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Fabrication of DNA nanotubes with an array of exterior magnetic nanoparticles

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ABSTRACT

Described here a methodology for arraying of magnetic nanoparticles (MNPs) on the surface of DNA nanotubes (DNTs). Positioning of magnetic nanoparticles at exterior surface of DNTs were shaped after self-assembling of oligonucleotide staples within an M13mp18 DNA scaffold via an origami process. The staples were partially labeled with biotin to be arrayed at the surface of DNTs. Gel retardation assay of the DNTs carrying magnetic nanoparticles indicated a reversely behavioral electrophoretic movement in comparison to the nanotubes have been demonstrated previously. Also, high resolution transmission electron microscopy confirmed positioning magnetic nanoparticles at the exterior surface of DNTs, correctly. Ultrastructural characteristics of these DNA nanotubes using atomic force microscopy demonstrated topographic heights on their surfaces formed through positioning of magnetic nanoparticles outside the tubules. This nanoarchitecture would be potential for multiple arraying of nanoparticles that those be useful as functionalized chimeric nanocarriers for developing novel nanodrugs and nanobiosensors.

1. Introduction

Fabrications of hybrid nanomaterials have been considered by scientists due to their applications from as diverse as gene or drug delivery to bioelectronics [1–4]. Particularly, the incorporations of metallic and magnetic nanoparticles in hybrid or chimeric nanomaterials have expanded potentials of these nanomaterials for employing in nanotherapeutics and nanodiagnostics [5–8]. This will change physical properties of the nanocomplexes; however, the incorporation of a metallic nanoparticle within an organic matrix such as a biomaterial could be possible using the recent methodologies in nanobiotechnology [9,10]. Progress on any aspects of these challenges can greatly expand the range of applications of theses nanoarchitectures in many areas of science and technology [11–12].

Structural DNA nanotechnology [13] has recently opened a new window for the fabrication of nano-devices [14] and the massively parallel construction of artificial chimeric nanostructures with complex geometries or patterns by DNA self-assembly phenomena [14–18]. When functional groups and materials are incorporated in and out of self-assembled DNA nanoarray, they can serve as excellent platform for the assembly of other species such as metal nanoparticles [19–21] antibodies, [19,22,23] and proteins [24,25]. The DNA nanotubes showed greatly promising application that a range from fabrication of nano-electronic devices to biological analyses and studies has been provided in playing role of the assay platform or array because of their specifications such as their high aspect ratio and a long narrow central channel generated by DNA self-assembly that it can be readily functionalized inside the central channel or at the position facing out of their tubular sidewalls [26–28].

To achieve the surface patterning or positioning, the functionality could come from covalently attached functional groups or molecules (e.g. Thiol, amino, and carboxylic groups or biotin) that those chemically linked to their specific targeted molecules species, such as nanoparticles or proteins [29,30]. Hence, DNA nanotubes play nanocarrier roles for functional hybrid materials and also possess the functional agent properties [31]. Such functionalized DNA nanotubes can serve as excellent platforms for the assembly or capturing of other target molecules with nanometer precision in nanobiosensors designs.

The precise positioning of encapsulated nanomaterials and biomolecules along the nanotube length, whether at interior or exterior surface, has the potential to create chimeric nanotube architectures that those transport materials as a cargo to target point not as a common carrier. Hence, we describe a methodology for fabrication of DNA nanotubes as hybrid nanocarriers for MNPs at their exterior surfaces (Fig. 1) with a high aspect ratio could be used for trapping or carrying biomolecules.

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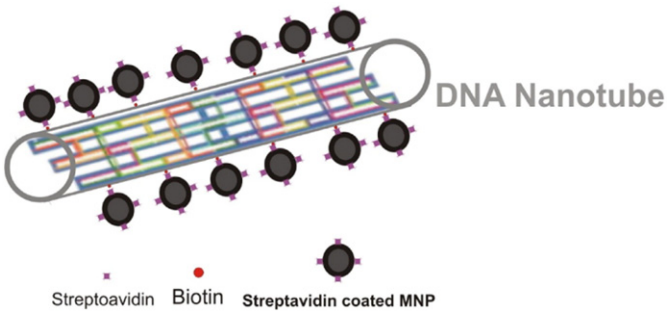

Fig. 1. Schematic of DNA nanotube with an array of exterior magnetic nanoparticles.

2. Materials and methods

2.1. Chemicals and instruments

Thermal condition for self-assembly of DNA nanotube in origami reaction was set using Rotor Gene Q machine (QIAGEN, Germany). Gel electrophoresis experiments were performed using electrophoresis mini set from Bio-Rad (USA). Transmission electron microscopy was done using TEM EM900 (Zeiss EM028, Germany). The micrographs were obtained by JPK-AFM (JPK Instruments AG, Berlin, Germany). Mica was prepared from Nano-technology Systems Corporation, Tehran, Iran. M13mp18phage genome and T4 DNA ligase were purchased from New England Biolabs (Massachusetts, USA). Desired single-stranded oligonucleotides (simple and biotinylated) were synthesized and desalted by Bioneer (Korea). Quantum Prep Freeze 'N Squeeze DNA gel-extraction spin columns were from Bio-Rad. SYBR Gold nucleic-acid gel stain was purchased from Molecular Probes Inc. (Eugene, Oregon, USA). GeneRuler DNA Ladder Mix was from Thermo Fisher Scientific, Inc. (Waltham, MA, USA). Streptavidin (fluidMAG-Streptavidin) magnetic nanoparticles in 100 nm diameter size and MagnetoPURE-Micro-separator were purchased from Chemicell (Germany).

2.2. Computational modelling of nanotube-based templates with sticky ends

Recently caDNAno is introduced as an attractive software to design variable origami shapes. It commonly applies two inputs, including a lengthy scaffold and a group of crossing staples. Using the CadNano software with honeycomb style, staple strand sequences for the folding and fabrication of DNA nanotubes were selected. The M13mp18 phage genome was used as the scaffold DNA strand, and the staples were designed based on their complementarities with the special sites of the scaffold sequence for shaping sticky-ended nanostructures. For the fabrication of surface patterning magnetic DNA nanotubes, considering to the staple strands by surface positioning on DNA nanotube out walls, a group of staple strand were choice for biotinylation and synthesized 5′-biotin staple strands (Table 1).

2.3. Self-assembly condition of DNT structures

In general condition for fabrication of simple DNA nanotubes, the origami reaction was prepared by combining 20 nM DNA scaffold M13mp18 single-stranded DNA and 100 nM of each staple oligonucleotide that were diluted in 1 × Tris base, acetic acid, and EDTA buffer (40 mM Tris–acetic acid buffer, pH 8.0, and 12.5 mM magnesium acetate) and then the mixtures were kept at 95 °C for 5 min, and then annealed from 95 °C to 20 °C with a constant rate of − 1 °C/min in the thermocycler. For the fabrication of long and sturdier DNA nanotubes, the origami products were treated by ligation process with T4 DNA ligase. The ligation-reaction mix was prepared containing 2 μL of 10× T4 DNA ligase reaction buffer, 10 μL of self-assembled DNA nanotubes, 2 μL of 50% polyethylene glycol, and 1 μL of T4 DNA ligase enzyme. Finally, the ligation mix was incubated at 37 °C for 1 h.

Table 1
Staple oligomer sequences for self-assembly of DNA nanotubes.

No.	Sequence (5′ to 3′)
1	Bio-CCAACGTGCAGGTCATTCGTA
2	Bio-CACTATTCCGGTTCATGGTCG
3	Bio-TTCCAGTTCCCTTAAGCAGGC
4	Bio-GAGATAGGGTTGACGCGCGGGGAGAGGCGGT
5	Bio-ACGGCCAGTGCCTGTTTCCTG
6	CATGCCTCAAAGGGGCGCTCA
7	GAGGATCAAAGAACGTCGGGA
8	GGCAAAATTGGAACGCTGCAT
9	ATCATGGGCTCACAAATGAGTGAGCTAACTCAC
10	GGTACCGACGAGCCAGTGTAA
11	GAAAATCTTGCCCTCACCAGT
12	Bio-CATGCCTCAAAGGGGCGCTCA
13	Bio-TGTGAAATTGTTATCCTCATAGCAAGCTTG
14	ACAACATAGCTCGAGACTCTA
15	CAGCTGACTGTTTGCGAAATC
16	CTGGCCCTTGCCCCTAAATCAAAAGAATAGCCC
17	AGCCTGGCTTTCCAGTGGACT
18	GAGACGGCGTGCCAAAGAGTC
19	GTGGTTTTCGGCCAAGTGTTG
20	Bio-TTGCGTATTGGGGTTGCAGCA
21	Bio-ATTAATTGCGTTCGAAAAACCGTCTATCACG
22	Bio-CTGCCCGGGTGCCTATTCCAC
23	Bio-AACCTGTGCCATAAGGAAGAA
24	Bio-TAATGAATTCTTTTTCACCGC

2.4. DNT exterior surface positioning of MNPs

After fabrication of biotinylated DNTs, The nanotubes were separated from the reaction materials via electrophoresis in 1% agarose gel. The attended bond on the gel for long and sturdier DNA nanotubes was extracted by quantum prep freeze N squeeze DNA gel extraction spin columns according to the manual instruction. The extracted DNTs were mixed with 2.5 × 10–3 mg/mL streptavidin coated MNPs and then incubated at 37 °C for 5 min.

2.5. Transmission electron microscopy of magnetic DNTs

The TEM was used to determine and conform the size and morphology of DNA nanotubes. For this purpose, the magnetic DNA nanotubes fabricated were immobilized by syringe spraying on Agar Scientific (Stansted, Essex CM24 8GF, United Kingdom) holey carbon film with 300-mesh Cu(50) and micrograph of DNTs was obtained by TEM EM900 (Zeiss EM028, Germany).

2.6. Atomic force microscopy of magnetic DNTs

Five microliter of fabricated magnetic DNA nanotubes was immobilized on a mica surface for 4 h at room temperature (25 °C) to be dried. The samples were studied using contact mode with JPK-AFM, with 150 Hz IGain, 0.0048 PGain, and 1.0 V set point via a JPK NanoWizard control. The cantilever was ACTA-10 probe model (material: silicon, N-type, 0.01–0.025_/cm). Rough data were graphically processed with the JPK nano-analyzer software.

3. Results and discussions

3.1. Computational architecture of DNA nanotubes

The architecture nanotube obtained from caDNAno software was demonstrated in Fig. 2. The model consisted of a cylindrical scaffold assembled with the staples from the oligonucleotides. The scaffold has been formed from six single-stranded DNA with the M13mp18