Nanoparticles

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Photoswitchable Nanoassemblies by Electrostatic Self-Assembly

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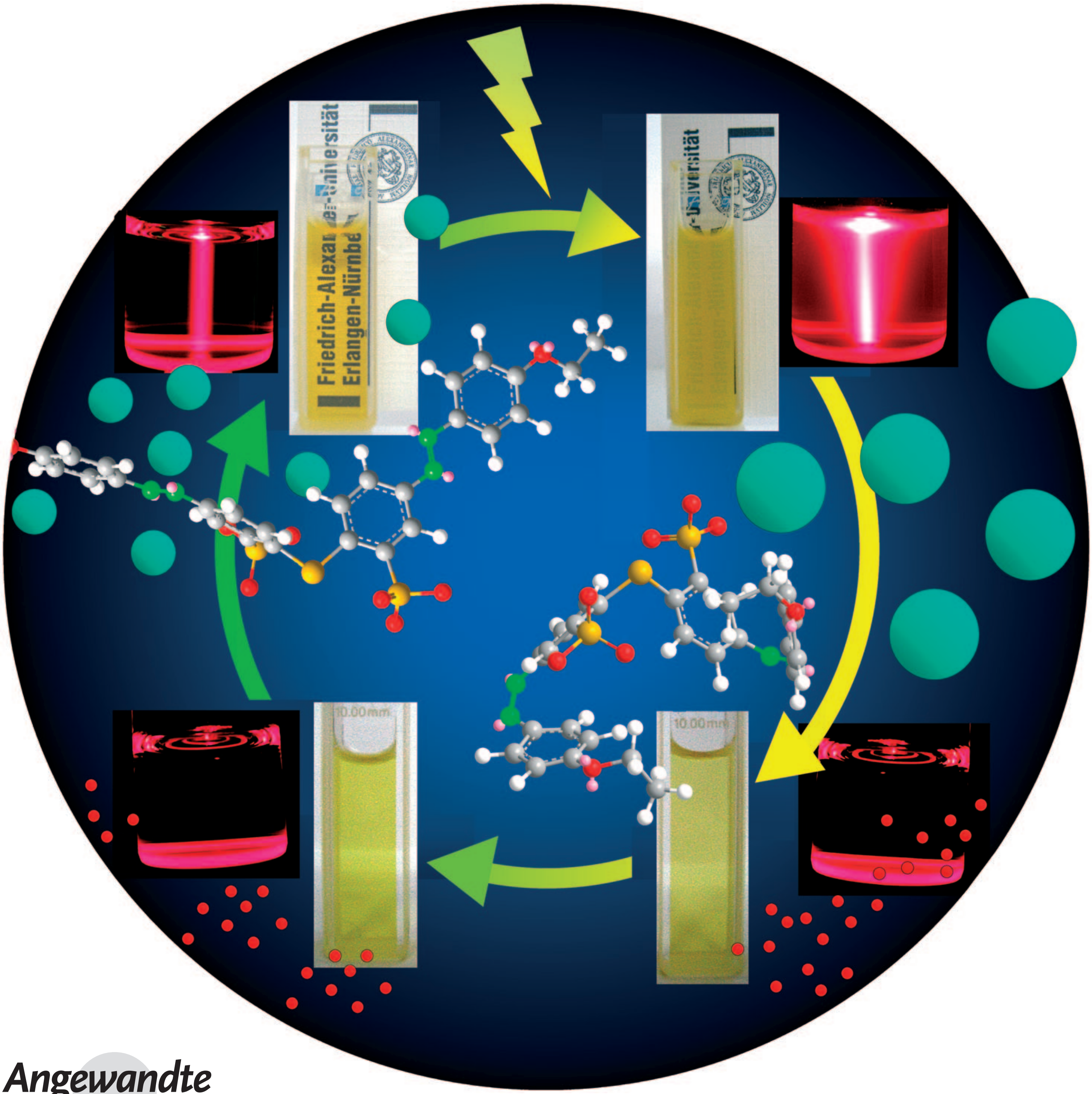

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The design of supramolecular nanostructures is of great importance, as self-assembly allows the production of a variety of structures for many applications, such as carrier systems, sensors, or transducers.[1] Particular potential lies in assemblies that can respond to external triggers. Recently, light-responsive structures have attracted much attention, as light is an elegant, non-invasive stimulus that offers possibilities for new functional nanostructures, for example as optical materials or switches in biological systems.[2]

Several ways to achieve light-responsiveness of nanoparticles in solution exist; for example, light-induced chemical reactions.[3] Very versatile structures are obtained by self-assembly: H-bridges and metal coordination yield diverse photoresponsive structures with defined local binding motifs.[4] However, the formation of "nano-objects" with controllable size remains a challenge. Surfactants undergoing isomerization or dimerization in UV light form light-responsive micelles,[2a,5] and transitions between vesicles and micelles of a surfactant/dye mixture were recently described.[5i] In these, the basic driving force for association is amphiphilicity. Recently, we established electrostatic self-assembly as an alternative route to supramolecular structures in solution.[6] Combining macroions with multivalent oppositely charged organic ions gives rise to an interplay of ionic interactions and π–π stacking or ionic interaction and geometric factors, yielding self-assembled nanoparticles with various shapes. Thus, it will be highly interesting to investigate whether this concept can also lead to new light-responsive nanoassemblies with photo-addressable size.

Herein we present a dually responsive system based on the combination of light- and pH-responsiveness of electrostatically self-assembled nanoparticles (Scheme 1). The model system consists of a fourth-generation poly(amidoamine) dendrimer, which previously led to pH-responsive dye–polyelectrolyte assemblies[6b] and an ionic photoisomerizable diazo dye. As the molecular structure of the dye counterion influences size and shape of the aggregates,[6] the conformation change from *trans* to *cis* has significant influence on the assembly. This differs fundamentally from famous host–guest systems based on individual dendrimers,[7] but focuses on the inter-connection of ionic dendrimers with dye ions as linkers. For Acid Yellow 38, UV/Vis spectroscopy gave a thermal *cis–trans* isomerization constant of $K = 1.63 \times 10^{-5}\,\mathrm{s}^{-1}$ at pH 3.5, in agreement with literature.[8] With a 12 hour half-life and 80 % azo groups in the *cis* form in the photostationary state, it is suitable for use in the studies described herein.

Assemblies are formed by mixing aqueous solutions of the building blocks and subsequent adjustment to pH 3.5. At pH 3.5, primary and tertiary dendrimer amine groups become protonated, that is, positively charged, and can associate with anionic dye counterions. Upon irradiation, an increased opalescence was partly visible by eye; in other words, the particle size increases (transition from A to B). Dynamic light scattering (DLS) was performed to characterize size distributions of assemblies before and after irradiation. Figure 1 shows results for the loading ratio (molar ratio of dye sulfonate groups to primary dendrimer amine groups) $l = 4.5{:}1$. Autocorrelation functions and corresponding distributions of relaxation times show the difference before and after irradiation with UV light (wavelength 380 ± 20 nm, 20 min). The hydrodynamic radius R_H increases from 32 nm to 165 nm.

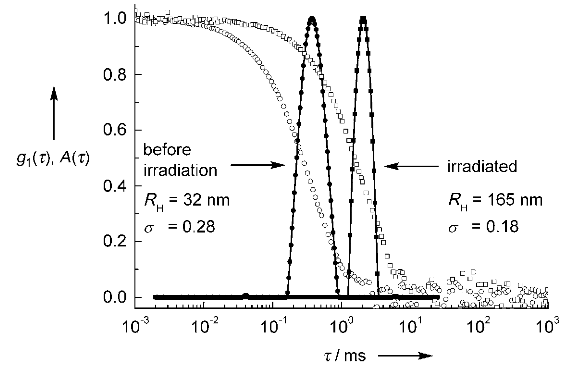

Figure 1. Dynamic light scattering on a dendrimer–dye assembly with loading ratio $l = 4.5{:}1$ before and after UV irradiation: Electric field autocorrelation function $g^1(\tau)$ and distribution of relaxation times $A(\tau)$ show the increase in assembly size. R_H = hydrodynamic radius; σ = standard deviation of the distribution.

UV/Vis spectroscopy was performed to show that the supramolecular change is caused by *trans–cis* isomerization of the dye building block. Dye spectra (Figure 2) are known for its nonirradiated (*trans*) and irradiated (80 % *cis*) form.[8] Spectra of samples with the dye pre-irradiated prior to assembly formation are very similar. The difference between pure dye and assembly is in accordance with the spectral changes observed for dye molecules binding to polylelectrolytes.[7,9] Thus, absorption spectroscopy is evidence of photoisomerization and for both dye isomers binding to dendrimer macroions. The spectrum of a sample that was irradiated as an assembly again indicates isomerization. Its difference to other irradiated samples is due to a photoprotective effect limiting dye isomerization to the *cis* state when bound to the macroion (resulting in 47 % *cis*) and the scattering of the sample due to the increased size.[10]

The existence of different particle sizes before and after irradiation are confirmed by atomic force microscopy (AFM). It is of interest as to whether the self-assembled photoswitched structures stay intact upon deposition onto the surface. Figure 3 shows AFM images for two samples before and after irradiation. Sizes observed are 140 ± 15 nm diameter and 32 ± 9 nm height prior to irradiation, and 480 ± 70 nm diameter and 180 ± 60 nm height for the irradiated samples. Thus, the size difference is in accordance with DLS results.[11]

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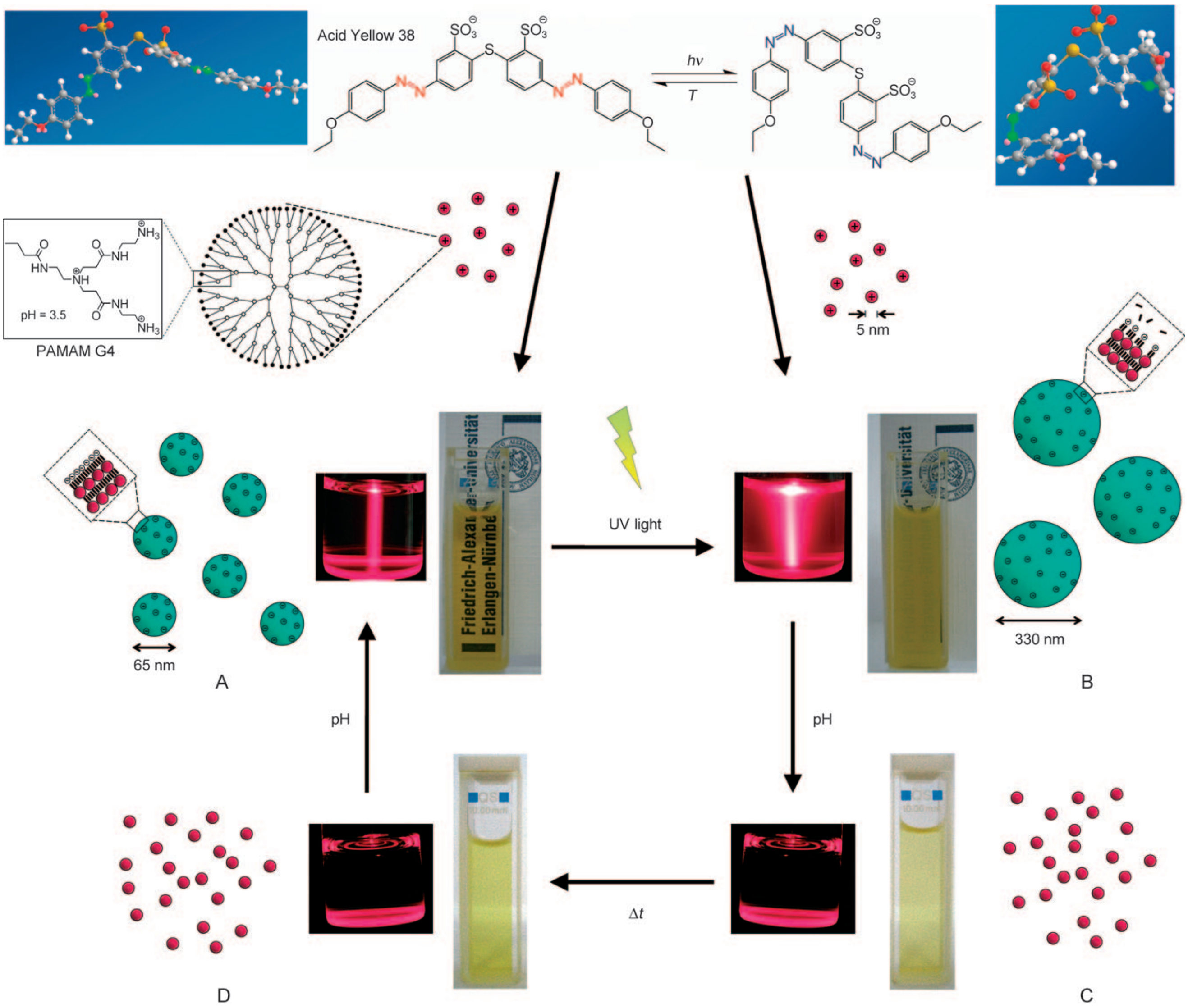

Scheme 1. Representation and photographs of a light- and pH-switchable electrostatically self-assembled system with photoaddressable particle size. Starting from a divalent anionic azobenzene dye and cationic dendrimeric macroions, self-assembled nanoparticles result (A), which grow in size upon irradiation with UV light (B) and further disassemble, triggered by the pH (C); after re-isomerization (D), building blocks can be reassembled into the original structure (A) by another pH change. Photographs indicate scattering power with a red laser and turbidity of the solution. Results are shown for a loading ratio (dye sulfonate groups/dendrimer amine groups) $l=4.5:1$. In (A) to (D), there are additional free dye molecules in the solution.

Samples with different loading ratios give further insight (for DLS, see the Supporting Information, Figure S1). Almost no size change is observed for dendrimer excess at $l=1.85:1$ (charge stoichiometry is at $l=2:1$ for primary and tertiary amine groups protonated at pH 3.5). For $l=7.2:1$, a size increase from r_H from 30 nm to 90 nm is observed. In contrast, for a large excess of dye ($l=12.5:1$), only a very small size increase again occurs. Furthermore, the narrow size distribution after irradiation is striking (standard deviation $0.07 \leq \sigma \leq 0.18$).

The reason for a particle size increase upon irradiation may be a decrease in steric or electrostatic stabilization. In this type of aggregate, the major source of stability results from the particle charge.[6] Thus, changes in the ζ potential are considered in Figure 4. Prior to irradiation, samples with dye excess exhibit a negative ζ potential, that is, they are negatively charged. In contrast, for excess dendrimer, the ζ potential is positive (+50 mV, not shown), indicating that excess dendrimer charges stabilize the assembly. The origin of the negative ζ potential for samples with excess dye must be over-stoichiometric binding of dye ions to the assembly, which most likely arises from π–π interactions to electrostatically bound dye molecules. Binding excess dye ions should thus be weaker than binding to charge stoichiometry. Upon irradiation, the ζ potential does not significantly change for the samples with excess dendrimer. In contrast, the (negative) ζ potential increases for samples with excess dye, indicating that the particles become less strongly negatively charged.[12] Such a change can only be caused by dye ions dissociating from the assembly; that is, the more loosely bound dye ions

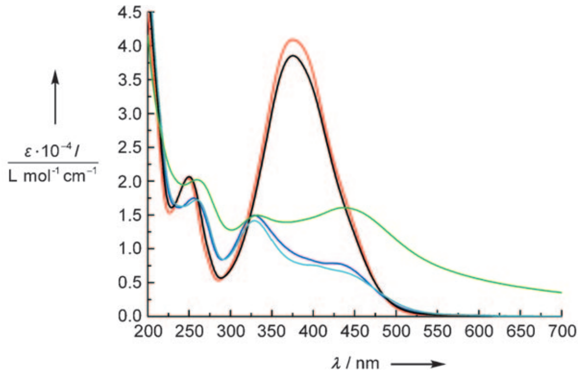

Figure 2. UV/Vis spectra of dye and dendrimer–dye assemblies before and after irradiation. Red: dye before irradiation, dark blue: dye after irradiation, black: dendrimer–dye assembly before irradiation, green: dendrimer–dye assembly after irradiation, turquoise: dendrimer–dye assembly with pre-irradiation of the dye.

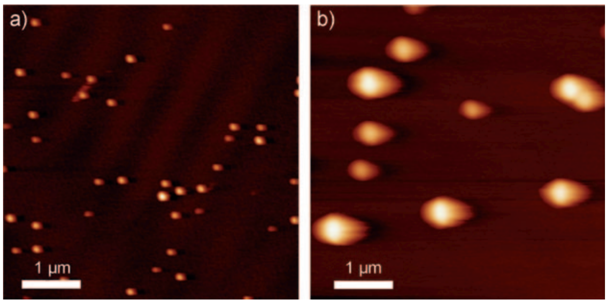

Figure 3. AFM images for dendrimer–dye assemblies ($l=5{:}1$) a) before and b) after UV irradiation. The solution was irradiated prior to deposition onto modified mica.

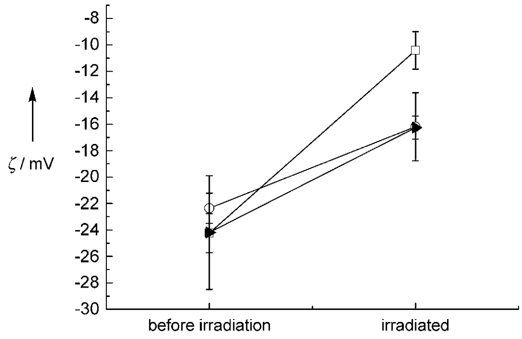

Figure 4. ζ Potential for dendrimer–dye assemblies before and after irradiation for different loading ratios l; □ $l=4.8{:}1$, ○ $l=7.2{:}1$, ▲ $l=12.5{:}1$. The change is due to a change in particle charge.

are partly released from the aggregate. This reduces the stability of a charge-stabilized particle and consequently causes the combination of aggregates into larger ones.

Evidently, the *trans* dye binds to the dendrimers up to a larger excess than the *cis* dye, which is most likely due to geometric effects allowing for hosting more *trans* dye molecules in stacks under the given constraints of the dendrimer assembly. Furthermore, a different polarity of the two isomers may cause the *cis* form to interact less strongly with other aromatic dye moieties through π–π interactions and hydrophobic effects. Also, in dendrimer excess samples, the dye conformation changes from *trans* to *cis* to a substantive degree and relative inter-dye interactions influence the assembly formation,[6d] but no change in size and ζ potential is observed. This change is not due to kinetic effects, as association of dendrimer with pre-irradiated dye yields aggregates comparable in size to those formed upon irradiating the assemblies. Thus, the crucial difference is that excess dye samples contain additional free dye ions in the solution,[13] which may play a major role in the reorientation process.[14] For a large excess of dye ($l=12.5{:}1$), only a small change in average assembly size occurs upon irradiation, whilst the ζ potential increases moderately. Thus, dye ions partly dissociate from the aggregate, decreasing its charge, but less than for a moderate dye excess. This effect is most likely due to a higher concentration of free dye in the solution. The remaining charge is sufficient to stabilize the aggregate. Rearrangement processes however take place, as evidenced by the narrowing size distribution.

We were also interested in the dual responsiveness of the system. Evidently, the size of electrostatically assembled supramolecular structures can be changed through light irradiation (A to B). After reisomerization of the dye to the *trans* form, assemblies do not diminish to their original size; for example, a sample with $l=7.2{:}1$ is stable with a constant size for at least one week. Kinetic effects probably play a role; therefore, pH was used as a second trigger. Changing the pH of the irradiated sample (B) from pH 3.5 to pH 10.5 causes the electrostatically self-assembled aggregates to disassemble into its building blocks as the dendrimer becomes uncharged (C). The absence of larger aggregates is evident from a decrease in turbidity and scattering power. Thereafter, in time reisomerization of the dye molecules into the *trans* state (D) occurs. The pH was then changed to pH 3.5, causing the dendrimers to recharge and assemble with the *trans* dye. By electrostatic self-assembly, the nanoaggregates of original size and charge are rebuilt (A); that is, a complete cycle has been accomplished by combining photoswichting and pH switching.

In conclusion, we have shown that electrostatic self-assembly can lead to photoswitchable nanoparticles in solution. Supramolecular assemblies of dendrimer macroions and divalent azobenzene counterions can respond to light with a size increase from 32 nm to 165 nm radius. The change in size is due to dissociation of dye molecules from the assembly, which causes a decrease in charge and further growth. Combining light and pH responsiveness, the electrostatically self-assembled system can undergo a complete cycle from small assemblies to larger assemblies formed by irradiation. These larger assemblies are subsequently split into their building units by a pH switch and after re-isomerization by the time they are assembled into the original assemblies by a further pH change. This new type of nanoassembly with light-switchable size may open the way to novel sensors, actuators, or molecular machines.

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[10] Disassembling by increasing pH and carrying out spectroscopic investigations prior to re-isomerization allowed UV/Vis data to be analyzed without a scattering contribution.

[11] AFM diameters given are measured at the surface but half widths that are much smaller are the basis for a volume comparison with DLS. Based on this, the volume change upon irradiation is in the same order of magnitude.

[12] The change is not due to the size change, as the particle size increases upon irradiation.

[13] This is evident from UV/Vis measurements.

[14] Furthermore, because the *cis*/*trans* ratio for free and bound dye differs, there may be a readjustment in the equilibrium between *trans* dye in the assembly and in solution.