporting Information. The analytical and spectroscopic data for **G1** are consistent

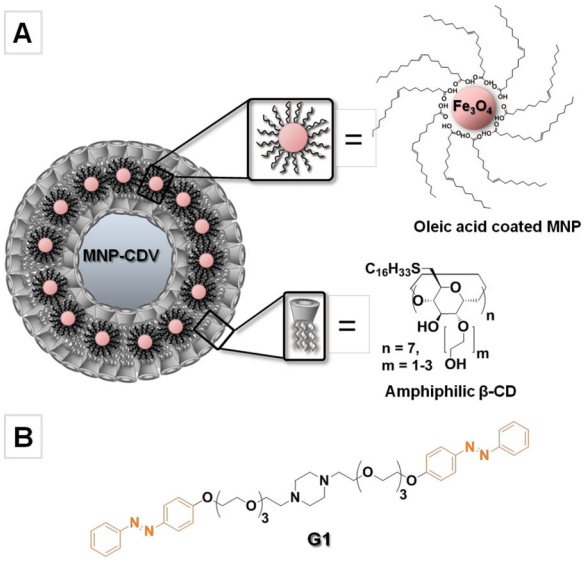

Figure 1. (A) Schematic representation of magnetic nanoparticle-cyclodextrin vesicle hybrids (**MNP-CDV**). (B) Photoresponsive azobenzene cross-linker (**G1**).

with its molecular structure. Oleic acid coated iron oxide nanoparticles were synthesized as described.[19] The average size of the **MNP** is around 9 nm according to TEM and DLS (see **Figure 2**). These **MNP** are highly superparamagnetic (e.g. they can be easily precipitated with a permanent magnet).

Superparamagnetic cyclodextrin vesicles (**MNP-CDV**) were obtained by absorbing hydrophobic **MNP** into the hydrophobic bilayer domain during preparation of the vesicles. To this end, a mixture of the oleic acid coated **MNP** and amphiphilic β-CD was dissolved in chloroform and a thin film was made by rotary evaporation of the solvent. The film was hydrated by 20 mM phosphate buffer (pH 7.2) and the suspension was stirred for 12 h. The resulting **MNP-CDV** were examined by TEM, AFM and DLS. In TEM, it could be observed that the **MNP** are confined to the **CDV** (see Figure 2 and additional images in Figure S1 in Supporting Information) and that the **MNP-CDV** have a diameter of around 500 nm. With AFM, it was observed that the **MNP-CDV** are rather soft and flexible particles that adsorb and spread on the mica substrate (see Figure S2). These findings were confirmed by DLS (see Figure 2). In aqueous medium the amphiphilic β-CD self-organize in a molecular bilayer so that the hydrophobic alkyl chains minimize their exposure to water while the CD and oligo(ethylene glycol) moieties cover the surface the membrane. These bilayers can obviously accommodate hydrophobic **MNP** in the hydrophobic membrane interior, even though the average diameter of the particles (9 nm) is substantially larger than the thickness of the bilayer (5 nm).[12] We note that our observations are consistent with several literature reports describing the absorption of hydrophobic nanoparticles in liposomes.[11]

The **MNP-CVD** were fluorescently labeled by including 10% sulforhodamine B labeled amphiphilic β-cyclodextrin.[20] The sulphorhodamine B labeled **MNP-CDV** hybrids can be observed in fluorescence microscopic images (see **Figure 3**). It is evident from Figure 3A that the hybrid vesicles are spherical and the diameter is around 500 nm (consistent with TEM and DLS). However, the **MNP-CDV** hybrids align in the direction of an applied external magnetic field and form linear aggregates with a length of around 10 µm within a few seconds (see Figure 3B). We assume that the **MNP-CDV** align due to the attractive dipole-dipole interactions of the superparamagnetic **MNP** in the membrane of the **CDV**. Indeed, the aggregates spontaneously dissociate when the magnetic field was switched off within a few seconds (see Figure 3C). It can be concluded that the magnetic field assisted self-assembly of the **MNP-CDV** into linear aggregates is completely reversible. A real time video of the formation and disassembly of the linear aggregates is available as Supporting Information with this article. In the video, it can be seen that formation and disassembly of the aggregates occurs within seconds upon application or removal of the magnetic field. Also, it can be seen that the formation and disassembly can be repeated multiple times, indicating the reversible nature of the self-assembly process induced by the magnetic field. Furthermore, it was observed that the linear aggregates can reorient with a changing direction of the applied magnetic field, thus acting as "magnetic stirring bars" that can be manipulated by the external field.[3c]

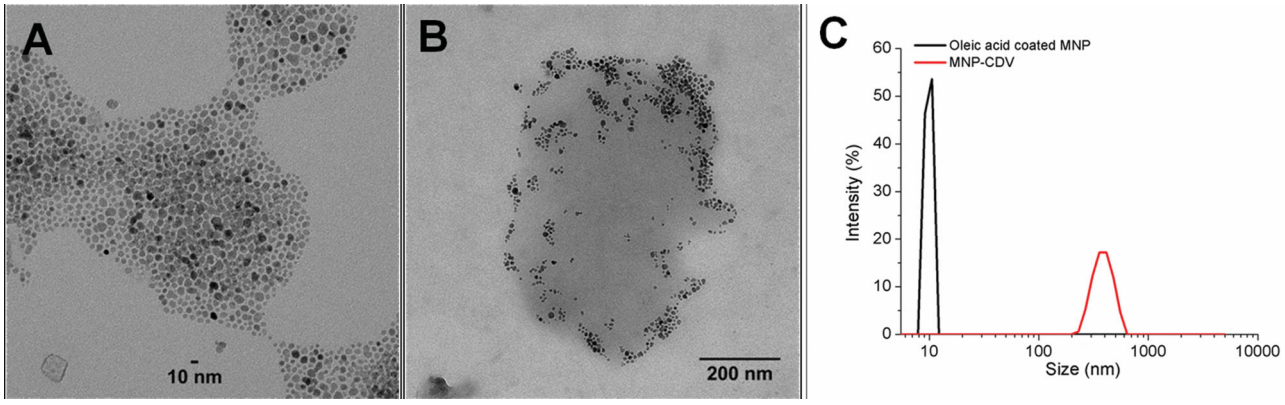

Figure 2. (A) TEM image of iron oxide **MNP**. (B) TEM image of **MNP-CDV** hybrid. (C) DLS size distribution of **MNP** and **MNP-CDV** hybrids. Conditions: [**MNP**] = 0.67 mg mL^{-1}, [**MNP-CDV**] = 0.5 mg mL^{-1} **MNP** in 100 µM of **CDV** in aqueous solution.

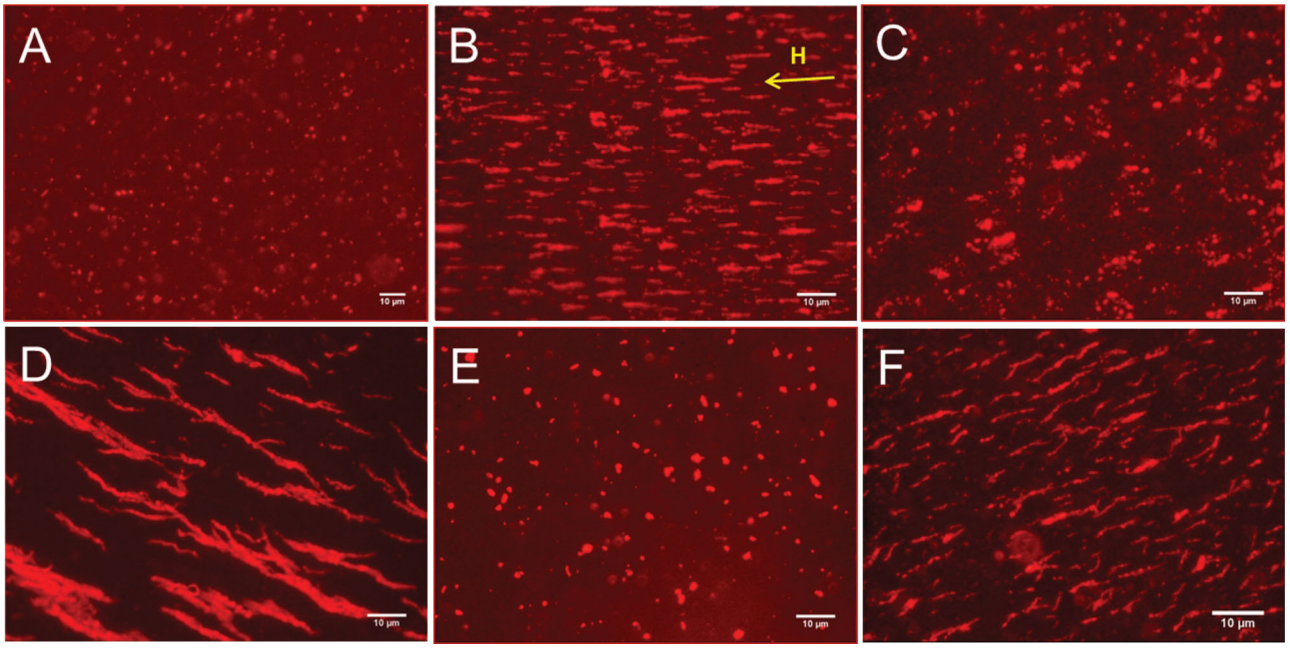

Figure 3. Fluorescence microscopy images of sulforhodamine B labeled magnetic vesicles. (A) **MNP-CDV** in the absence of an external magnetic field. (B) Formation of linear aggregates of **MNP-CDV** in a magnetic field (H). (C) Spontaneous disassembly of linear aggregates of **MNP-CDV** after switching off the magnetic field. (D) Linear aggregates of **MNP-CDV** formed in an external magnetic field and stabilized by the cross-linker *trans*-**G1**. The aggregates deform but persist after switching off the external field. (E) Disaggregation of **MNP-CDV** and *cis*-**G1** after UV irradiation for 30 min in the absence of an external magnetic field. (F) Re-aggregation of **MNP-CDV** and *trans*-**G1** in a magnetic field after visible light irradiation for 30 min. Conditions: [**MNP-CDV**] = 0.4 mg mL^{-1} **MNP** in 50 μM of **CDV** (90% of amphiphilic β-CD and 10% sulforhodamine B labeled amphiphilic β-CD) in 20 mM phosphate buffer at pH 7.2, [*trans*-**G1**] = 20 μM. The scale bars denote 10 μm.

The microscale aggregates of **MNP-CDV** are not stable in the absence of a magnetic field since the **MNP** are superparamagnetic. We hypothesized that the aggregates of **MNP-CDV** can be stabilized using divalent guest **G1** that cross-links the CDV.[18] The formation of an inclusion complex of **G1** and **CDV** is light-responsive since the *trans* isomer of azobenzene is a suitable guest for β-CD (K_a = 6000 M^{-1}), but the *cis* isomer is not (K_a~1 M^{-1}). The azobenzene moiety can be reversibly photoisomerised from *trans* to *cis* by irradiation at 350 nm and from *cis* to *trans* by irradiation at 455 nm. We have previously shown that a divalent guest very similar to **G1** can induced the photoresponsive adhesion of **CDV** into amorphous microscale clusters.[18] Similarly, addition of *trans*-**G1** to a solution of **MNP-CDV** induces a rapid aggregation and adhesion of **MNP-CDV** (see **Figure 4**). Optical density measurements at 600 nm were performed with **MNP-CDV** after extrusion through a polycarbonate membrane, which reduced the initial average particle size to around 150 nm, i.e. similar to **CDV** that are not loaded with **MNP**. It can be taken from Figure 4A that the OD600 of a solution of 50 μM solution of **MNP-CDV** is around 0.05. When 100 μM *trans*-**G1** was added (after 2 min) to the **MNP-CDV**, the OD600 gradually increased to a maximum of 0.25. These measurements confirm the spontaneous aggregation and adhesion of **MNP-CDV** in presence of *trans*-**G1**, consistent with our reported findings for **CDV** not loaded with **MNP**.[18] UV irradiation of the mixture of **MNP-CDV** and *trans*-**G1** induces the dispersion of the aggregates leading to a decrease of OD600. The reversibility of the light-induced formation and dispersion of **MNP-CDV** aggregates is almost quantitative over 2 cycles (see Figure 4B), provided the irradiation time is sufficient (30 min at both 350 and 455 nm).

Having established that **MNP-CDV** can be reversibly cross-linked by photoresponsive **G1**, their interaction in an external magnetic field was investigated under the fluorescence microscope (see Figure 3). It was observed that if **MNP-CDV** were first exposed to a magnetic field and then cross-linked with **G1**, ca. 100 μm long threads of compactly clustered **MNP-CDV** were formed (see Figure 3D). These aggregates could also be observed by AFM, although they are difficult to characterize due to their soft nature (see Figure S2 in the Supporting Information). Importantly, these aggregates persist for several hours also in the absence of the external magnetic field. We assume that these large aggregates result from the formation of small linear aggregates of **MNP-CDV** in the magnetic field (as shown before in Figure 3B) which are subsequently stabilized and interconnected by numerous intervesicular non-covalent cross-links. The aggregates reorient according to the direction of the external magnetic field and gradually deform due to Brownian motion, but they do not disaggregate by switching off the magnetic field (see video provided as Supporting Information). However, UV irradiation of the cross-linked aggregates of **MNP-CDV** and *trans*-**G1** at 350 nm for 30 min leads to the dispersion of the thread like aggregates and the **MNP-CDV** recover their initial size and spherical shape (see Figure 3E). This observation is fully consistent with the photoisomerization of *trans*-**G1** to *cis*-**G1**, which eliminates the cross-links in the aggregates. The resulting **MNP-CDV** self-organize into linear aggregates again as soon as the external

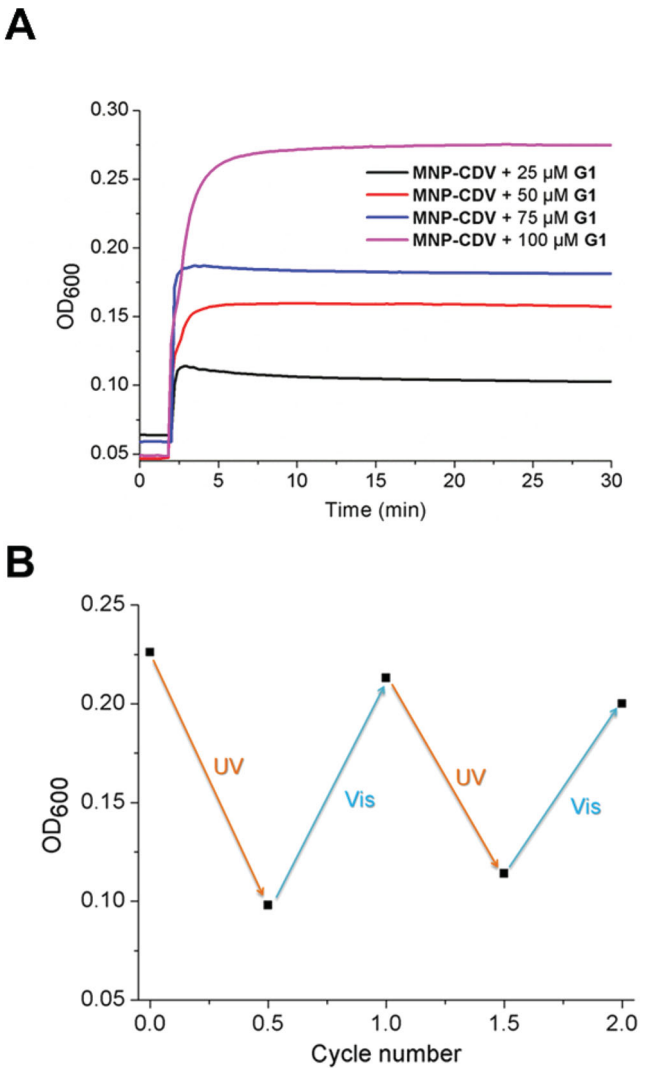

Figure 4. Photoresponsive aggregation of **MNP-CDV** and *trans*-**G1**. (A) Time-dependent optical density measurements at $\lambda = 600$ nm (**G1** added after 2 min) (B) Aggregation and dispersion of **MNP-CDV** by **G1** under alternate irradiation with UV light (350 nm) and visible light (455 nm). Conditions: [**MNP-CDV**] = 0.4 mg mL^{-1} **MNP** in 50 μM of **CDV** in 20 mM phosphate buffer at pH 7.2.

magnetic field is reapplied. Upon subsequent irradiation of visible light at 455 nm for 30 min (to obtain *trans*-**G1** from *cis*-**G1**) the 100 μm thread-like aggregates slowly form again (see Figure 3F). These experiments show that a metastable linear assembly of **MNP-CDV** can be stabilized by photoresponsive noncovalent cross-linking.

In conclusion, we have developed a magnetic soft material based on iron oxide nanoparticles absorbed in amphiphilic cyclodextrin vesicles. **MNP-CDV** form 10 μm linear aggregates in aqueous solution if exposed to an external magnetic field. The assembly of **MNP-CDV** in a magnetic field results in a metastable state that is only accessible as long as the field is present. However, the metastable state can be stabilized using noncovalent cross-linking by a divalent azobenzene guest. Due to the photoresponsive nature of the cross-links, the linear aggregates are stable under visible light irradiation (and in the absence of any irradiation) but disintegrate under UV irradiation. Thus, we have made a soft material that responds to magnetic field as well as to light, and the combination of both leads to superstructures that are not accessible when only one external stimulus is applied. We envisage that these magnetic hybrids may be of potential use as a drug delivery system, contrast agent in MRI and also in hypothermia therapy. The biocompatibility of the hybrid material can be significantly enhanced by using host-guest chemistry to functionalize the outer surface with carbohydrates, peptides and/or proteins.

Experimental Section

Materials: All chemicals used in this study were purchased from Acros Organics (Schwerte, Germany) or Sigma–Aldrich Chemie (Taufkirchen, Germany) and were used without further purification. β-Cyclodextrin was kindly donated by Wacker Chemie (Burghausen, Germany). All solvents were dried according to conventional methods before use.

Synthesis: The synthesis of divalent azobenzene (**G1**) was carried out in four steps. Commercially available tetraethyleneglycol was monotosylated, and further treated with 4-phenylazophenol in the presence of K_2CO_3 to give (E)-2-(2-(2-(2-(4-(phenyldiazenyl)phenoxy) ethoxy)ethoxy)ethoxy)ethanol. The second hydroxyl group was mesylated, and further treated with piperazine in the presence of Et_3N to give rise to the target **G1**. Details of the synthesis are reported in the Supporting Information. The spectroscopic and analytical data for **G1** are consistent with its molecular structure. The synthesis of **CDV** was performed as described in the literature.[12b] Chemical reactions were carried out in oven-dried glassware under an inert gas atmosphere. Analytical TLC was performed on Merck silica gel 60 F254 plates. All compounds were visualized by dipping in alkaline permanganate solution. Column chromatography was carried out by using Kieselgel 60 (230–400 mesh). ^1H and ^{13}C NMR spectroscopic measurements were carried out by using Bruker ARX 300 MHz or Varian 500 MHz INOVA spectrometers. Chemical shifts were referenced to internal standards $CDCl_3$ (δ = 7.26 ppm for ^1H and 77.0 ppm for ^{13}C) or TMS (δ = 0.00 ppm for ^1H and ^{13}C). HRMS was performed by using a Bruker MicroTof instrument.

Preparation of MNP: Oleic acid coated **MNP** were synthesized by co-precipitation of ferric and ferrous salts in alkaline medium as described in the literature.[19] To this end, 2 g of ferrous sulfate heptahydrate ($FeSO_4$ $7H_2O$ > 99%) and 3.49 g of ferric chloride hexahydrate ($FeCl_3$ $6H_2O$ > 99%) were dissolved in 100 mL Milli Q water in a clean flask. Next, 25 mL of 25% (w/w) NH_3 H_2O was added to the mixture and the solution was kept stirring at room temperature. The solution turned black, leading to a black precipitate. Then ~1 mL of oleic acid was added dropwise into the dispersion at 80 °C under argon atmosphere. The resulting **MNP** were well dispersed into water and protected by a double layer of oleic acid. The water dispersion of nanoparticles was extracted with toluene. By addition of NaCl, **MNP** coated with a monolayer of oleic acid were transferred into the toluene phase. Finally the toluene dispersed **MNP** were refluxed under argon atmosphere to remove the water.

Preparation of MNP-CDV: Amphiphilic β-CD and oleic acid coated MNP were taken in a 25 mL flask. The mixture was dissolve in 2–3 mL of chloroform and dried by slow rotary evaporation to yield a thin film at the bottom of the flask. Residual solvent was removed under high vacuum. 10 mL of aqueous buffer (100 mM phosphate buffer, pH 7.2) was added and the suspension was stirred overnight. Fluorescent **MNP-CDV** hybrids were prepared by incorporating 10 mol% sulforhodamine labeled amphiphilic β-CD[20] with amphiphilic β-CD.

Light microscopy and fluorescence microscopy: Microscopic images were recorded with an Olympus inverted research microscope CKX41.

The microscope was equipped with a DX 20 L-FW camera (Kappa opto-electronics GmbH), which was controlled by the program Kappa CameraControl (version 2.7.5.7032). A mercury burner U-RFL-T was used for the generation of the excitation light. 10 μL of **MNP-CDV** solution was taken on a microscopy slide. A magnetic field was introduced by bringing a hand-held rectangular permanent magnet in close proximity of the microscopy slide.

UV/Vis Spectroscopy: Optical density measurements were carried out at in 1.5 mL disposable cuvettes with dimensions 12.5 × 12.5 × 45 mm and 10 mm path length using a Uvikon 923 double-beam spectrophotometer. The optical density was measured at $\lambda = 600$ nm (OD600), which is far from absorption of the azobenzene chromophore. Measurements were performed for 30 min to 40 min, unless otherwise noted, with data points collected every 12 s. The freshly prepared solution of **MNP-CDV** was extruded through a polycarbonate filter resulting in an average particle size of around 150 nm at the starting point of each experiment.

Irradiation Experiments: Two different light sources were utilized for light irradiation experiments. One source was a Rayonet photochemical reactor (The Southern New England Ultraviolet Company) equipped with 16 RPR- 3500 lamps used to generate UV light (350 nm) to photo-isomerize azobenzene moieties from *trans* to *cis*. The other source was a Philips Lumileds royal blue LUXEON K2 emitter (LXK2-PR14-Q00) used to generate visible light (455 nm) to isomerize azobenzene moieties from *cis* to *trans*. The **MNP-CDV** were irradiated for 30 min in disposable plastic cuvettes.

Transmission Electron Microscopy (TEM): **MNP** were deposited on a covered holey copper grid, by applying a drop of NPs dissolved in toluene on the surface. TEM analyses were performed by using a Zeiss 200 FE electron microscope with schottky emitter and energy Ω filter operating at 200 kV. The microscope was equipped with the CCD camera Gatan USC 4000. The electron microscope was constructed by Carl Zeiss ag, Oberkochen and the camera by Gatan Gmbh, München. The size of the nanoparticles was determined with ImageJ version 1.39u, Java 1.6.0_02 (National Institutes Of Health, USA).

Supporting Information

Supporting Information is available from the Wiley Online Library or from the author.

Acknowledgment

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[1] a) G. M. Whitesides, B. Grzybowski, *Science* **2002**, *295*, 2418–2421; b) A. Mulder, J. Huskens, D. N. Reinhoudt, *Org. Biomol. Chem.* **2004**, *2*, 3409–3424; c) S. G. Zhang, *Nature Biotechnol.* **2003**, *21*, 1171–1178.

[2] a) R. Eelkema, M. M. Pollard, J. Vicario, N. Katsonis, B. S. Ramon, C. W. M. Bastiaansen, D. J. Broer, B. L. Feringa, *Nature* **2006**, *440*, 163–163; b) R. Klajn, P. J. Wesson, K. J. M. Bishop, B. A. Grzybowski, *Angew. Chem. Int. Ed.* **2009**, *48*, 7035–7039; c) Y. Takashima, S. Hatanaka, M. Otsubo, M. Nakahata, T. Kakuta, A. Hashidzume, H. Yamaguchi, A. Harada, *Nature Commun.* **2012**, *3*, Art. Nr. 1270.

[3] a) Y. Sahoo, M. Cheon, S. Wang, H. Luo, E. P. Furlani, P. N. Prasad, *J. Phys. Chem. B* **2004**, *108*, 3380–3383; b) S. B. Lecommandoux, O. Sandre, F. Checot, J. Rodriguez-Hernandez, R. Perzynski, *Adv. Mater.* **2005**, *17*, 712–718; c) W. H. Chong, L. K. Chin, R. L. S. Tan, H. Wang, A. Q. Liu, H. Chen, *Angew. Chem. Int. Ed.* **2013**, *52*, 8570–8573; d) M. B. Bannwarth, S. W. Kazer, S. Ulrich, G. Glasser, D. Crespy, K. Landfester, *Angew. Chem., Int. Ed.* **2013**, *52*, 10107–10111.

[4] a) M. Grzelczak, J. Vermant, E. M. Furst, L. M. Liz-Marzan, *ACS Nano* **2010**, *4*, 3591–3605; b) S. Das, P. Ranjan, P. S. Maiti, G. Singh, G. Leitus, R. Klajn, *Adv. Mater.* **2013**, *25*, 422–426; c) O. Chovnik, R. Balgley, J. R. Goldman, R. Klajn, *J. Am. Chem. Soc.* **2012**, *134*, 19564–19567; d) H. Han, J. Y. Lee, X. Lu, *Chem. Commun.* **2013**, *49*, 6122–6124.

[5] J. Gao, H. Gu, B. Xu, *Acc. Chem. Res.* **2009**, *42*, 1097–1107.

[6] A. Jordan, R. Scholz, P. Wust, H. Fahling, R. Felix, *J. Magn. Magn. Mater.* **1999**, *201*, 413–419.

[7] H. Lee, E. Lee, D. K. Kim, N. K. Jang, Y. Y. Jeong, S. Jon, *J. Am. Chem. Soc.* **2006**, *128*, 7383–7389.

[8] a) G. H. Gao, G. H. Im, M. S. Kim, J. W. Lee, J. Yang, H. Jeon, J. H. Lee, D. S. Lee, *Small* **2006**, *6*, 1201; b) H. J. Lee, K. S. Jang, S. Jang, J. W. Kim, H. M. Yang, Y. Y. Jeong, J. D. Kim, *Chem. Commun.* **2010**, *46*, 3559.

[9] P. E. L. Renard, O. Jordan, A. Faes, A. P. Fink, H. Hofmann, D. Rüfenacht, F. Bosman, F. Buchegger, E. Doelker, *Biomaterials* **2010**, *31*, 691–705.

[10] X. Shi, S. H. Wang, S. D. Swanson, S. Ge, Z. Cao, M. E. V. Antwerp, K. J. Landmark, J. R. Baker Jr., *Adv. Mater.* **2008**, *20*, 1671–1678.

[11] a) G. Beaune, B. Dubertret, O. Clément, C. Vayssettes, V. Cabuil, C. Ménager, *Angew. Chem. Int. Ed.* **2007**, *46*, 5421–5424; b) O. T. Bruns, H. Ittrich, K. Peldschus, M. G. Kaul, U. I. Tromsdorf, J. Lauterwasser, M. S. Nikolic, B. Mollwitz, M. Merkel, N. C. Bigall, S. Sapra, R. Reimer, H. Hohenberg, H. Weller, A. Eychmüller, G. Adam, U. Beisiegel, J. Heeren, *Nature Nanotechnology* **2009**, *4*, 193–201; c) F. de Cogan, A. Booth, J. E. Gough, S. J. Webb, *Angew. Chem. Int. Ed.* **2011**, *50*, 12290–12293; d) N. Lozano, Al-W. Jamal, A. Taruttis, N. Beziere, N. C. Burton, J. V. D. Bossche, M. Mazza, E. Herzog, V. Ntziachristos, K. Kostarelos, *J. Am. Chem. Soc.* **2012**, *134*, 13256–13258; e) G. Balle, R. D. Corato, J. K. Tabi, V. Dupuis, O. Clément, F. Gazeau, C. Wilhelm, C. Ménager, *Langmuir* **2012**, *28*, 11834–11842.

[12] a) B. J. Ravoo, R. Darcy, *Angew. Chem. Int. Ed.* **2000**, *39*, 4324–4326; b) P. Falvey, C. W. Lim, R. Darcy, T. Revermann, U. Karst, M. Giesbers, A. T. M. Marcelis, A. Lazar, A. W. Coleman, D. N. Reinhoudt, B. J. Ravoo, *Chem. Eur. J.* **2005**, *11*, 1171–1180.

[13] a) J. Voskuhl, M. C. Stuart, B. J. Ravoo, *Chem. Eur. J.* **2010**, *16*, 2790–2796; b) D. A. Uhlenheuer, D. Wasserberg, C. Haase, H. D. Nguyen, J. H. Schenkel, J. Huskens, B. J. Ravoo, P. Jonkheijm, L. Brunsveld, *Chem. Eur. J.* **2012**, *18*, 6788–6794.

[14] a) X. Liao, G. Chen, X. Liu, W. Chen, F. Chen, M. Jiang, *Angew. Chem. Int. Ed.* **2010**, *49*, 4409–4413; b) H. Yamaguchi, Y. Kobayashi, R. Kobayashi, Y. Takashima, A. Hashidzume, A. Harada, *Nature Commun.* **2012**, *3*, Art. Nr: 603; c) A. Harada, R. Kobayashi, Y. Takashima, A. Hashidzume, H. Yamaguchi, *Nature Chem.* **2011**, *3*, 34–37.

[15] Y. P. Wang, N. Ma, Z. Q. Wang, X. Zhang, *Angew. Chem. Int. Ed.* **2007**, *46*, 2823–2826.

[16] D. P. Ferris, Y. L. Zhao, N. M. Khashab, H. A. Khatib, J. F. Stoddart, J. I. Zink, *J. Am. Chem. Soc.* **2009**, *131*, 1686–1688.

[17] a) S. K. M. Nalluri, J. Voskuhl, J. L. Bultema, E. J. Boekema, B. J. Ravoo, *Angew. Chem. Int. Ed.* **2011**, *50*, 9747–9751; b) A. Samanta, M. C. A. Stuart, B. J. Ravoo, *J. Am. Chem. Soc.* **2012**, *134*, 19909–19914.

[18] S. K. M. Nalluri, B. J. Ravoo, *Angew. Chem. Int. Ed.* **2010**, *49*, 5371–5374.

[19] Y. Sun, X. Ding, Z. Zheng, X. Cheng, X. Hu, Y. Peng, *Eur. Polym. J.* **2007**, *43*, 762–772.

[20] J. Voskuhl, T. Fenske, M. C. A. Stuart, B. Wibbeling, C. Schmuck, B. J. Ravoo, *Chem. Eur. J.* **2010**, *16*, 8300–8306.