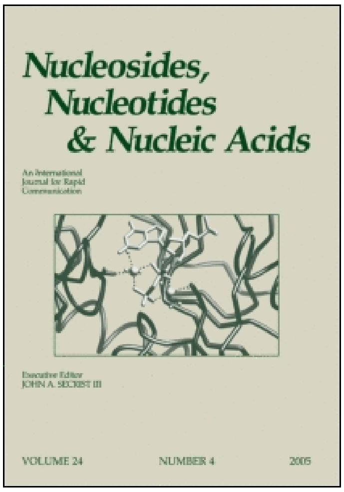

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Nanoparticles and DNA Probes Based on DNA-Fluorophore Conjugates

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The assembly of synthetically controllable molecular systems is one of the major goals of nanotechnology[1–3] and branched motifs of DNA can provide suitable building units for the assembly of nanoscale objects.[1,4,5] The key advantage of using DNA lies in its well defined binding properties, which means that DNA may be the molecule with the most readily predictable and programmable intermolecular interactions.

Different approaches have been taken to exploit the key properties of DNA. For example, Seeman has demonstrated the construction of non-mobile DNA junction architectures,[6,7] which through the use of "sticky end" techniques and ligation enzymes, led to the formulation of a cube,[1] a truncated octahedron[8] and a nanomechanical device.[9] Mirkin's experiments[10] include the mixing of two non-complementary oligonucleotide-modified gold nano-particles and subsequent introduction of a DNA linking duplex which contain "sticky ends" where one end was complementary to the oligonucleotides in one nanoparticle and the other complementary to the oligonucleotides in the second nanoparticle. Hybridization of the oligonucleotides resulted in a polymeric DNA-gold colloid.

Perylene dyes, which possess high fluorescence quantum yield and excellent photostability, can be coupled to complementary oligonucleotides which will allow

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us to make structures on a nanometer length scale and to use them as DNA probe. Oligonucleotides labelled with fluorescent dyes are extensively utilized for the detection of nucleic acids.[11,12] The application of fluorescent dyes as reporter molecules has been largely developed to avoid the handling of radioactive probes.[13] However, it has been demonstrated that the sensitivity limit observed with these probes was not as high as for the radioactive labeled oligonucleotides.[14] Polyphenylene dendrimers, which have been developed in our group, are not only chemically stable and shape-persistent, but also provide a large surface area that can be decorated with several chromophores. This leads to an increase in the absorption and emission intensity of the dendrimer functionalized with the chromophores.[15–17] The use of rigid polyphenylene dendrimers as carriers for several reporter molecules (fluorescence dyes) overcomes many difficulties which can appear by using other flexible systems. A typical problem is conformational mobility which leads to undesired chromophore-chromophore interactions such as self-quenching and low fluorescence quantum yield. The role of a dendrimer as a carrier for several reporter molecules in DNA probing is herein combined with the formation of oligonucleotide-dendrimer hybrids en route to novel multi-dimensional DNA architectures. We want to exploit the molecular recognition property of DNA and the possibility of using multifunctional fluorophores and dendrimers to build up well-defined 1-D, 2-D and 3-D DNA- fluorophore networks and to study the electronic properties of such structures. This programmed assembly methodology, by virtue of the oligonucleotide sequence, provides an opportunity to tailor the architectural parameters of nanoparticle-based structures linked with DNA which are expected to influence the electronic properties. These parameters include the size of the nanoparticle, particle periodicity and interparticle distance.

The oligonucleotide sequences have been synthesized via solid-phase synthesis using phosphoramidite chemistry and purified by HPLC. UV-spectroscopy and MALDI-TOF analysis have been used to characterize and confirm the structure of the oligonucleotides. A perylene dye functionalized with two carboxylic acid groups

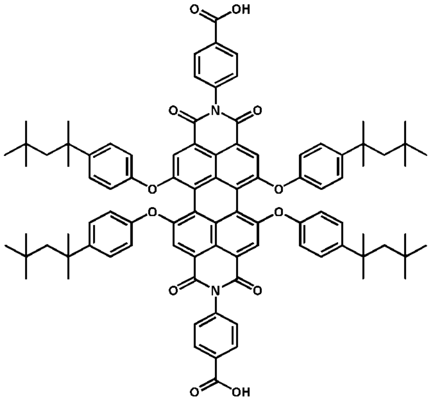

Figure 1. The structure of the perylene dye for the construction of linear conjugates.

(Fig. 1) has been synthesized and coupled to the oligonucleotide (16 mer). The conjugate has been purified by polyacrylamide gel electrophoresis. Fluorescence Correlation Spectroscopy (FCS) shows that the conjugate exhibits fluorescence in water and tends to aggregate weakly. A three component fit to the FCS correlation function yields hydrodynamic radii, R_H, from 1.5 nm to 152 nm. With the help of cationic detergents the conjugate can be dispersed in n-decane ($R_H = 1.3$ nm). After having shown the solubility of the molecule in different media, we plan to characterize the hybridization properties in more detail.

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