Design and Imaging
DNA Nanostructures

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Molecular Self-assembly

Synthesis, SPM microscopy, DFT theory
Molecular self-assembly is the spontaneous association of molecules under equilibrium conditions into stable, structurally well defined aggregates joined by non-covalent bonds.
DNA bases as building blocks

Watson and Crick (53 years ago)

2 strands linked by H-bonds between complementary bases A-T and G-C

15 bases can form $4^{15}$ different sequences
Increasing the complexity

Using SPM techniques to study the self-assembly of:
- Individual Nucleobases
- Complementary Nucleobases
- Nucleosides
- Nucleotides
- Nucleobases with amino acids
- etc....
SPM studies in ambient conditions

- DNA Nanostructures
  - DNA nucleobases
  - DNA modified bases
  - DNA origami
  - DNA 3D objects
  - DNA nanowires
- DNA with amino acids
- DNA with Carbon nanotubes (CNT)
- DNA with proteins
- Locked Nucleic acids (LNA)
- Peptide Nucleic acids (PNA)
- Human Chromosomes
- Force Spectroscopy of Collagen Fibrils
- ...
Self-assembly of Individual DNA/RNA nucleobases at the Liquid-Solid Interface
Scanning Tunneling Microscope (STM)

measuring current [nanoAmperes (nA)]
STM at the Solid-Liquid Interface

STM Probe

Solvent

Monolayer

Substrate

Sample

Highly oriented pyrolytic graphite (HOPG)
Adenine

2D supramolecular network

J. Am. Chem. Soc. 2006, 128, 13305-13311
2D supramolecular networks versus 1D chains

Guanine

Adenine

Cytosine

Thymine

Self-assembly of Complementary DNA/RNA nucleobases at the Liquid-Solid Interface
Can the SPM techniques be used to visualize the base-pairing between complementary nucleobases??
G-U Base pairs

*J. Am. Chem. Soc.* **2008**, *130*, 695-702
Self-assembly of Complementary nucleobases

G-C Base pairs
(Watson-Crick G-C dimers)

NanoLetters, 2006, 6, 1434-1438
A-T Base pairs
(Reverse Hoogsteen ATAT-quartets)

These systems could be useful for host-guest complexation.

J. Am. Chem. Soc. 2006, 128, 13305-13311
### Binding energies of homo-dimers, hetero-dimers, and A-T-A-T Reverse Hoogsteen Quartets

<table>
<thead>
<tr>
<th>Dimer Type</th>
<th>Energy (eV/dimer)</th>
<th>Energy (eV/quarter)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Homo-dimers</strong></td>
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<tr>
<td>A-A dimer</td>
<td>0.486</td>
<td></td>
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<tr>
<td>T-T dimer</td>
<td>0.609</td>
<td></td>
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<tr>
<td><strong>Hetero-dimers</strong></td>
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<td></td>
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<tr>
<td>WC A-T dimer</td>
<td>0.425</td>
<td></td>
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<tr>
<td>Reverse WC A-T dimer</td>
<td>0.418</td>
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<tr>
<td>Hoogsteen A-T dimer</td>
<td>0.423</td>
<td></td>
</tr>
<tr>
<td>Reverse Hoogsteen A-T dimer</td>
<td>0.422</td>
<td></td>
</tr>
</tbody>
</table>

**Quartets**

<table>
<thead>
<tr>
<th>Quartet Type</th>
<th>Energy (eV/quarter)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WC A-T-A-T quartet</td>
<td>0.35</td>
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<tr>
<td>Reverse WC A-T-A-T quartet</td>
<td>0.01</td>
</tr>
<tr>
<td>Reverse Hoogsteen A-T-A-T quartet</td>
<td>1.20</td>
</tr>
<tr>
<td>Hoogsteen A-T-A-T quartet</td>
<td>1.24</td>
</tr>
</tbody>
</table>
A-T-A-T Reverse Hoogsteen quartet

2D monolayer of A-T-A-T Reverse Hoogsteen quartets stabilized by A dimers chains

Summary 1

- STM technique is a very powerful Nano-tools” which allows us to extract a wealth of information from self-assembled molecular systems with much higher resolution at the single molecule level than any other technique.

- The non-covalent” interaction can steer the molecular self-assembly process, leading to the creation of supramolecular nanostructured surfaces.

- Watson-Crick and Reverse Hoogsteen base pairing can be visualized for the first time by STM with submolecular resolution.

- DNA/RNA nucleobases are good candidates to create 1D and 2D surface functionalized patterns and host-guest complexation with amino acids, other nucleobases, other guest molecules, etc..

- DFT Calculations are very useful in predicting the molecular structures.
DNA Nanostructures
Introducing Complexity
DNA assembly of 2D Nanostructures

- Parallel double helices
- Very rigid
- Has been used as building block in many different structures


A) A 4×4 DNA tile used for construction of a DNA lattice or a DNA wire.

B) Individually addressable 16 pixel DNA print board used for writing D-N-A; structures were imaged by AFM on mica.

C) Self-Assembling molecular pegboard containing individually addressable sequences

Au nanoparticle arrays assembled on the 2D DNA nanogrids. a) shows the A and B tile sequences used for the nanogrid assembly. A tile contains an A15 sequence protruding out of the tile. T15 conjugated 5nm gold nanoparticle is represented as yellow ball. b) Hybridization of the DNA-Au conjugate to A tile leads to periodical 2D Au-nanoparticle arrays. c) AFM images of the Au nanoparticle arrays. d) a 3D view of the 2D Au nanoparticle array.

• DNA Origami (Folding Paper) method
  (Rothemund, Nature 2006)

1 x M13 ssDNA + 200 x staples
DNA origami

Modifying the Origami
Trapping DNA origami structure with dielectrophoresis

a) Schematic view of the origami trapping experiments. b) AFM image of origami structures used for DEP trapping. The image is taken on a MICA surface using tapping mode AFM in liquid. c) AFM image of a single smiley. d) Rectangular origami trapped with the optimal DEP parameters (on SiO₂ surface, tapping mode AFM in air). The scale bar is 100 nm.

Anton Kuzyk et al., Small 2008, 4, 447–450
DNA Origami Design of Dolphin-Shaped Structures with Flexible Tails

Ebbe S. Andersen, et al. ACS NANO 2008, 2, 6, 1213-1218
DNA-programmed assembly of 2D DNA nanostructure

Ebbe S. Andersen, et al. ACS NANO 2008, 2, 6, 1213-1218
Design of an unsymmetrical dolphin

- Dolphin structure provides complexity
  1. eye (hollow structure)
  2. fin (accurate 90 degree)
  3. tail (narrow part with higher flexibility)

- Unsymmetrical structure

Complexity
Flexibility
AFM Manipulation
Dimerization
Recognition
Chirality
World’s smallest dolphin
Observation of Flexible Origami Tails

Ebbe S. Andersen, et al. ACS NANO 2008, 2, 6, 1213-1218
Origami recognition

Positioning DNA origami structures placed by specific interconnections at well-defined and known positions

The assembly of 2 dolphins can be accomplished by placing sticky end and receptor sites on the abdomen and on the back which help to identify two types species (even identical origami)

Ebbe S. Andersen, et al. ACS NANO 2008, 2, 6, 1213-1218
Self-Organisation

- To form any useful macroscopic function, the structures must be placed into *well defined and known positions*, with specific interconnections.

- Key techniques to produce *ordered* or *interacting* structures are based on chemical interactions between *specific molecules or parts of molecules*.

- Design *different molecules interact* is the key to unlocking this technology.

- Ideally, complete *structures or circuits* will be grown from *solution* by single or multiple interaction.
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