

Programmed Assembly of Nanoparticles on DNA Templates*

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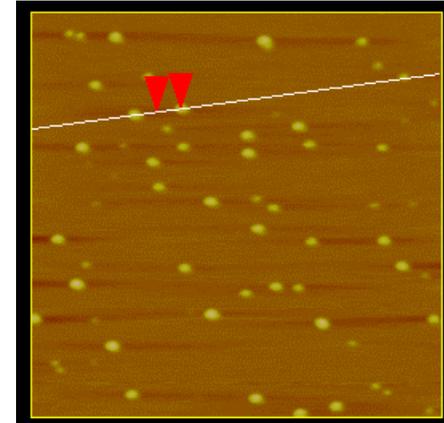
Oak Ridge National Laboratory
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Abstract

The ability to assemble nanoparticles into wires, arrays, networks, and circuits in a precise and controlled manner is key to the fabrication of a variety of nanodevices. The challenge is that fabrication with nanoscale precision of nanoparticle arrays in a time and cost effective manner remains a formidable task. Interest in the concept of self-assembled nanostructures led to the idea of using DNA as a scaffold or template for the programmed assembly of nanoscale arrays. We will describe a new approach for binding nanoparticles to DNA. Functionalized gold nanoparticles have been covalently bound to internal, modified sites on double-stranded DNA. Gold nanoparticles coated with mercaptosuccinic acid or thioctic acid were bound to amino-modified thymine bases on double-stranded DNA. Visible absorption spectra and atomic force microscopy (AFM) were used to analyze the products. Absorption spectra of gold particles in the presence of DNA show a significant hypochromic effect when the gold binds to the DNA and the absorption peak of the particles shifts to a longer wavelength after incubation with DNA. Analysis of AFM images shows that the average height of the DNA between gold particles is 0.74 nm, in good agreement with published values, while the height of the DNA bound to the particles is approximately 3 nm. Thiol groups were added to one end of the gold/nanoparticle product, which was then attached to a gold surface. This method has the potential to allow controlled placement of particles with sub-nanometer precision and to allow attachment of the product to fixed contacts for nanodevice fabrication.

I. Synthesis of Au Clusters

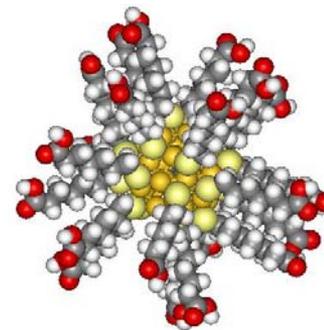
- Produced metal (Au) monolayer-protected clusters (MPC) about 1-2 nm in diameter.
 - Ensure room-temperature “single-electron” operation
 - Passivation plays multiple roles
 - Barrier for cluster growth
 - Defines chemical functionality
 - Contributes to charge transport properties.



• Synthesis Needs:

- Size distribution
- Chemical functionality
- Conducting ligands
- # active chemical functional groups

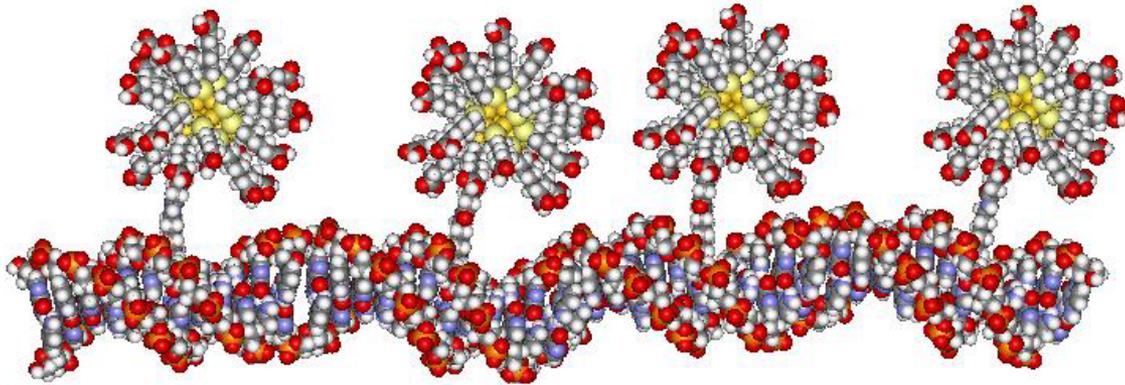
Multiple Carboxyl Groups



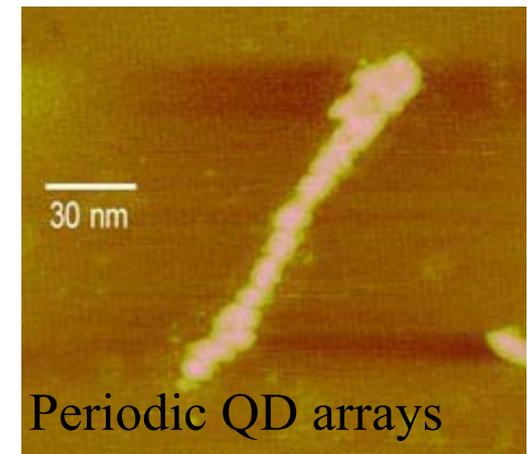
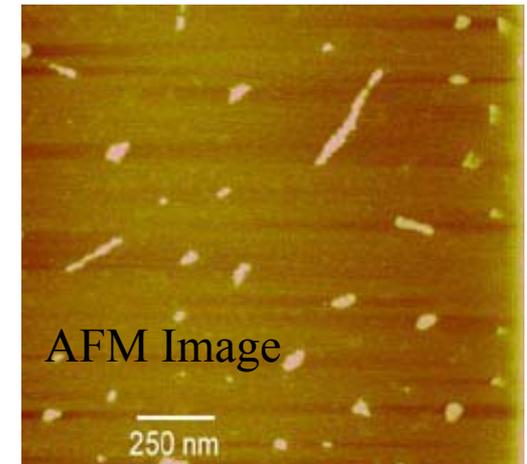
L.Maya, G. Muralidharan, T.G. Thundat, E.A. Kenik, *Langmuir* (2000).
L. Maya, K.A. Stevenson, G. Muralidharan, T.G. Thundat, E.A. Kenik, *Langmuir* (2001).

II. Directed assembly of Au clusters along engineered DNA

- DNA modified with amine groups as binding sites.
- Covalent QD attachment to DNA.

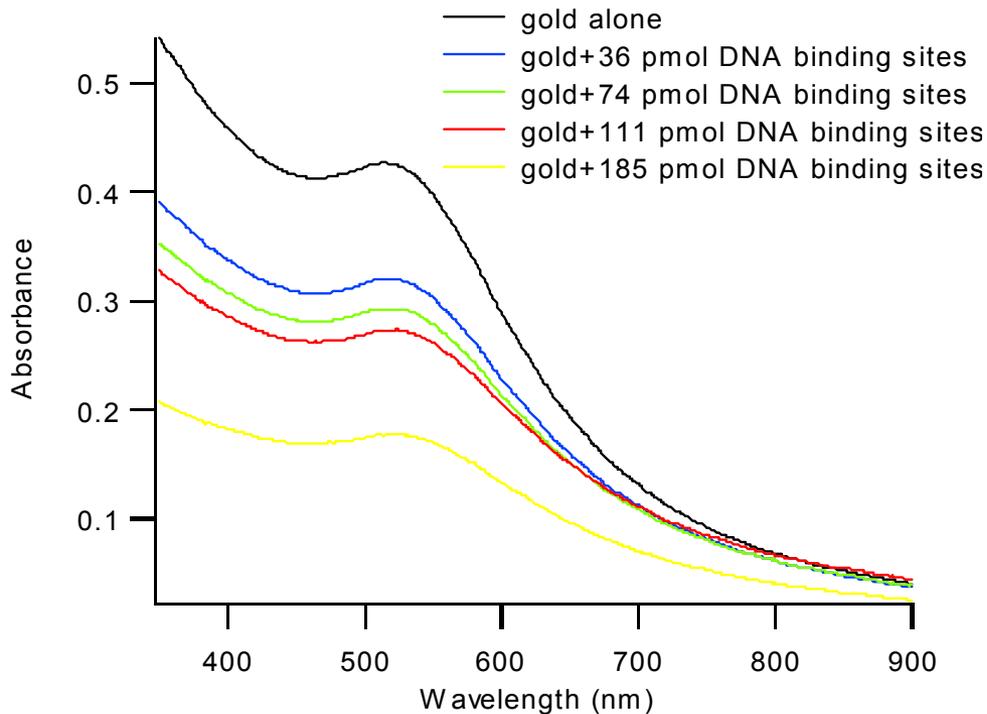


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J. Nanosci. Nanotech. **2**, 397-404 (2002).

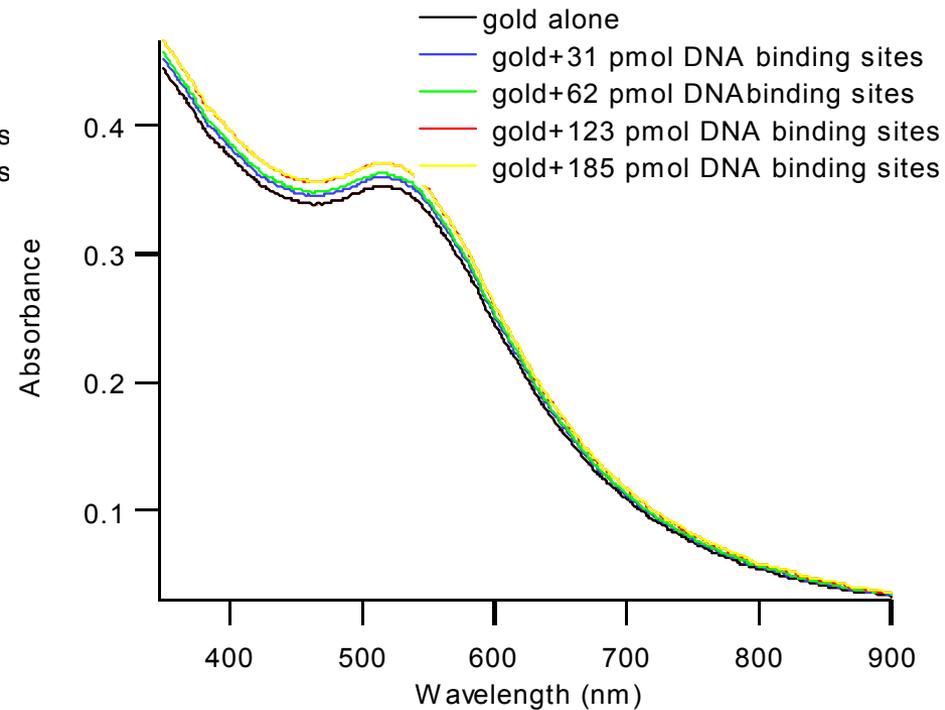


Spectrophotometric Evidence of Nanoparticles Bound to DNA

Activated Gold Bound to DNA

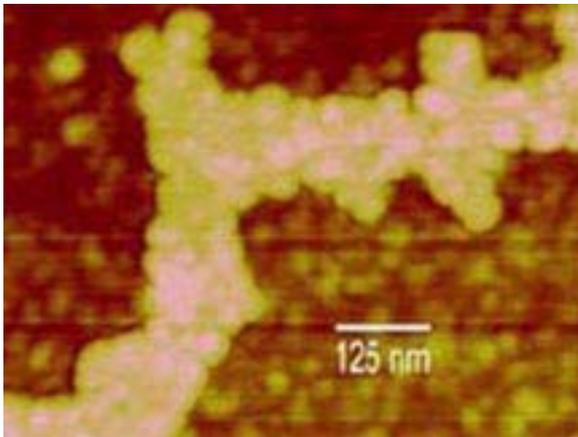


Untreated Gold Mixed with DNA

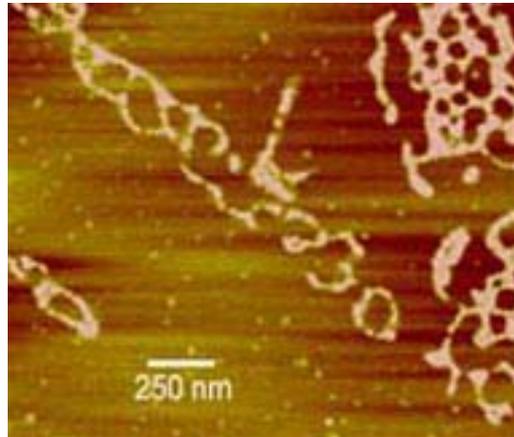


Methyl-Amine “Blockers”

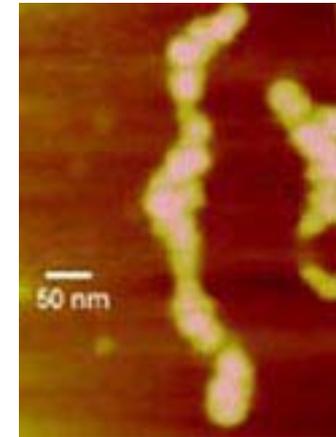
- Use methyl amine (CH_3NH_2) to prevent aggregation.
- This approach:
 - Blocks excess functional units on Au QD.
 - Allows multiple QDs to bond to single DNA template.



Without methylamine



With methylamine



With methylamine

AFM Images

Gel Electrophoresis of DNA+MPC Complex

Gel electrophoresis of DNA and MPC's.

Lane 2: MPC's + DNA in the absence of methylamine.

Lane 3-6: MPC's + DNA and increasing amounts of methylamine.

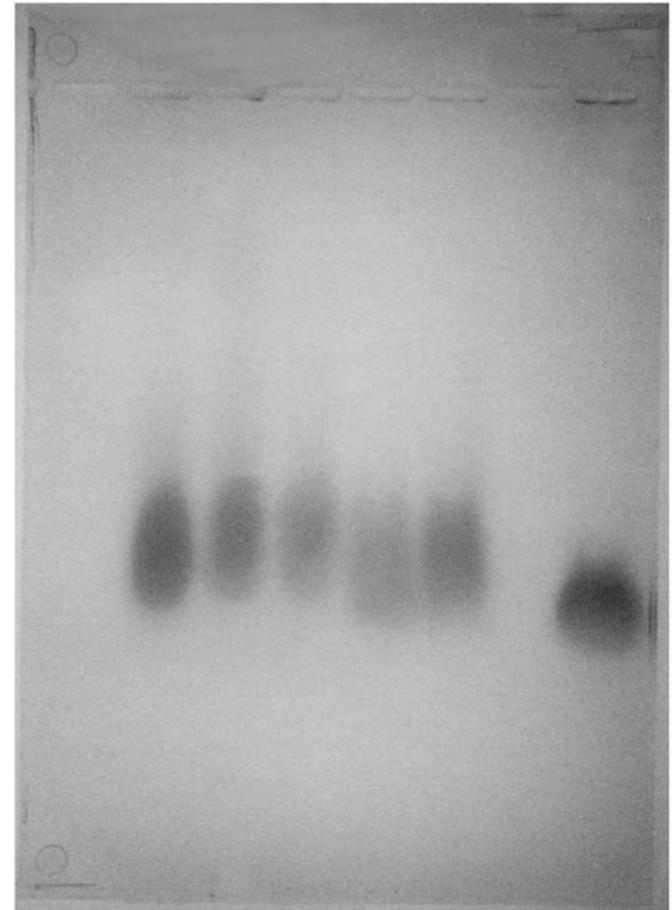
Lane 3: Methylamine concentration twice the concentration of MPC binding sites on the DNA.

Lane 4: Methylamine concentration four times the concentration of MPC binding sites.

Lane 5: Methylamine concentration ten times the concentration of MPC binding sites.

Lane 6: Methylamine concentration twenty times the concentration of MPC binding sites.

Lane 8: Activated gold particles alone.



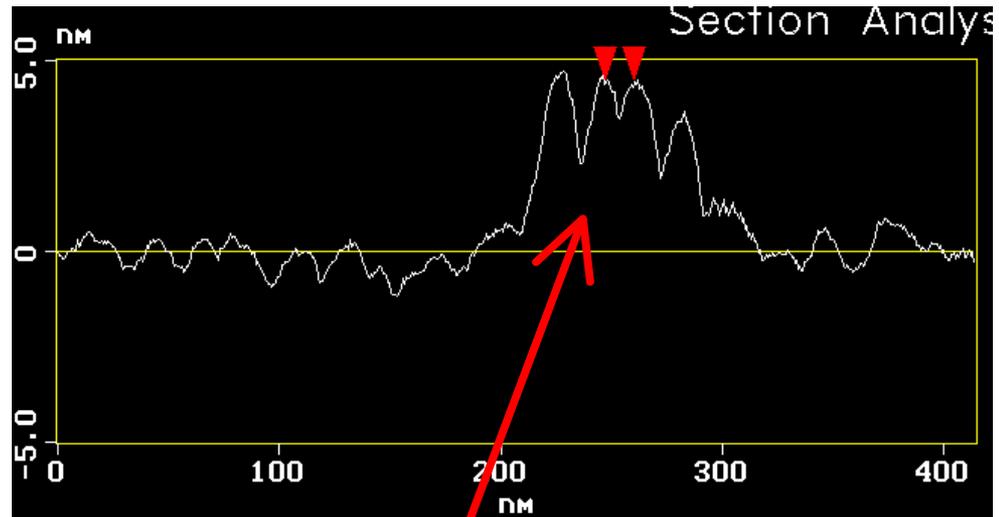
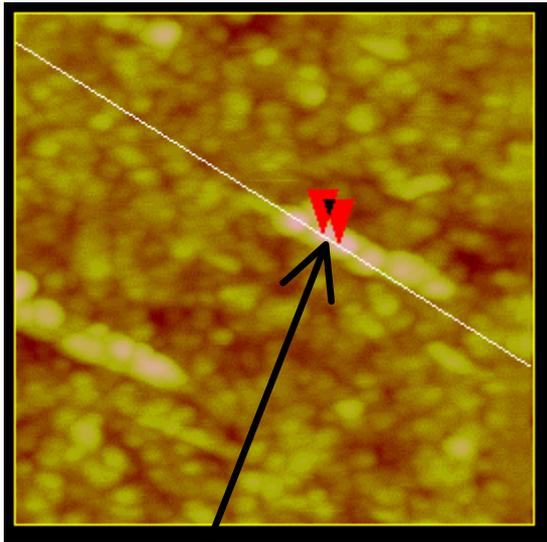
1 2 3 4 5 6 7 8

†Carboxyl groups on nanoparticles were activated with EDC and NHS, then incubated with ligated DNA in the presence or absence of methylamine.

‡The gel was silver-stained to visualize gold.

Periodicity in QD Placement

- Regular 1D Arrays
- Method to covalently bond inorganic nanoparticles to duplex DNA in a programmable fashion.
- Fabrication of nanostructures with nanoscale periodicity.

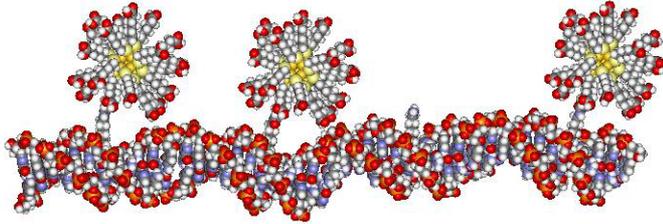


Gold nanoparticles bound to DNA strand with 10 nm spacing.

Small, periodic structures

III. Occupancy Control for QD Assembly

Occupancy Problem: Chemically control the binding site occupancy along the DNA template.



Solution: Synthesize QDs with discrete, controllable number of active functional groups.

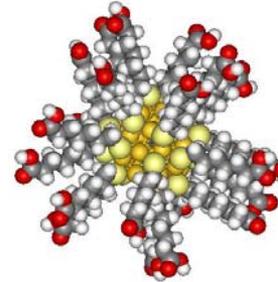
- Allows CH_3NH_2 to be eliminated from the assembly procedure.
- Greater precision & efficiency in assembly.

Approach:

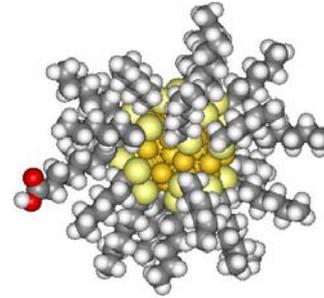
- Ligand exchange reactions to produce distribution of the # binding ligands.
- Separation techniques (e.g., electrophoresis) to identify and isolate ensembles with discrete # of functional groups.

DNA+QDs with 100% COOH coating with a small amount of methylamine present.

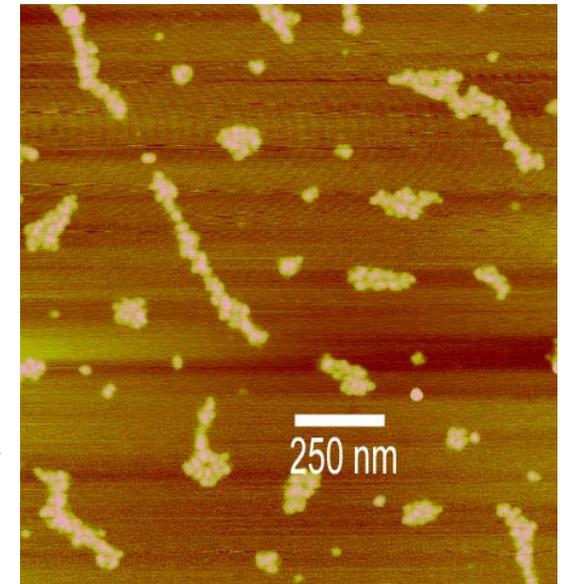
* Notice Over binding & Cross linking.



Each ligand contains active binding site, Resulting in a redundancy of binding.

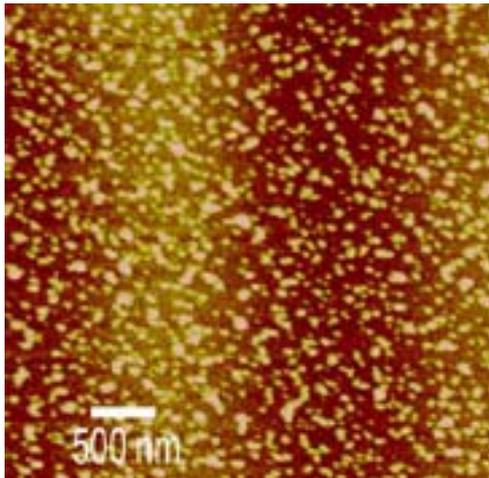


Nanocluster with one active binding site. All other ligands are inactive.

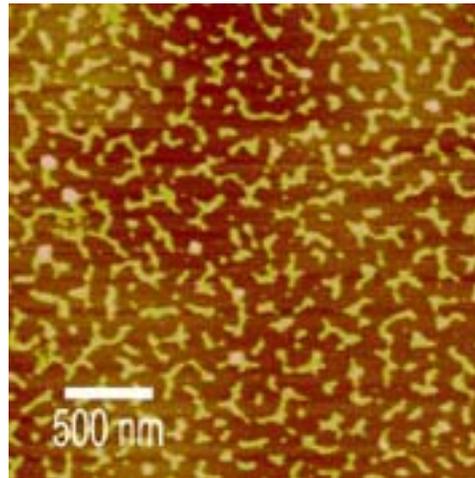


Studies of Occupancy Problem

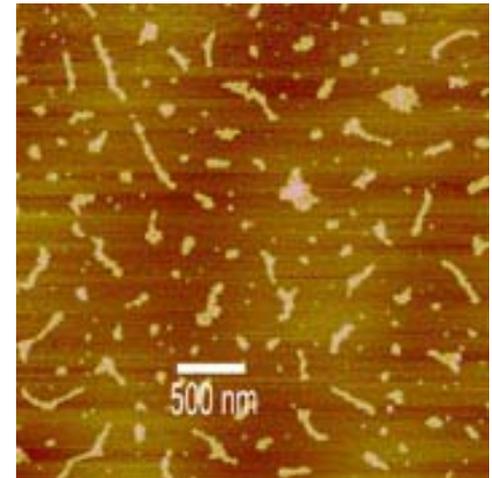
- Reduce amount of methylamine present
- Synthesize nanoparticles with a mixture of reactive carboxylic acid side chains and non reactive alcohol side chains



10% carboxylic acid
little binding



25% carboxylic acid
good binding,
some crosslinking



100% carboxylic acid
good binding,
some crosslinking

Unique Features of MPC Assembly via DNA

DNA is one of the most programmable assemblers available.

Advantages of DNA as assembler:

- Synthesized in any sequence in various lengths and geometries,
- Assembly in massively parallel fashion,
- Modified for attachment of other molecules in a specific manner with subnanometer resolution,
 - Molecular recognition is built into building blocks and template.
- Potentially sub-nanometer resolution (1 nucleotide is 0.34 nm),
- Long-range order/periodicity.
- May be easily removed when role in assembly is complete.

Research Issues: Control site occupation along DNA template.

- Methylamine blocks excess binding sites.
- Improved control of chemical binding sites on QD.

Conclusions

- We have covalently attached functionalized gold along engineered internal sites of double-strand DNA.
 - No “nicks” along the DNA backbone.
 - Double-stranded product retains the regularity that makes DNA an attractive template for assembly.
 - Thiolation after attachment allows greater flexibility in manipulating the DNA+cluster complex.
- Occupancy control is major challenge for approach.
 - Methylamine blocks excess binding sites.
 - Need improved control of chemical binding sites on QD.
- Programmable materials synthesis via DNA templates opens revolutionary vistas:
 - Templated assembly of nanostructures.
 - Synthesis, assembly, and engineering of quantum dot arrays.
 - Innovative nanosensors.
 - Nanoelectronic designs.