In solution, amphiphilic block copolymers self-assemble into a large variety of different morphologies. These include most commonly spheres, rods, and vesicular assemblies.[1,2] Occasionally, also lamellae, tubes, large compound vesicles, hexagonally packed hollow hoops, large compound micelles, and onions have been obtained.[3] In recent years, it has become a challenge to manipulate these morphologies in solution through different strategies. For a given block copolymer, composition reorganization of the micelle architectures has been achieved by changing the salinity as well as the solution pH,[4–6] the polymer concentration,[7,8] and the solvent composition.[9–11] Other approaches to change the structures of block copolymer supramolecular assemblies include chemical modification of the polymers in situ[12] and thermally induced melting and crystallization.[13]

Recently, a new type of hybrid material (or molecular chimera) containing a nucleic acid segment and an organic polymer unit have been introduced.[14–16] These amphiphilic DNA block copolymers, like other polyelectrolyte block copolymers, form micelles of spherical shape in aqueous solution. The micelles with a corona of single-stranded (ss) DNA were applied for the delivery of antisense oligonucleotides (ODNs)[17] for the hybridization with DNA-coated gold nanoparticles[18] and as programmable, three-dimensional scaffolds for DNA-templated organic reactions.[19]

Micelles composed of this material were hybridized with the complementary sequence (5'-TAACAGGATTAGCA-GAGCGAGG-3'). As a result, DNA block copolymer micelles were formed that contain a shell of ds-DNA (Figure 1a). To investigate whether hybridization with the complementary sequence influenced their structural features, the micelles were visualized in hybridization buffer solution on a mica surface by SFM in soft tapping mode. Although the immobilization and the imaging process might alter the morphologies of the micelles, SFM has been proven to be a powerful tool for imaging amphiphilic DNA block copolymer aggregates[17–19]. Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.
obtained. For ds micelles, a mean height of (5.8 ± 1.6) nm was determined (calculated for 116 micelles from nine SFM images). The SFM measurements suggest that hybridization of ss-DNA block copolymer micelles with the complementary sequence does not change the overall shape of the spherical aggregates. The deviations in the mean heights of ss and ds micelles might result from different charge densities in the corona and micelle deformations induced by variations in the adjusted soft-tapping-mode parameters. To exclude surface effects, it is necessary to investigate the structural properties of the micelles in solution. For this reason, FCS experiments with ss and ds micelles containing a dye label (Alexa 488) were carried out.

FCS is an ultrasensitive analysis method[20] that is generally used to monitor binding affinities for fluorescence-labeled biomacromolecules. For instance DNA-hybridization events have been detected at the single-molecule level.[21] Furthermore, FCS has been employed to detect conformational transitions of enzymes[22] or polymers[23] by changes in the diffusion properties. The transit times of the freely diffusing fluorescent micelles through the excitation volume of 4.5 fL were measured in buffer solution by using a confocal microscope setup.[24] The translational diffusion coefficients D were calculated from the mean diffusion times. As the diffusion coefficient D is related to the frictional coefficient f of the hydrated micelles, the shape information of the immobilized DNA block copolymer aggregates could be used to calculate the radius r0 for the spherical micelles from the FCS diffusion data (see the Supporting Information). A mean radius of (5.6 ± 0.5) nm was found for the ss-DNA micelles. The radius of the ds-DNA micelles was (5.3 ± 0.5) nm. These values are in good agreement with the AFM measurements as they confirm similar dimensions for ss and ds micelles. Moreover, it can be concluded from the FCS data that upon immobilization, the micelles are flattened owing to the interaction with the surface and/or the SFM imaging process.

After hybridization of ss micelles with the complementary sequence, the changes of the morphology of the DNA block copolymer assemblies were investigated employing long DNA molecules. The sequence of these templates was chosen so that they encode the complementary sequence of DNA-b-PPO several times. On the template T110 (sequence: 5’-(TAACAGGATTACGAGGGGAGG)5-3’), and T88 (sequence: 5’-(TAACAGGATTACGAGGGGAGG)5-3’), five and four DNA-b-PPO polymers can be annealed, respectively. For the hybridization experiments, the ratios of block copolymers to long DNA molecules were adjusted so that the templates were completely hybridized. The resulting structures were visualized by SFM on a mica surface. For the DNA-b-PPO-T110 hybridization product, no spherical objects were detected. Instead, rodlike structures were observed (Figure 3a–e). Histograms of the height distribution of the rodlike objects were compiled which revealed an average height of (1.95 ± 0.1) nm (Figure 3f). The rods exhibited a length of (29.1 ± 6.5) nm. The shape and the dimensions of these structures are consistent with the model shown in Figure 1b. Upon hybridization, disintegration of the spherical ss-DNA block copolymer micelles occurs and DNA-b-PPOs are organized in a linear fashion along the template molecule. Thereby, the nucleic acid segment of the DNA block copolymer is involved in forming the double helix with the template while the hydrophobic blocks stick out of the ds-DNA. This process is accompanied by dimerization of two of these ds-DNA-PPO hybrids forming rodlike micelles, induced by the hydrophobic interactions of the PPO moieties (Figure 3b–e). The parallel alignment of two double helices with a spacing of 3–4 nm can be proven by a cross-sectional analysis perpendicular to the long axis of the assembly (Figure 3g).
The height of the rodlike aggregates is in very good agreement with values that have been obtained previously for ds-DNA.[25] The length of the rodlike micelles is slightly smaller than expected for ds-DNA exhibiting the same number of nucleotides as present in the template T110 (37.4 nm) when assuming a contribution of 0.34 nm per base pair.

Two different control experiments were carried out. On the one hand, DNA-b-PPO micelles were incubated with a 110-mer ODN that did not show any sequence complementarity with that of the micelles. As a result the structural properties of the spherical micelles remained unchanged (data not shown). On the other hand, the template T110 was hybridized with a non-polymer-modified ODN that encodes the complementary sequence of the micelles. By SFM the expected ds-DNA molecules were detected but no dimer formation occurred.

To prove that in general spherical DNA block copolymer micelles can be transformed into amphiphilic rods by using long DNA templates, DNA-b-PPO was hybridized with T88. Again, SFM analysis revealed the disappearance of spherical micelles and the formation of rodlike structures consisting of two parallel aligned double helices with a length of (22.7 ± 5.1) nm and a height of (1.72 ± 0.2) nm (see the Supporting Information). The longitudinal extension is again slightly reduced compared to ds-DNA that contains 88 nucleotides (29.9 nm).

The SFM results were complemented by FCS experiments to prove the formation of rodlike micelles also in solution. For that purpose, spherical ss-DNA block copolymer micelles were hybridized with T110 templates with a fluorophore (Cy3). As a control, the labeled template T110 was hybridized with the DNA sequence present in DNA-b-PPO without polymer attachment, which results in the formation of a ds-DNA molecule. The 3D shapes of the rodlike aggregates and the ds-DNA controls were investigated in buffer solution by diffusion measurements. As for the spherical micelles, the frictional coefficient \( f_{\text{rod}} \) of rodlike micelles is related to an effective radius of these objects. By using the measured aspect ratio \( P_{\text{dimer}} = 6.3 \) of the dimer and \( P_{\text{DNA}} = 19 \) of the ds-DNA molecule, the diffusion times were predicted to increase by a factor of 1.16 from the control to the amphiphilic DNA rods (see the Supporting Information). In Figure 4, the autocorrelation functions of the rodlike micelles and the ds-DNA controls are shown with mean diffusion times of \( t_{\text{D0}} = (1.9 ± 0.1) \) ms for the DNA-b-PPO-T110 hybridization products and \( t_{\text{D0}} = (1.47 ± 0.1) \) ms for the controls. The diffusion-time ratio of 1.29 strongly supports the expectation that the rodlike properties of the hydrated micelles and of the ds-DNA molecule are also maintained in solution.

In summary, a conceptually new approach for selectively manipulating the structural features of polyelectrolyte block copolymer micelles, which relies on molecular recognition, has been presented. Although hybridization of DNA block copolymer aggregates with short DNA strands has no significant impact on the structural properties, base pairing with long DNA templates induced a transformation from spherical into rodlike micelles. The Watson–Crick motif aligned the hydrophobic polymer segments along the DNA double helix, which resulted in selective dimer formation on the surface. Even the length of the resulting rodlike micelles could be adjusted by the number of nucleotides of the templates. Characteristics of this novel strategy are the sequence specificity and the structural uniformity of the

Figure 3. a) SFM topography image of the hybridization products of DNA-b-PPO and T110. b–e) Close-up images of rodlike micelles consisting of two DNA helices arranged parallel to each other forming a dimer. b, c) Enlarged images recorded at higher resolution than in (a). d, e) Topography images taken from other experiments obtained under similar conditions. f) Histogram showing the height of the rodlike aggregates. g) The line profile along the indicated line in (b). 

\[ h = \text{height}, \quad d = \text{distance}. \]

Figure 4. Normalized autocorrelation functions of the hybridization products of DNA-b-PPO and T110 in solution (——), the ds-DNA from T110 and oligonucleotides without PPO attached as the control (——), and rhodamine 6G in water (-----) as the reference. \( t_{\text{corr}} = \text{correlation time} \)
resulting micelle aggregates. This study, for the first time, demonstrates that DNA nanostructures, which are usually generated by using base pairing of complementary ss-ODN sequences,[26–28] can be built up with hydrophobic interactions. This technique adds a new tool to the field of DNA nanotechnology with respect to structure formation.

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