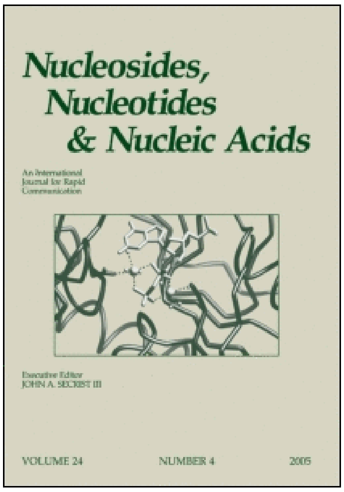

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Novel DNA Nanoparticles and Networks

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NOVEL DNA NANOPARTICLES AND NETWORKS

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▫ *Joining the thrombin-binding aptamer 5′-d(GGTTGGTGTGGTTGG) and the minihairpin 5′-d(GCGAAGC) leads to new DNA nanoparticles, which are different from rod-like helical double-stranded DNA. Covalent interstrand cross-links in DNA duplexes generated by bifunctional alkadiyne chains were used to build-up the DNA networks.*

Keywords DNA Nanoparticles, DNA Networks, Aptamers, Minihairpins

INTRODUCTION

The powerful molecular recognition property of the DNA molecule has appealing features in the bottom-up nanotechnology and can be used to direct the assembly of highly structured materials with specific nanoscale features. Single-stranded DNA of particular sequences can self-assemble into secondary structures such as cubes, octahedrons,[1] hairpins and aptamers.[2] This self-assembly and scaffolding may provide useful applications in nanoelectronics, biosensors, and gene delivery systems. In order to exploit the DNA for material science we have focused our attention on the engineering of DNA constructs containing different structural motifs as well as DNA networks.

RESULTS AND DISCUSSION

Aptamer-Minihairpin Conjugates

The aptamer 5′-d(GGTTGG*TGT*GGTTGG) (**1**)[2] forms a chair-like structure in the presence of K^+ or Na^+ ions and shows a T_m value of 48°C. It binds to the

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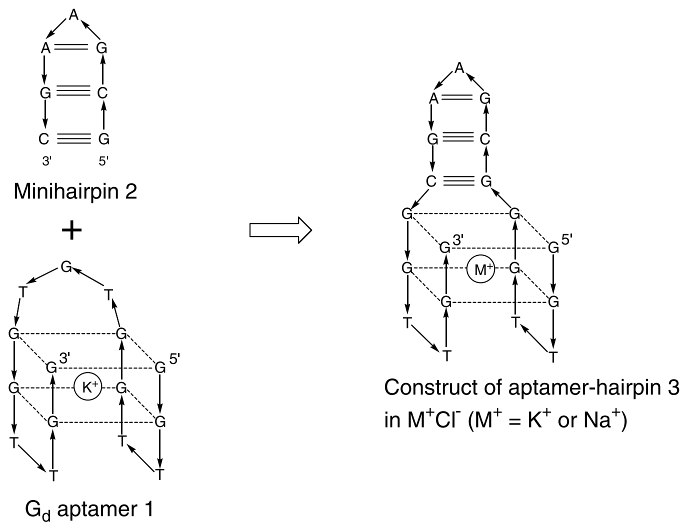


FIGURE 1

serine protease thrombin and results in the inhibition of thrombin-catalyzed fibrin clot formation. The short DNA fragment 5′-d(GCGAAGC) (**2**) (Figure 1) occurs frequently in biologically important regions and creates an extraordinarily stable minihairpin (T_m = 70°C).[3] We have combined these two structural units **1** and **2**, forming d(GGTTGG*GCGAAGC*GGTTGG) (**3**) (Figure 1). This shows two phase transitions with T_m values of 43°C and 70°C (20 mM Li_3PO_4, 50 mM KCl (pH 7), revealing the separate melting of the aptamer (43°C) and of the minihairpin elements (70°C).

As like the thrombin-binding aptamer **1**, the newly formed construct **3** shows the same ion dependence in such a way that neither Li^+ nor Cs^+ ions form the structure while in the presence of Na^+ the molecule exhibits T_m values of 40°C and 70°C. Replacement of the external 2-base loops [d(TT)] of **3** by the minihairpin **2**

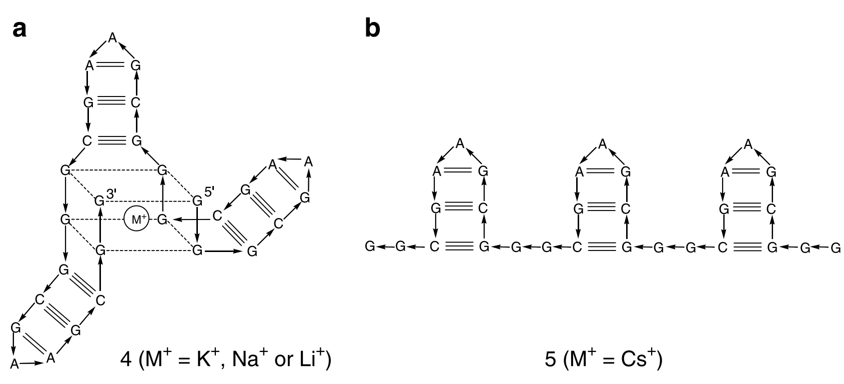


FIGURE 2

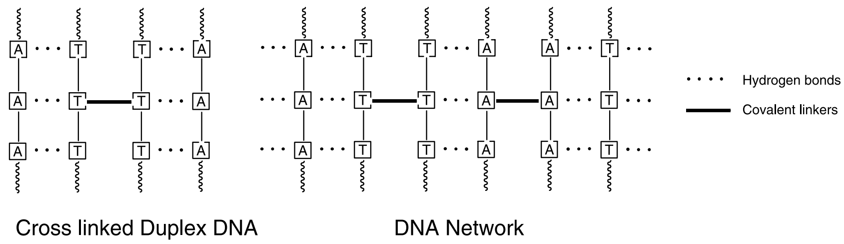
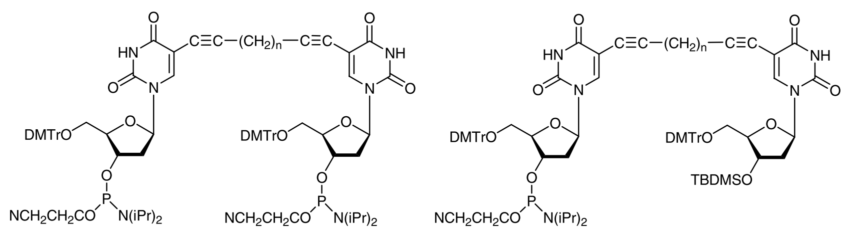


FIGURE 3



1 2

SCHEME 1

results into the new propeller-shaped nanostructure **4** (Figure 2). It shows different behavior from that of **3** as not only in the presence of K^+ and Na^+ ions, but also in Li^+ solutions it exhibits two melting temperatures, from which the higher one–referring to the minihairpins (72°C)–is almost independent from the ion type. The lower one is ion dependent showing a T_m value in the presence of Na^+ (60°C). In a Cs^+-containing solution only the transition of the minihairpin is observed (72°C), implying the absence of the tetrade and the presence of a linear chain with three minihairpin loops (**5**, Figure 2b).

From these findings it is obvious that this DNA construct shows rather different properties as the rod-like helical double-stranded DNA. This allows the formation

TABLE 1 T_m Values and Thermodynamic Data of Oligonucleotides Containing Regular and the Base-Modified Nucleoside T*–T*

Duplex	T_m (°C)	$\Delta H°$ (kcal/mol)	$\Delta S°$ (cal/K mol)	$\Delta G°_{310}$ (kcal/mol)
5′-d(TTTTTTTTTTTT) 3′-d(AAAAAAAAAAAA)	44	−84	−238	−9.8
3′-d(AAAAAAAAAAAA) 5′-d(TTTTTT*TTTTTT) | 5′-d(TTTTTT*TTTTTT) 3′-d(AAAAAAAAAAAA)	58	−133	−377	−16.0

Buffer: 1 M NaCl, 100 mM $MgCl_2$, 60 mM Na-cacodylate, pH 7.

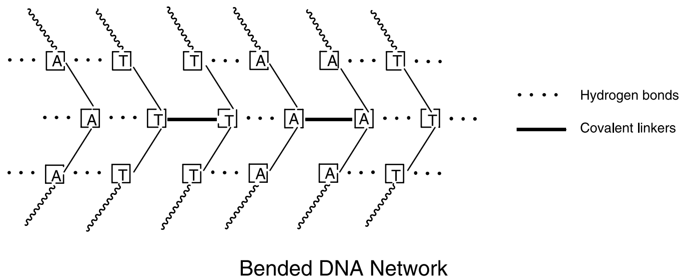


FIGURE 4

of "globular" DNA nanoparticles which show controllable structural properties on the same molecule.

DNA Networks

Interstrand cross-links in DNA duplexes generated by bifunctional alkylating agents are of considerable interest in forming DNA which inhibit DNA transcription and replication.[4] To explore this we have focused our interest in constructing polymeric networks from double stranded DNA. They are cross-linked by alkadiyne chains of various lengths and rigidity (Figure 3). This approach can be used to generate super supramolecular assemblies of highly ordered materials.

For this we have synthesized base-modified cross-linked building blocks **1** and **2** with various alkadiyne chains (Scheme 1). The oligonucleotides incorporating these building blocks were obtained by solid-phase synthesis. Already, the cross-linked duplex DNA shows significantly higher thermal stability than that of the individual DNA duplexes of identical length and composition (Table 1).

These structures might be deposited on surfaces thereby forming regular pattern of DNA networks. They can act as protein binding sites or might be used to generate particular patterns on a polymeric surface. According to the persistence length of DNA (50 nm) the molecules described above form stiff rod-like structures. Future work will use bended DNA-fragments which are formed by particular sequence motifs. Thus, it will be possible to create bended DNA networks (Figure 4).

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