Today’s Overview

– Introduction to nanoscience and technology
  – How does light interact with matter on the nanoscale?
  – Emergent properties: Transition from the bulk to the nanoscale
  – Colloids
– Interfacing nanomaterials with DNA
  – Design rules for new materials
  – Applications of spherical nucleic acids

Image Courtesy of Bawendi and Coworkers.
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There’s Plenty of Room at the Bottom

“I am not afraid to consider the final question as to whether, ultimately—in the great future—we can arrange the atoms the way we want; the very atoms, all the way down!“

-- Richard Feynman

December 26, 1959
California Institute of Technology

Feynman, R. Engineering and Science 1960, 23(5), 22–36.
Historical Significance of Nanomaterials

Observation of Nanoscale Phenomena

1857

Early Understanding of the Nanoscale/Era of Miniaturization


Rational Design and Manipulation of Nanoscale Objects

83nm
Tools for Studying Nanoparticles

- **Scanning Electron Microscope (SEM)**
- **Transmission Electron Microscope (TEM)**
- **Scanning Tunneling Microscope (STM)**


Courtesy Hersam and Coworkers
1. Developing tools for making, characterizing, and manipulating materials on the nanometer (nm) length scale

2. Determining the chemical and physical consequences of miniaturization.
Size, Shape, and Composition Matter

Rayleigh Light Scattering of Nanoparticles

Ag Nanoprisms: ~100 nm
Au Spheres: ~100 nm
Au Spheres: ~50 nm
Ag Spheres: ~100 nm
Ag Spheres: ~80 nm
Ag Spheres: ~40 nm

200 nm (the same for all the images)
Defining Nanotechnology

1. Developing tools for making, characterizing, and manipulating materials on the nanometer (nm) length scale.

2. Determining the chemical and physical consequences of miniaturization.

3. Exploiting the ability to miniaturize and its consequences in the development of new technology.
Nanostructured Materials Can Improve Energy Generation, Conversion, and Storage

Catalysis

Solar Energy Harvesting

Nanoporous Materials for Energy Storage


The Importance of Surface Area in Nanotechnology

Total Surface Area = 1
Total Volume = 1

Total Surface Area = 1.26
Total Volume = 1

Total Surface Area = 1.58
Total Volume = 1

300 Million Trillion
5 nm Nanoparticles

= 

A volume of nanoparticles that can fit in the palm of the hand have the same surface area as a soccer field

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The Size of a Nanomaterial Changes How Light Interacts

• For many semiconductors, such as CdSe, their color can be tuned with size.
  – An electron is excited from the valence band to the conduction band by incident light. When the electron returns to the valence band, it releases light related to the band gap of the material.

![Conduction Band](image1)

![Valence Band](image2)

2.3 nm
4.2 nm
4.8 nm
5.5 nm
Larger Band Gap
Smaller Band Gap

Courtesy of Bawendi and Coworkers.
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Applications of Quantum Dot Emission

Light Emitting Diodes (LEDs)

Medical Imaging
Attachment of DNA to Nanoparticles

- DNA strands can be chemically modified with an “anchor” (a -SH end group) that attaches DNA to a nanoparticle surface.

Add DNA with -SH endgroup → Add salt

Citrate-capped nanoparticle

Spherical nucleic acid: a new form of DNA
Spherical Nucleic Acids: New Forms of Programmable Matter

• Two nanoparticles with single-stranded DNA can connect to each other via DNA hybridization.
  – When the nanoparticles are brought together, they interact with each other to produce a color change.

When a’b’ is a piece of DNA or RNA from a virus or bacteria – simple colorimetric detection at low target levels!

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A New Field of Chemistry: Nanoparticles as “Atoms” and DNA as Programmable “Bonds”

atoms → electron-based bonds (covalent, ionic, metallic) → molecules → materials

programmable-atom bonds → programmable materials
Programming Crystalline Architectures: Enthalpy is Dominant Consideration

FCC

CsCl

Cr$_3$Si

NaCl

BCC

AlB$_2$

Cs$_6$C$_{60}$

Simple Cubic

*Science* 2011, 334, 204.

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Comparison of Atomic Lattices and DNA-Nanoparticle Superlattices

Atomic Lattices

**Building block: Atoms**
- For a given element, with a given set of properties, there is **no control over size**.

DNA-Nanoparticle Superlattices

**Building block: Nanoparticles**
- Act as “programmable atom equivalents”
- For a given nanoparticle, the **size and composition can be changed** to change the properties.

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# Comparison of Atomic Lattices and DNA-Nanoparticle Superlattices

## Atomic Lattices

### Connection between building blocks:

*Atomic orbital overlap*

- Crystal structure will maximize the number of nearest neighbors.
- **Can not tune the structure or the spacing between atoms.**

![Gold atoms: FCC crystal structure 288 pm lattice spacing](image)

## DNA-Nanoparticle Superlattices

### Connection between building blocks:

*DNA*

- Overlap, or hybridization, between single DNA strands serves as “bonds.”
- The strength of these interactions can be manipulated by the length and sequence of the complementary DNA strands.
- **Can tune the spacing between nanoparticles by changing DNA.**


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DNA-Mediated Assembly of Gold Nanoparticles

• Together, this allows one to change:
  – The size of the building blocks (particle size)
  – The spacing between the building blocks (lattice parameters)
  – How the building blocks are arranged (crystallographic symmetry)
Q: Which of the following is NOT true about the difference between atomic lattices and DNA-Nanoparticle superlattices?

1. The distance between building blocks is fixed in both systems.
2. The size of a nanoparticle building block can be changed without changing composition.
3. The size of an atomic building block can not be changed without changing composition.
Design Rules for DNA-Mediated Nanoparticle Assembly

Rule 1: DNA-functionalized gold nanoparticles will assemble to maximize the number of nearest neighbors to which it can make connections.

- The more strands that a particle can bind to, the more stable it will be.
Q: Which atomic crystal lattices has the greatest number of nearest neighbors?

1. Simple Cubic
2. BCC
3. FCC
4. ZnS (Diamond)
Self-Complementary DNA Results in a Face-Centered Cubic Lattice (FCC)

- All particles are complementary to each other, which results in a FCC lattice with 12 nearest neighbors for each particle.
DNA-Mediated Assembly of Gold Nanoparticles

Self-complementary DNA sequences: a one-particle system

Complementary, but not self-complementary DNA sequences: a two-particle system

Science 2011, 334, 204.
Chad A. Mirkin
Complementary (but not *Self-Complementary*) DNA Sequences

- The crystal structure with the greatest number of nearest neighbors will still form, but now it’s a two-particle system.
  - Only complementary particles can attach to each other.
DNA-Mediated Assembly of Gold Nanoparticles

- Pauling’s Rules predict ionic crystal structures with two-component systems as well.
  - For Pauling’s Rules, they are cations and anions. Only cations were attracted to anions.

<table>
<thead>
<tr>
<th>Radius Ratio</th>
<th>Cation Coordination</th>
<th>Anion Geometry</th>
</tr>
</thead>
<tbody>
<tr>
<td>$0.225 &lt; \frac{r_c}{r_a} &lt; 0.414$</td>
<td>4</td>
<td>Tetrahedron</td>
</tr>
<tr>
<td>$0.414 &lt; \frac{r_c}{r_a} &lt; 0.732$</td>
<td>6</td>
<td>Octahedron</td>
</tr>
<tr>
<td>$0.732 &lt; \frac{r_c}{r_a} &lt; 1$</td>
<td>8</td>
<td>Cube</td>
</tr>
</tbody>
</table>

- For particles with similar size, the greatest number of nearest neighbors is 8.
DNA-Mediated Assembly of Gold Nanoparticles

- Pauling’s Rules predicted a BCC crystal structure for ions with approximately equal radii. This occurs for nanoparticles as well.

- Remember: Pauling’s rules depend on fixed cation and anion ratios.
DNA-Mediated Assembly of Gold Nanoparticles

- With DNA and gold nanoparticles, the crystal structure can be maintained, while the sizes of the building blocks are varied.
  - Decrease in nanoparticle size compensated by increase in DNA length.
  - For each set of nanoparticles, a BCC-like crystal structure will form.
Rule 2: The overall hydrodynamic radius of a DNA-NP dictates its assembly and packing behavior.
The Final Application: Spherical Nucleic Acids (SNAs) – A New Form of DNA

13-nm Au NP
~67,500 atoms

40-mer Oligo-Nucleotide 1,400 atoms

- Synthetically Programmable Recognition
- Multivalency and Multi-functionality
- New Properties: Cooperative binding, Catalysis

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Spherical Nucleic Acids for DNA Detection: HIV, Ebola Virus, Smallpox, and Hepatitis B

1. Target DNA
2. SNA Probe
3. Gold or Silver Reduction

Target is present
Target is not present

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Verigene™ System

- Direct genomic detection
- ~100 aM (10^{-18}) LOD
- Multiplexed targets
- Automated assay process
- Ease of use
  - Minimal training required
  - Automated data tracking
  - No interpretation required
  - Fast (less than 2 h)

https://www.luminexcorp.com/the-verigene-system/

FDA-Cleared Hypercoagulation, Warfrin Metabolism, Cystic Fibrosis, Influenza and Blood Stream Infection Assays
SNAs Enter Cells Rapidly And Efficiently

Free ssDNA (fluorophore labeled)

Fluorophore-labeled SNA

C166 Cells

0 h 0.5 h 1 h 2 h
Nano-Flares for mRNA Detection

Flare Bound – Flares are Dark

Short Duplexes

Target (mRNA)

Longer Duplex Formed

Flare Released – Flare Lights Up

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The Promise of Gene Regulatory Oligonucleotides

DNA → Transcription → Messenger RNA → Translation → Protein

Increase in disease
The Promise of Gene Regulatory Oligonucleotides

DNA → Transcription → Messenger RNA → Translation → Decreased to normal state → Protein

Antisense DNA → Small interfering RNA
Spherical Nucleic Acids for GBM Brain Tumors: New Treatments for Cancer

Saline  SNA

brain tumor

The skin  The brain
Topical intravenous injection delivery

Immuno
therapy
Subcutaneous injection

SNAs in brain cancer

SNA drugs are used in human as a brain cancer treatment with Phase 0 clinical trials ongoing (e.g., NU-0129)

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Conclusions

- **Concepts Learned**
  - DNA is a chemically rich biopolymer that can be used as a smart “glue” in nanomaterials science
  - Nanoparticles have size, shape, and composition-dependent properties
  - Programmable atom equivalents are analogous to atomic systems in many ways, but with key differences that enable novel technological development

- **Technologies Enabled**
  - Programmable atom equivalents are synthons in materials science
    - e.g., Colloidal crystals as metamaterials, lenses, catalysts
  - Spherical nucleic acids are powerful diagnostic probes and therapeutic agents
    - e.g., Verigene, Nano-Flares, gene regulation agents for cancer treatment