DNA Arrays with Site-Specific Labels

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DNA arrays on substrates are an increasingly popular tool for directed self-assembly of nanoscale architectures. They can be made by a variety of methods, including "DNA curtains" and DNA origami attached to on lithographically-defined surfaces.[1, 2] The resolution of such arrays can be further defined by functional nanostructures specifically attached to predetermined base pairs on DNA molecules, which are then anchored to nanoscale surface features. DNA labels can involve chimeras made with peptide nucleic acid (PNA) or locked nucleic acid (LNA). A third way is a nick-translation process. Because of their sequence tunability, PNA, LNA, and nick-translation can be useful new tools for enabling directed self-assembly of DNA structures on lithographically-patterned surfaces.

Au nanoparticles have been attached to double-stranded (ds) DNA via PNA triplex invasion.[3] In this method, 200 base-pair fragments of ds-DNA are incubated with 25 base-pair long single-stranded (ss) PNA-DNA chimeras at 50°C overnight. The elevated temperature activates "breathing modes" in which individual DNA strands come apart slightly. In contrast to DNA's negatively-charged sugar-phosphate backbone, PNA has a neutrally-charged peptide backbone,[4] allowing the ss-PNA-DNA chimera to preferentially invade the charged DNA helix. It is possible to tune the PNA sequence and incubation time and temperature in order to invade specific sites on λ-DNA, which measures 16μm in length.[5,6]. This could enable site-selective placement of nanoscale architectures over length scales far exceeding the dimensions of DNA origami.

LNA is another option for labeling DNA. In each LNA base pair, the furanose ring of the sugar-phosphate backbone is "locked" down by a methylene linker between the 2' oxygen position and the 4' carbon position. This modification raises the melting temperature of an LNA-DNA chimera by several degrees per LNA base pair, allowing preferential binding of the chimera to the base pairs of its target in a DNA fragment. In this work, annealing PNA and LNA to DNA has so far been done with short (45-200bp) double-stranded DNA fragments.

Placement of DNA molecules on a surface can be directed by DNA curtains[1] or by binding them between patterned nanodots, which are functionalized with complementary oligonucleotides. This is illustrated by the schematic in Figure 1. Figure 2 shows directed self-assembly of 60nm length double crossover (DX) DNA on these nanodots.

Nick-translation is another method by which DNA can be labeled.[7,8] Briefly, one strand of double-stranded DNA is nicked, or cut, at specific locations by an enzyme. DNA polymerase is then added to incorporate digoxigenin-dUTP base pairs into complementary nicked sites. These base pairs can then be attached to a fluorescent quantum dot coated with anti-digoxigenin, thus labeling the nicked site. Figure 3 shows a DNA curtain labeled via nick-translation.

Nanofabricated templates offer a starting point for directed self-assembly of double-stranded DNA arrays. Labeling this DNA via PNA, LNA, and nick translation increases the resolution of these methods by enabling the site-specific placement of functional nano-objects (e.g. Au nanoparticles, quantum dots, nanowires, etc.) on surfaces.

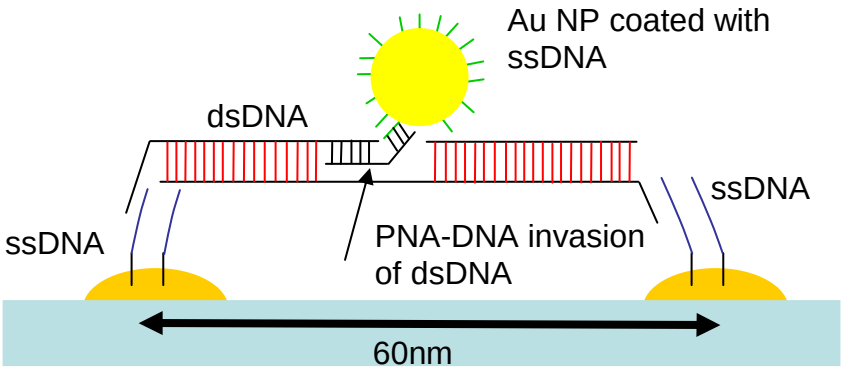

Figure 1. Schematic of labeled double-stranded DNA fragments attached to AuPd nanodots. The fragments have been invaded with a PNA-DNA chimera, which is then bound to an Au nanoparticle functionalized with single-stranded DNA .

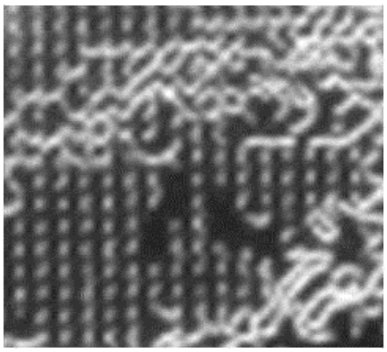

Figure 2. Double-crossover (DX) DNA attached to AuPd nanodots

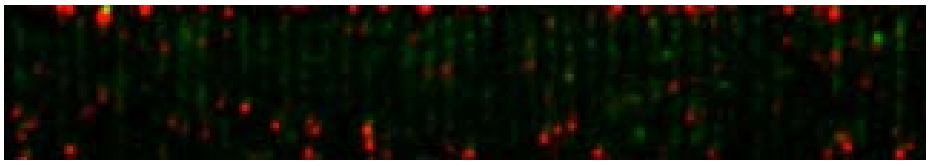

Figure 3. DNA curtain array labeled by nick-translation

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