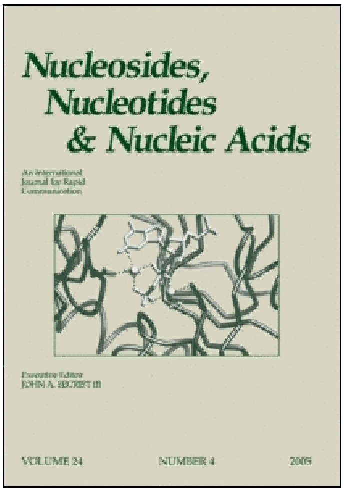

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GOLD DNA-CONJUGATES: ION SPECIFIC SELF-ASSEMBLY OF GOLD NANOPARTICLES VIA THE dG-QUARTET

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□ *The Oxytricha telomere DNA hairpin 5′-d($G_4T_4G_4$) immobilized on 13 nm gold nanoparticles forms a supramolecular assembly via dG-quartets, as determined by the color change and by SEM. The aggregation is ion-dependent and selective for sodium ions. K^+ is less efficient while Li^+ and Cs^+ do not drive the aggregation. This work is the first effort exploring the use of secondary structures of DNA (quadruplexes) for producing self-assemblies of gold nanoparticles.*

Keywords DNA, Gold-Nanoparticles, Self-Assembly, G-Quartet

INTRODUCTION

For several decades, gold has been known for its use in medicine. Recently, nanoshells consisting of a silica core covered by thin gold nanoparticles have proven effective for the treatment of cancer in first animal tests.[1] The gold-DNA-conjugate formation is a successful approach for the construction of highly ordered assemblies. Self-assemblies of gold nanoparticles via duplex formation are well known.[2] Such assemblies offer promising applications in the ultra-sensitive DNA detection, nanoscale electronics, biosensors, and in gene delivery systems. We focussed our interest in assembling gold nanoparticles using single-stranded DNA forming complex structures such as hairpins or aggregating to triplexes, quadruplexes and pentameric assemblies. For example, *Oxytricha* telomere DNA, 5′-d($G_4T_4G_4$) **1** (Scheme 1) forms quadruplex structures in the presence of Na^+ and K^+, while other cations such as Cs^+ and Li^+ are not effective.[3] They are the result of folded-back hairpins that dimerize, both inter- and intra-molecularly, to give the tetrads (Figure 1a). The dimer of two strands of **1** in antiparallel orientation forming a stack of four guanine-quartets held together with distinct diagonal

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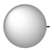
1 5'-d(GGGGTTTTGGGG)

2 5'-HS$(CH_2)_6O(PO_2H_2)$O-d(GGGGTTTTGGGG)

3 5'  -S$(CH_2)_6O(PO_2H_2)$O-d(GGGGTTTTGGGG)

SCHEME 1

loops.[4] We anticipated that the folding back property of *Oxytricha* telomere DNA, 5′-d($G_4T_4G_4$) **1** can be utilized to assemble gold nanoparticles (Figure 1b). Thus, the aggregation of gold-DNA nanoparticles might be controlled selectively by a particular cation.[5]

RESULTS AND DISCUSSION

For that, the 5′-(alkanethiol)-modified oligonucleotide **2** was synthesized and immobilized on Au nanoparticle surfaces to yield **3** (Scheme 1). This gold-DNA conjugate shows a plasmon resonance at 524 nm (Figure 2A-a). The aggregation of gold nanoparticles with different alkali metal ions was monitored as a function of the color change from red to purple, followed by UV-vis spectroscopy and by SEM (scanning electron microscopy).[2]

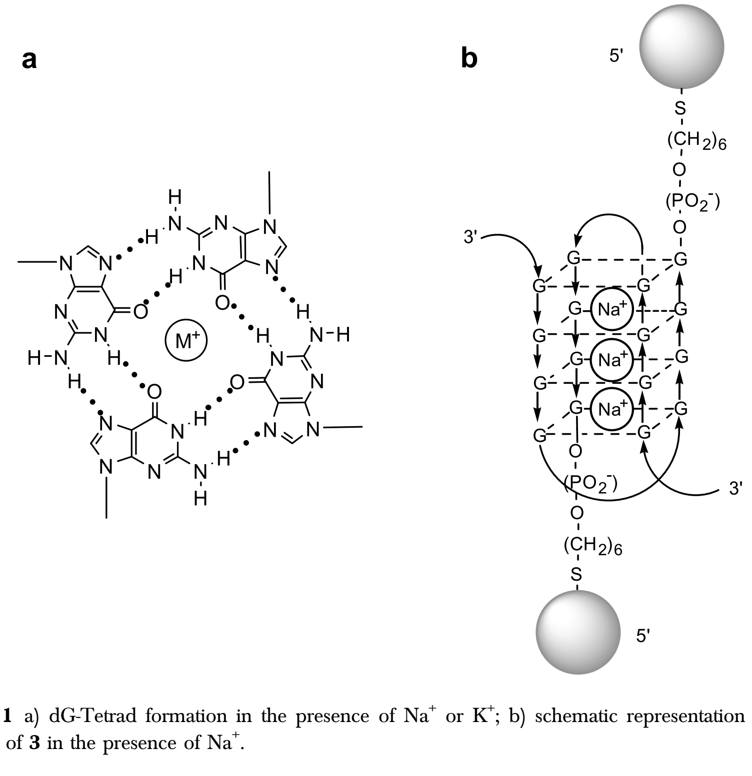


FIGURE 1 a) dG-Tetrad formation in the presence of Na^+ or K^+; b) schematic representation showing the aggregation of **3** in the presence of Na^+.

Ion-Dependent Self-Assembly of Gold Nanoparticles

The addition of 300 μL of 0.6 M NaCl in 10 mM phosphate buffer (pH 7.0) to 100 μL of gold probe **3** (0.3 M NaCl, 10 mM phosphate buffer, pH 7.0) (total concentration, 0.5 M NaCl), changes the color of the solution from red to purple within 5 min. If the solution was allowed to stand overnight precipitation of the gold oligonucleotide conjugate **3** occurs, and the solution becomes colorless. The initial color change, which is attributed to the formation of assemblies of oligonucleotide-modified Au nanoparticles leads to a red shift in the surface/plasmon resonance from 524 to 538 nm (Figure 2A-b).[2] Further evidence for the formation of the supramolecular assembly comes from the SEM studies. Figure 2B shows the SEM image indicating the formation of large assembled networks of Au-oligonucleotide hairpin aggregates.

The phenomenon of aggregation was also tested with other metal ions (K^+, Cs^+, and Li^+). In 0.6 M KCl, 10 mM phosphate buffer (pH 7.0), it took more than a week for the color change from red to purple, while in 1 M KCl, 10 mM phosphate buffer (pH 7.0) the purple color appeared within a week. No color change was noticed with 0.6 and 1 M CsCl or LiCl in 10 mM phosphate buffer (pH 7.0) even after a time period of more than a month. In contrast, the addition of 300 μL of 0.1–1 M NaCl, KCl, CsCl, or LiCl in 10 mM phosphate buffer (pH 7.0) to the unmodified Au nanoparticle solution (1 mL) results only in the growth of gold nanoparticles.[6] The ion selectivity of the hairpin gold conjugates **3** shows the same cation dependence as that observed for the parent hairpin 5′-d($G_4T_4G_4$) **1**.[3] The observed Au nanoparticles aggregation in **3** results from the interaction of a hairpin **1**, which dimerizes to form the dG-tetrads in the presence of Na^+ and K^+ ions (Figure 1b) but not with Li^+ or Cs^+. As shown in Figure 1b, the intermolecular interaction between two 5′-d($G_4T_4G_4$) (**3**) strands being in antiparallel orientation drive the process of gold nanoparticle assembly. Thus, the resultant aggregation

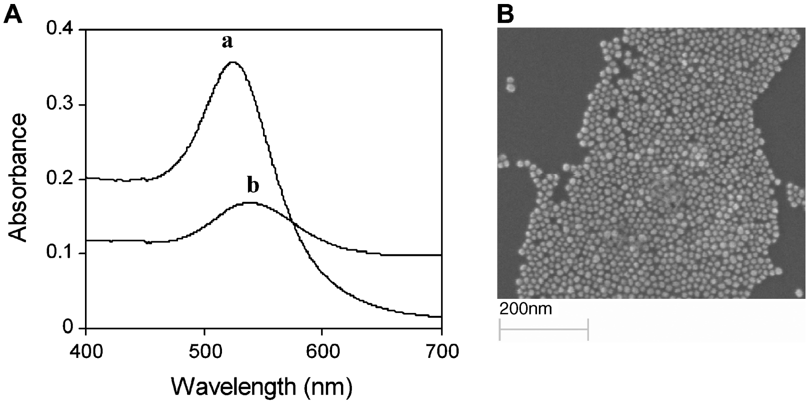


FIGURE 2 A) UV-visible spectra of Au nanoparticles functionalized with 5′-hexanethiol-d($G_4T_4G_4$) **3** before (a) and after (b) treatment with 0.6 M NaCl, 10 mM phosphate buffer (pH 7.0). B) SEM image of **3** in 0.6 M NaCl, 10 mM phosphate buffer (pH 7.0).

is caused by the hairpin-forming sequence 5′-d($G_4T_4G_4$) of the *Oxytricha* telomere DNA.

In conclusion, we have shown that the ion dependent property of the foldback hairpin can be used to control the self-assembly of gold nanoparticles. The supramolecular aggregate formation is selective for sodium ions, less effective for potassium ions. Other cations such as cesium and lithium do not drive the gold nanoparticles to cluster formation. Further studies on the assembly of Au-oligonucleotide conjugates with isoguanine (quartets or quintets) are under investigation.[7] Our approach has the potential to be utilized for the generation novel devices and materials, potentially useful for sensing and other applications in medicinal or engineering science, for the detection of alkali ions by the color change observed during quartet formation and for gene delivery as well as for diagnostic and therapeutic purposes.

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