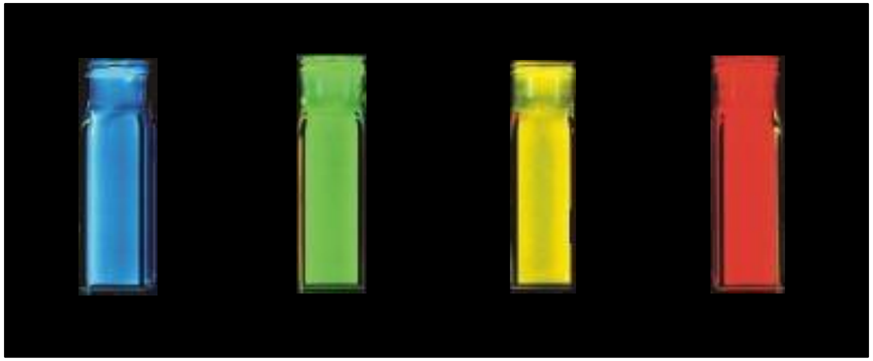
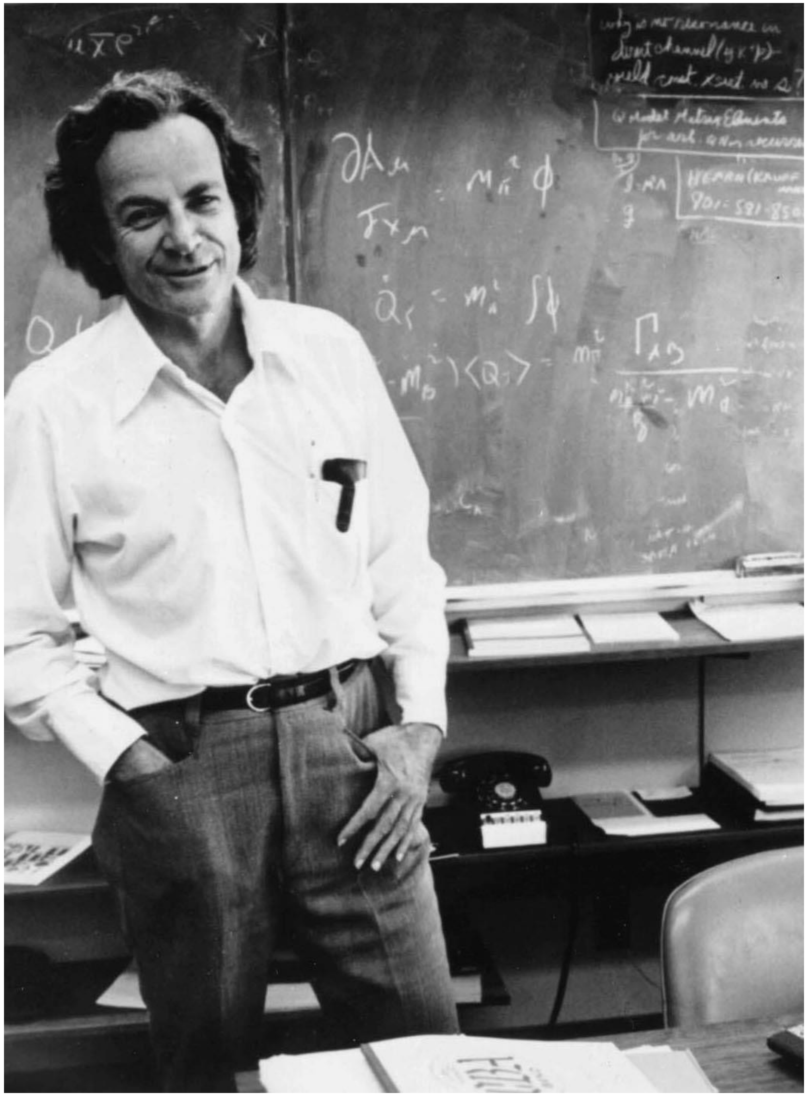
Today's Overview

- 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



There's Plenty of Room at the Bottom



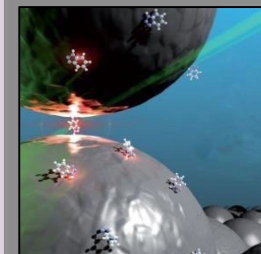
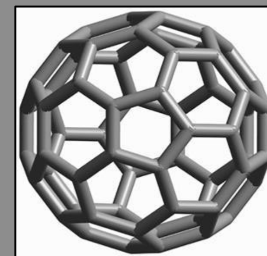
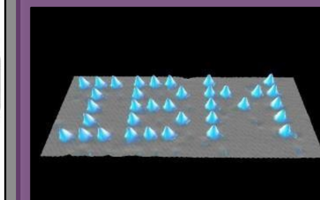
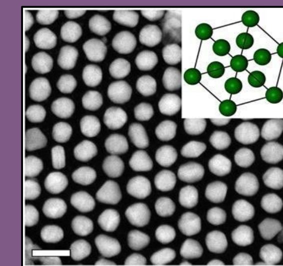
"I am not afraid to consider the final question as to whether, ultimately —in the great future — we can arrange the atoms the way we want; the very atoms, all the way down!"

-- Richard Feynman

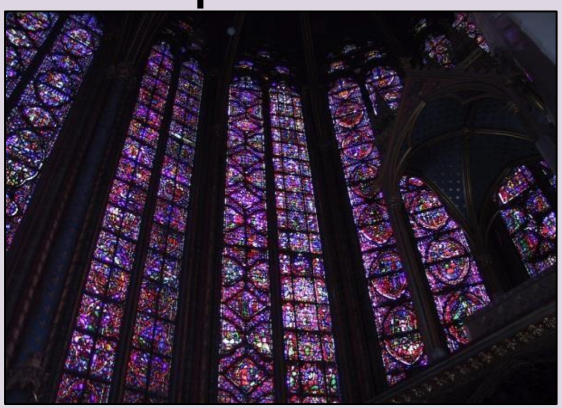
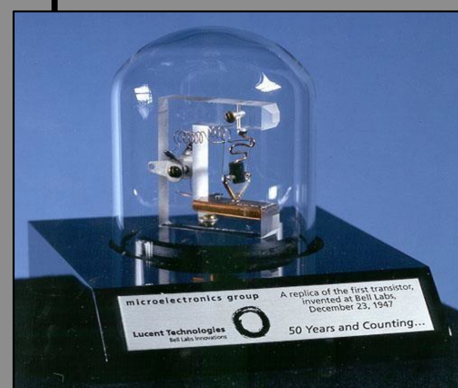
December 26, 1959
California Institute of Technology

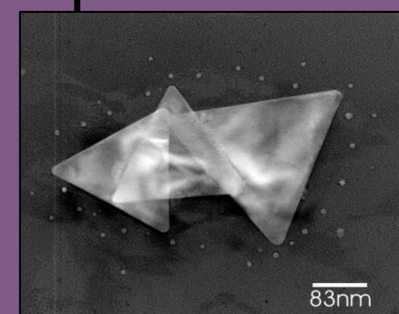
Historical Significance of Nanomaterials



300 | 1500 | 1857 | 1947 | 1974 | 1985 | 1990s | 2000s

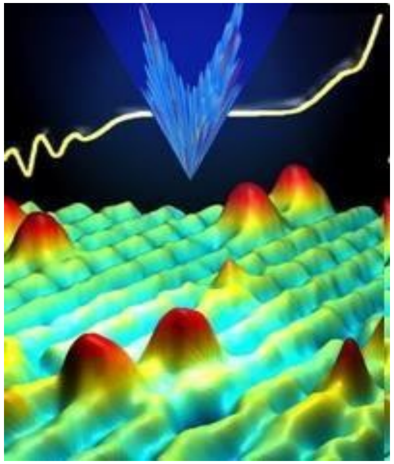


Observation of Nanoscale Phenomena

Early Understanding of the Nanoscale/ Era of Miniaturization

Rational Design and Manipulation of Nanoscale Objects

Tools for Studying Nanoparticles



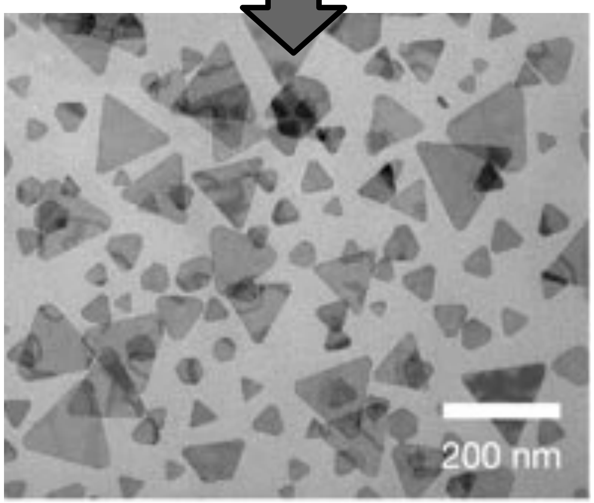
Courtesy Hersam and Coworkers

Scanning Electron Microscope (SEM)

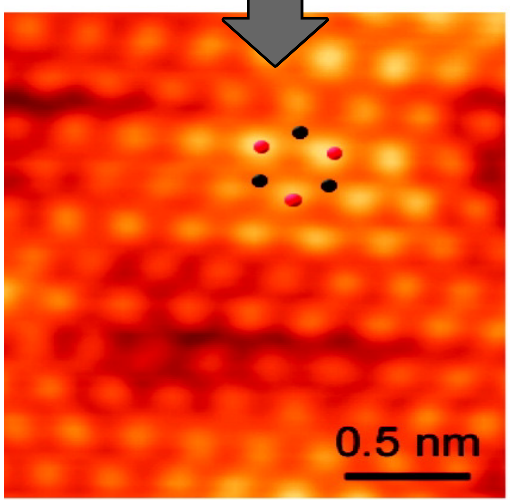
Transmission Electron Microscope (TEM)

Scanning Tunneling Microscope (STM)

Qin, L.; Mirkin, C. et al. *Science* **2005**, *309*(5731), 113.



Jin, R.; Mirkin, C. et al. *Nature* **2003**, *425*, 487.



Hossain, Hersam, et al. *JACS* **2010**, *132*, 43, 15399.

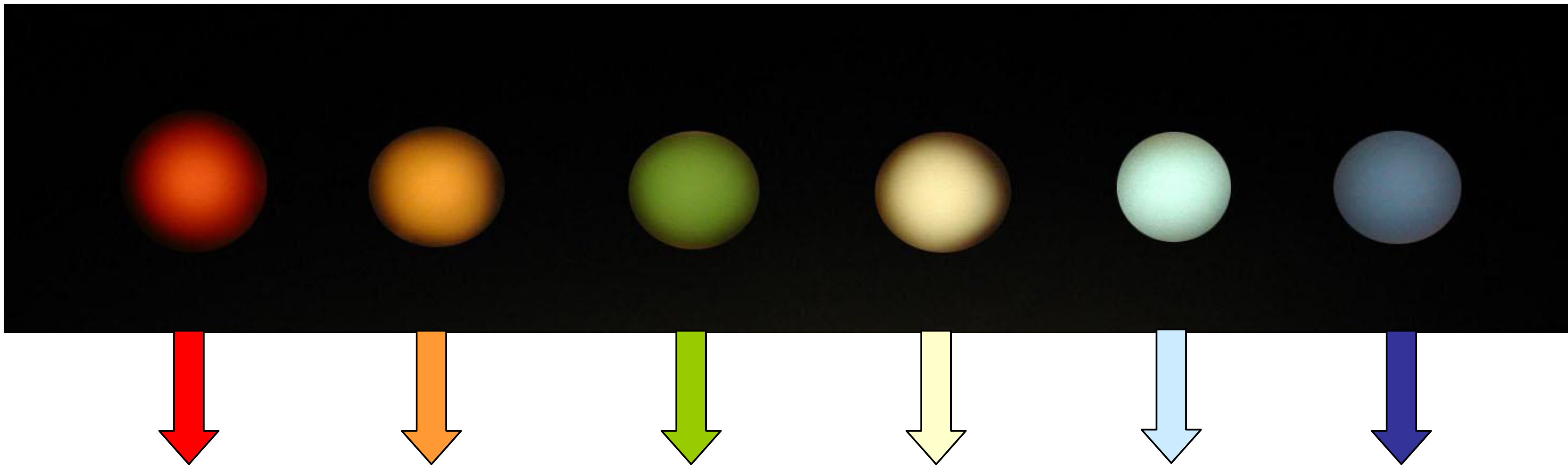
Defining Nanotechnology

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

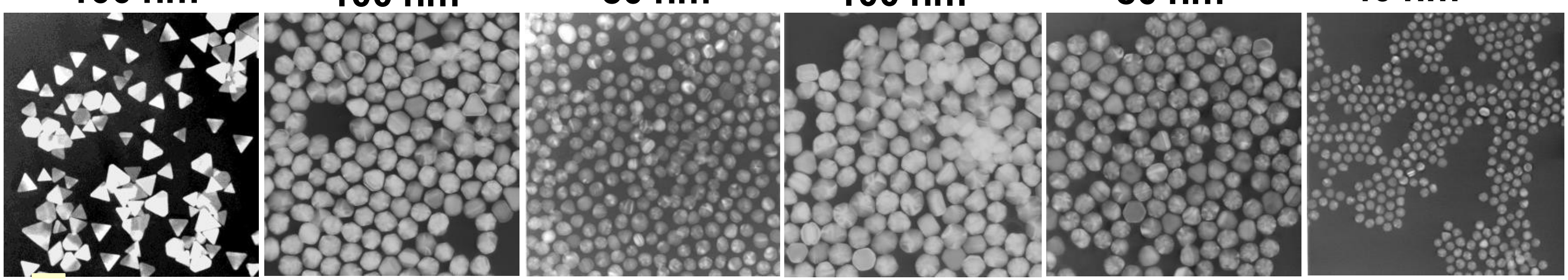
2. **Determining the chemical and physical consequences of miniaturization.**

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

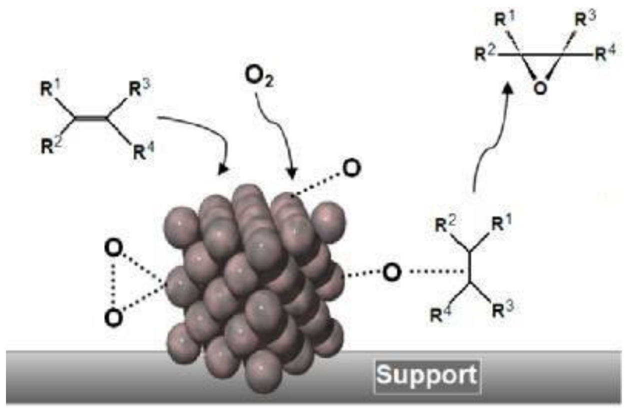
1. Developing tools for making, characterizing, and manipulating materials on the nanometer (nm) length scale

2. Determining the chemical and physical consequences of miniaturization.

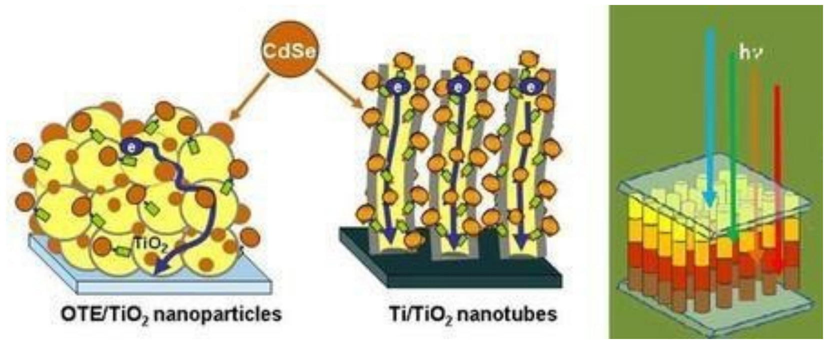
3. Exploiting the ability to miniaturize and its consequences in the development of new technology.

Nanostructured Materials Can Improve Energy Generation, Conversion, and Storage

Catalysis

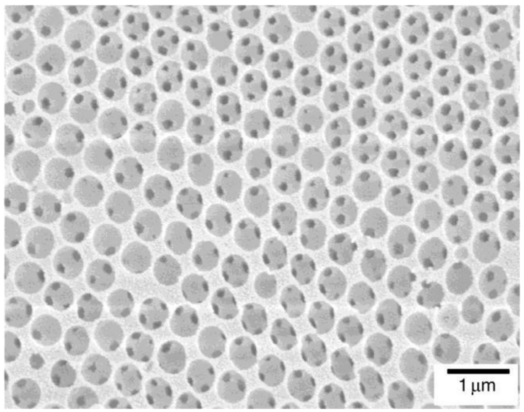


Solar Energy Harvesting

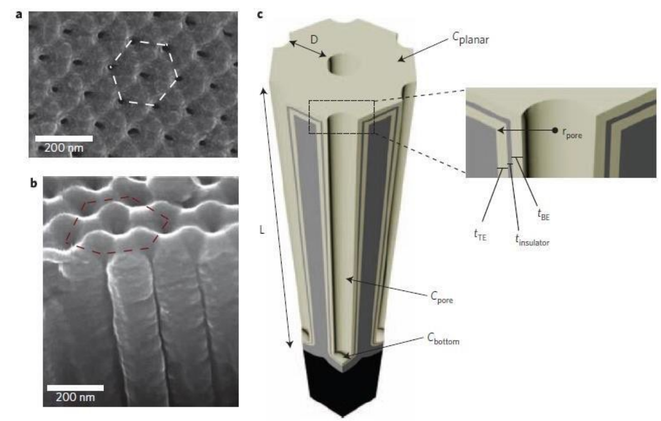


Kongkanand, A.; Kamat, P. V. et al. *J. Am. Chem. Soc.* **2008,** *130*(12), 4007.

Nanoporous Materials for Energy Storage

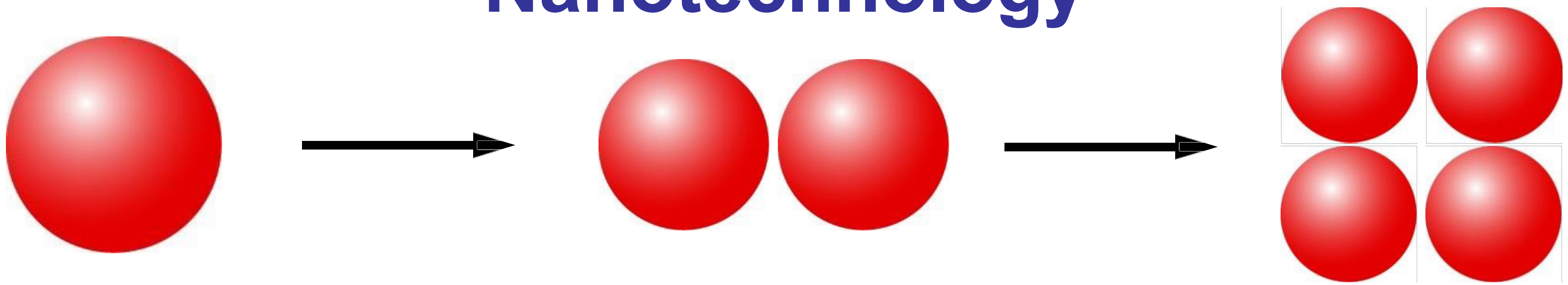


Subramanian, G.; Pine, D. J. *Adv. Mater.* **1999,** *11*, 1261.



Banerjee, P.; Lee, S. B.; Rubloff, G. W. et al. *Nat. Nanotechnol.* **2009,** *4,* 292.

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

…

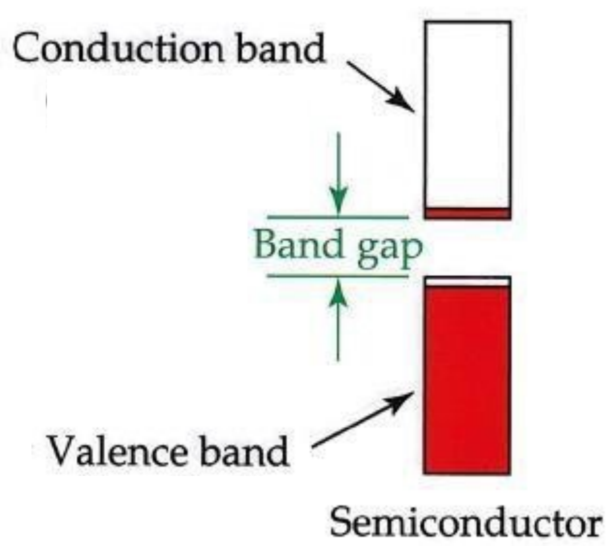
300 Million Trillion
5 nm Nanoparticles

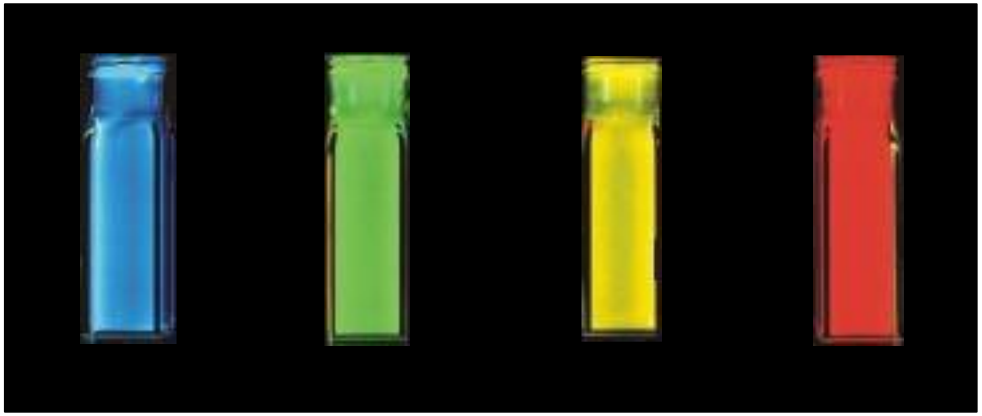
=

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

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.



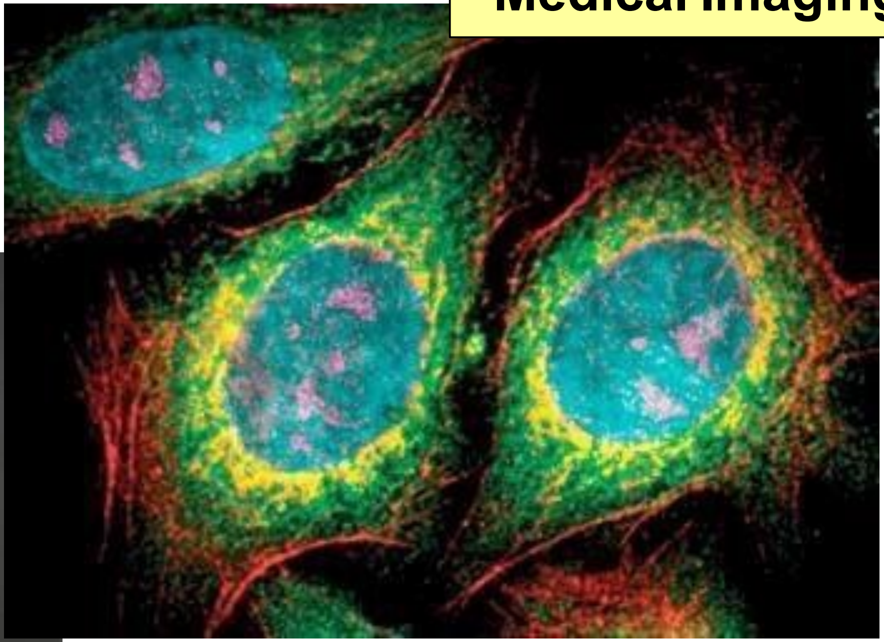


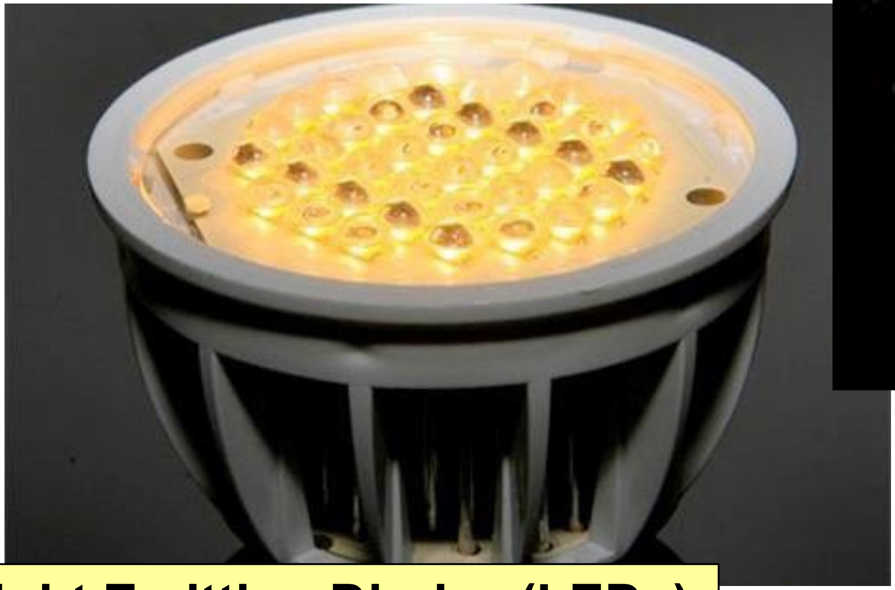
2.3 nm **4.2 nm** **4.8 nm** **5.5 nm**

Larger Band Gap ⟷ **Smaller Band Gap**

Applications of Quantum Dot Emission

Medical Imaging

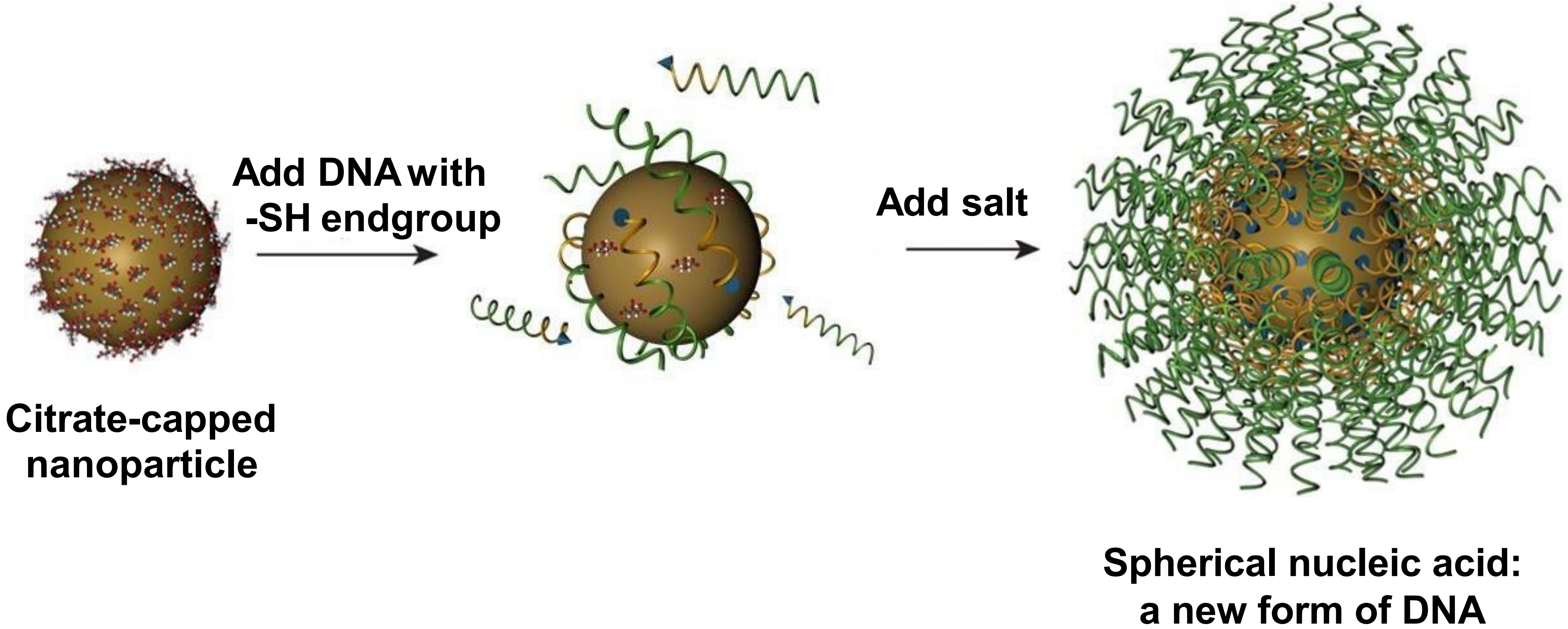




Light Emitting Diodes (LEDs)

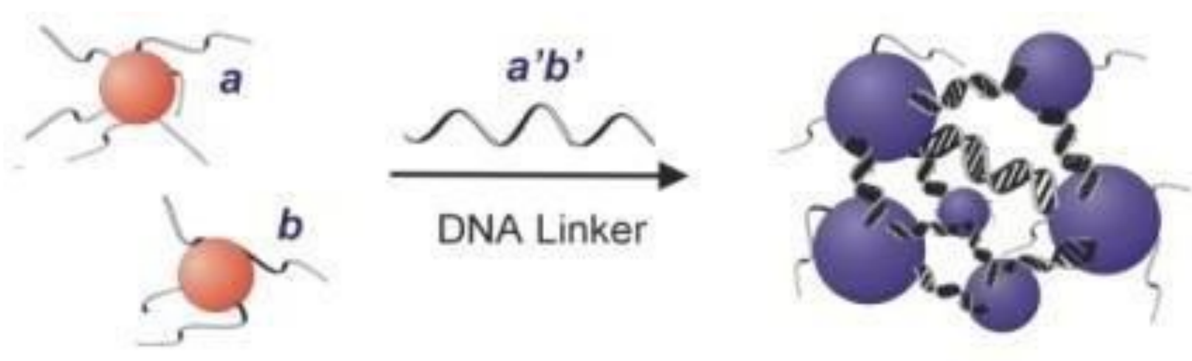
Attachment of DNA to Nanoparticles

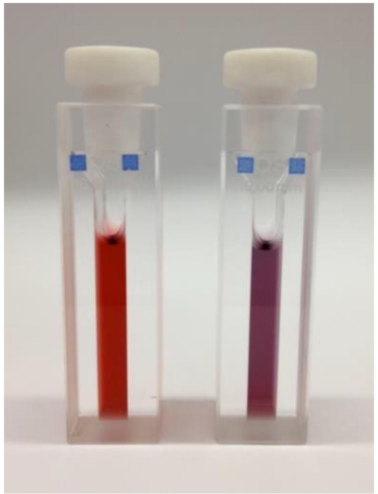
- DNA strands can be chemically modified with an "anchor" (a -SH end group) that attaches DNA to a nanoparticle surface.



Spherical Nucleic Acids: New Forms of Programmable Matter

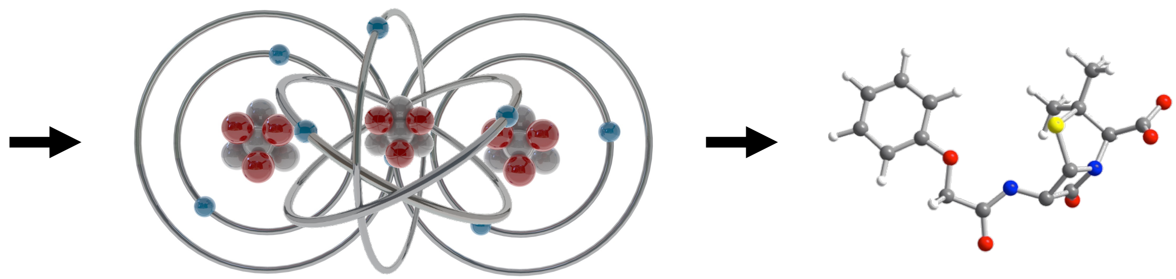
- **Two nanoparticles with single-stranded DNA can connect to each other via DNA hybridization.**
  - When the nanoparticles are brought together, they interact with each other to produce a color change.





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

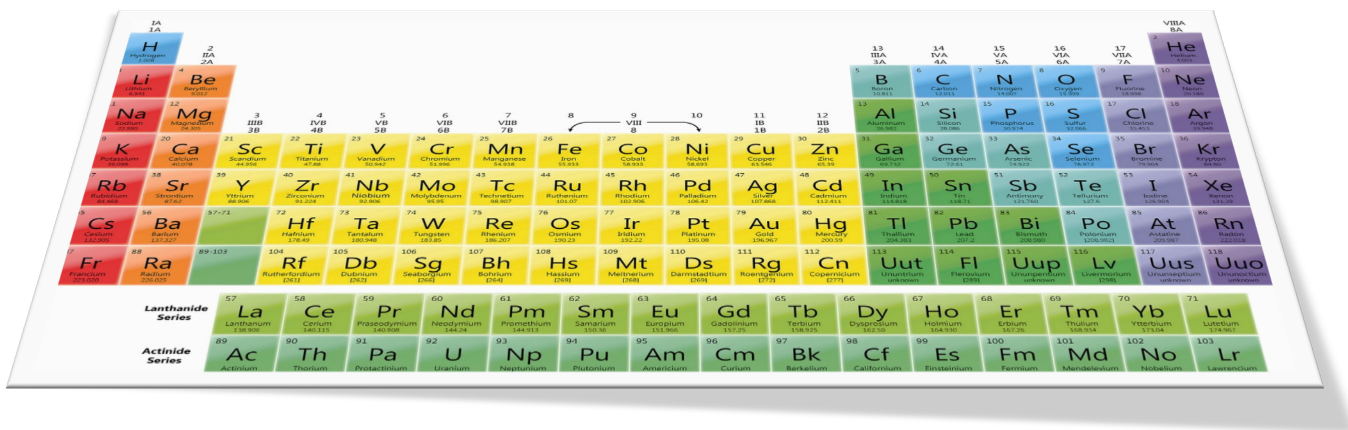
Conventional Chemistry



atoms

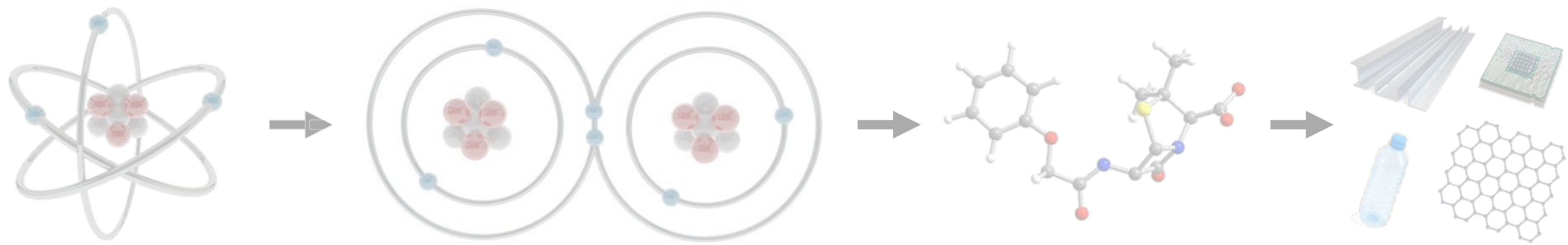
electron-based bonds
(covalent, ionic, metallic)

molecules



Angew. Chem. Int. Ed. **2013, 52, 5688.**
Chad A. Mirkin

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

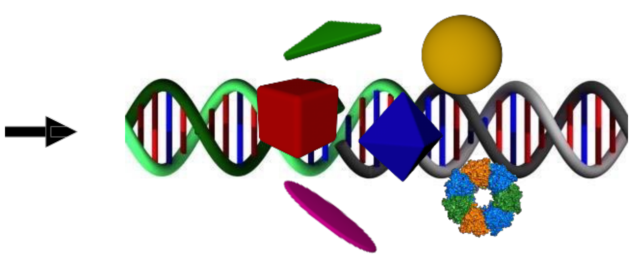


atoms

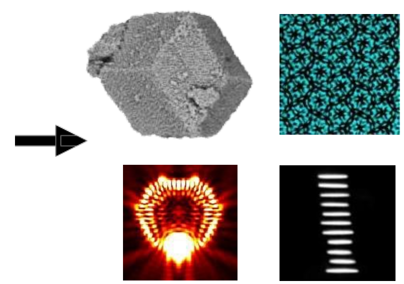
electron-based bonds
(covalent, ionic, metallic)

molecules

materials

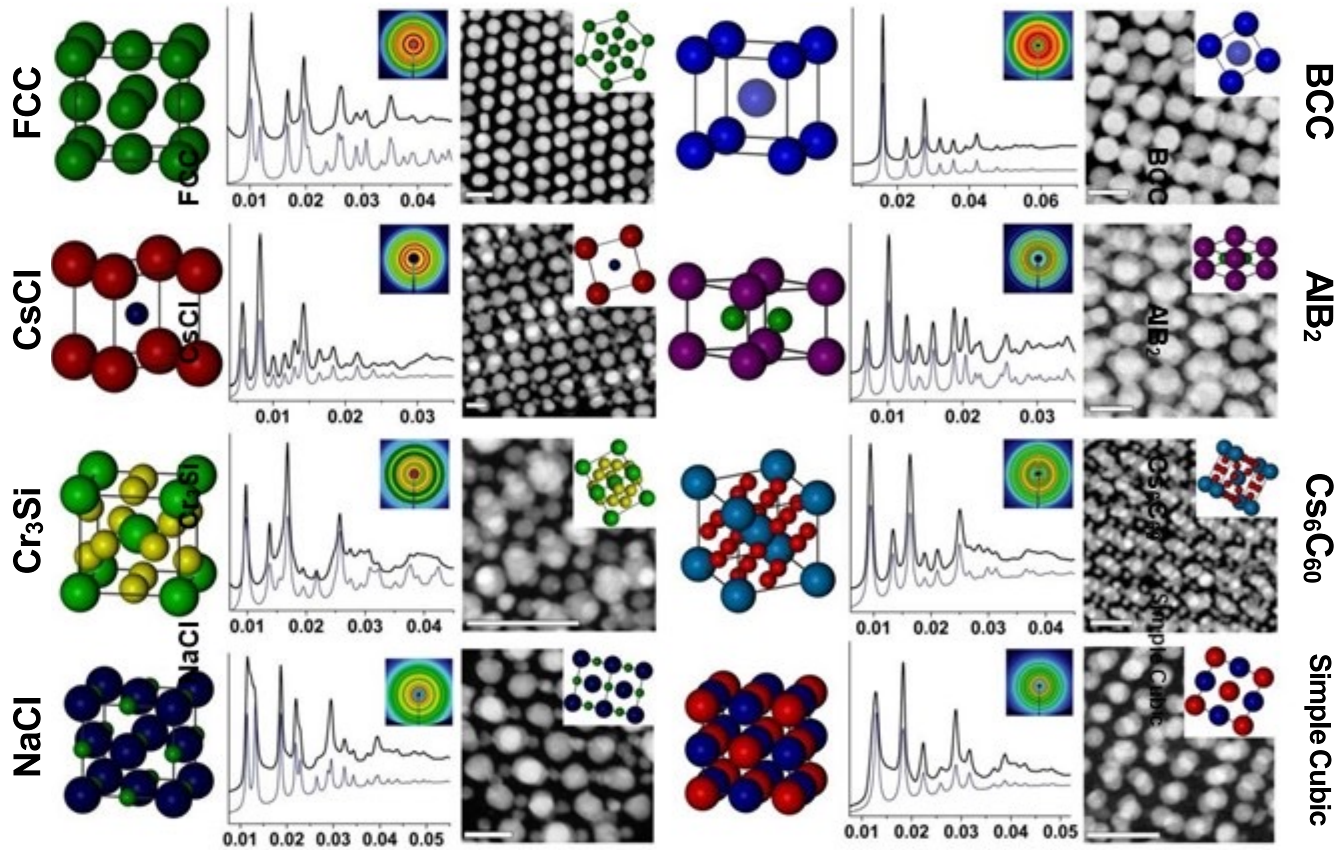


programmable-atom bonds



programmable materials

Programming Crystalline Architectures: *Enthalpy is Dominant Consideration*



Science 2011, ***334***, **204.**
Chad A. Mirkin

Comparison of Atomic Lattices and DNA-Nanoparticle Superlattices

Atomic Lattices

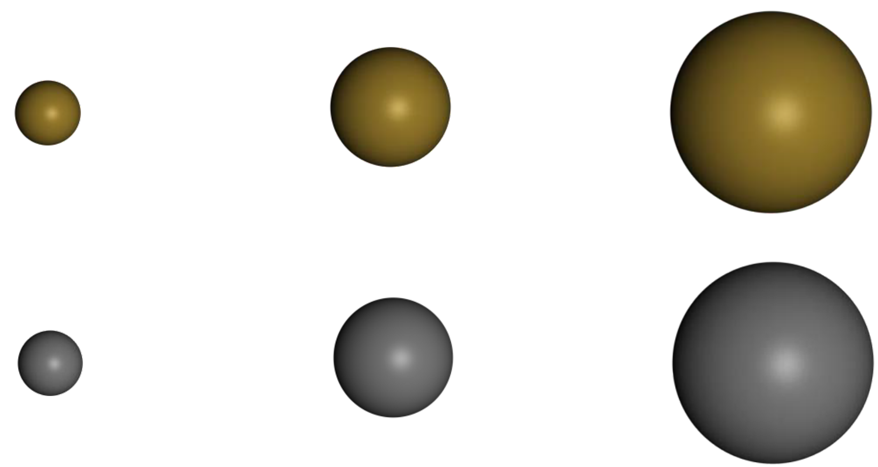
Building block: *Atoms*

- 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.

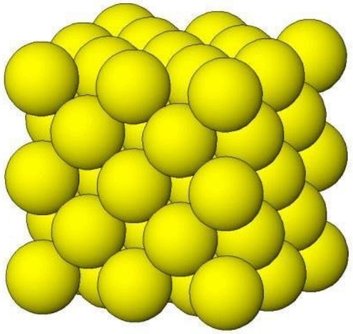


Comparison of Atomic Lattices and DNA-Nanoparticle Superlattices

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

DNA-Nanoparticle Superlattices

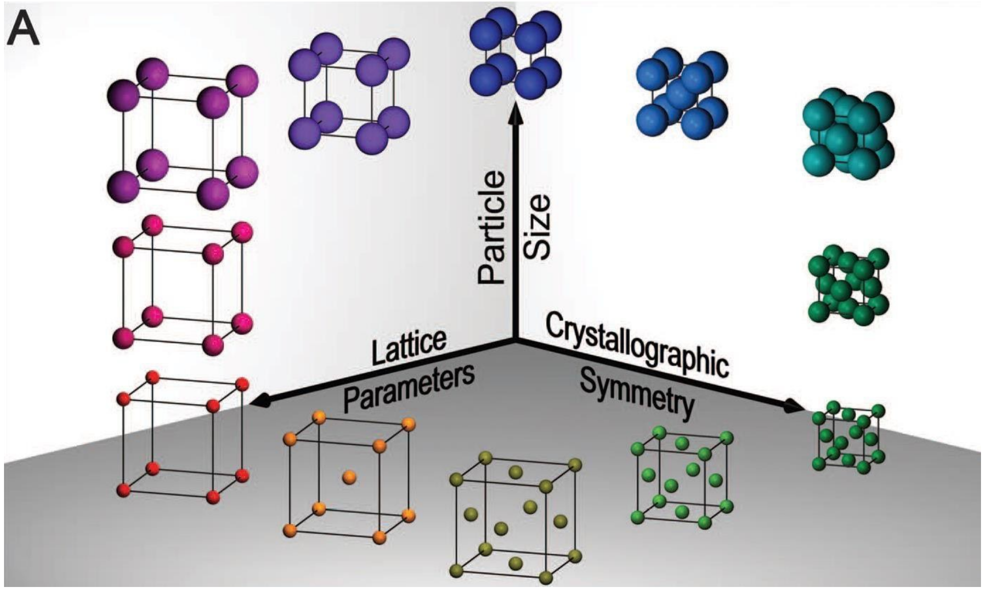
Connection between building blocks: *DNA*

- 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.**

Angew. Chem. Int. Ed. 2013, *52*, 5688.
Chad A. Mirkin

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)



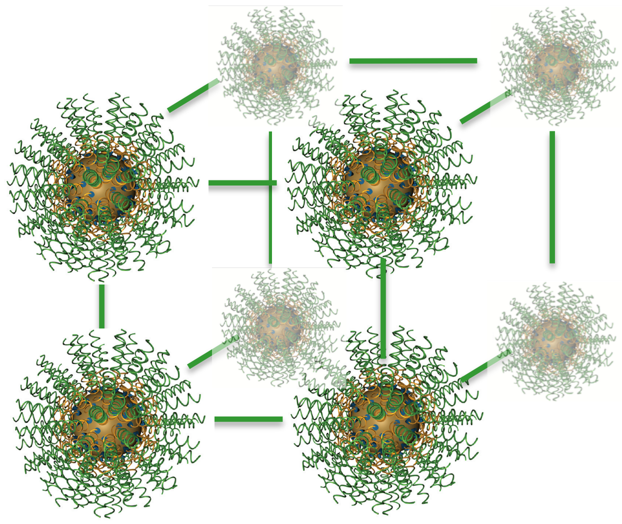
Q: Which of the following is NOT true about the difference between atomic lattices and DNA-Nanoparticle superlattices?

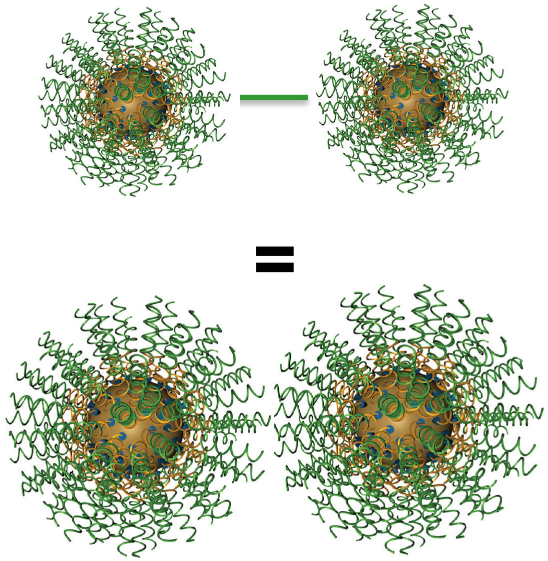
1. The distance between building blocks is fixed in both systems.
2. The size of a nanoparticle building block can be changed without changing composition.
3. The size of an atomic building block can not be changed without changing composition.

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.



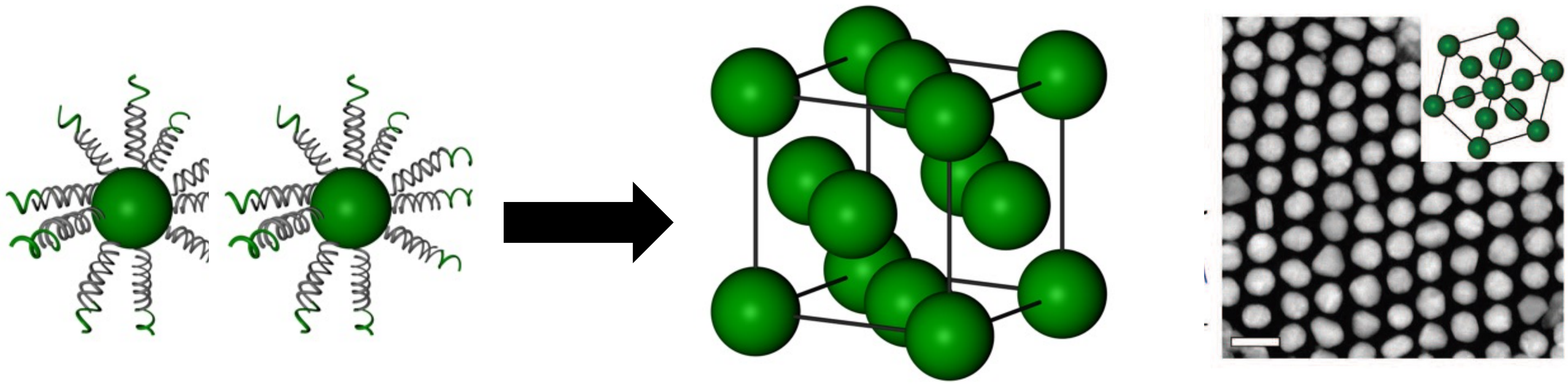


Q: Which atomic crystal lattices has the greatest number of nearest neighbors?

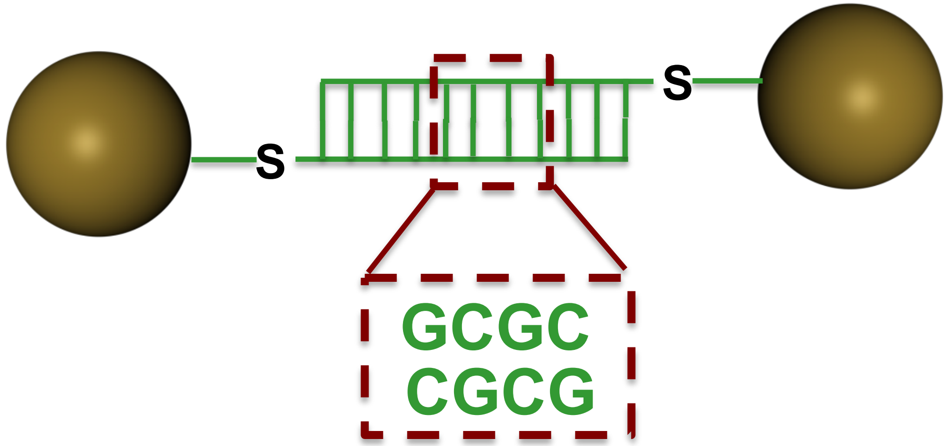
1. Simple Cubic
2. BCC
3. FCC
4. ZnS (Diamond)

Self-Complementary DNA Results in a Face-Centered Cubic Lattice (FCC)

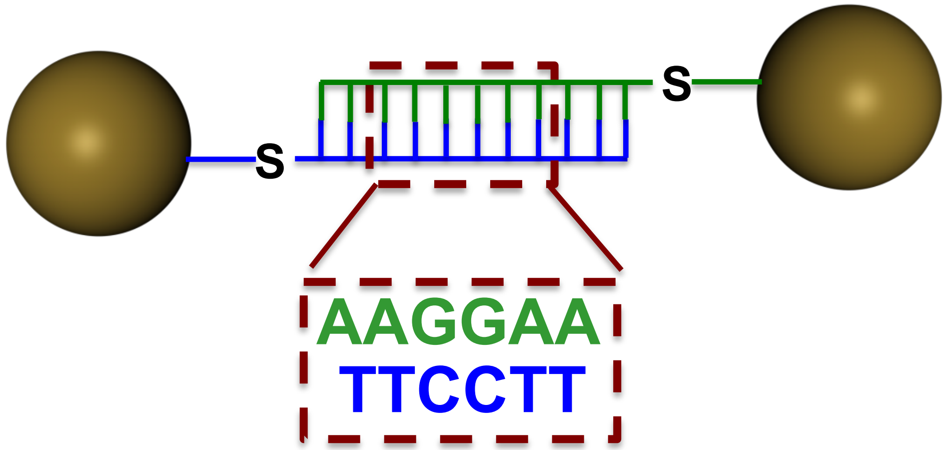
- **All particles are complementary to each other, which results in a FCC lattice with 12 nearest neighbors for each particle.**



DNA-Mediated Assembly of Gold Nanoparticles

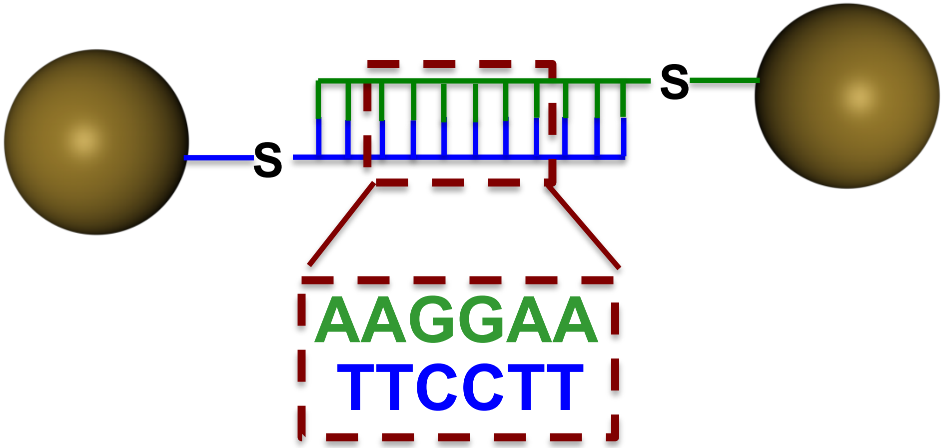


Self-complementary DNA sequences: a one-particle system



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

Complementary (but not *Self*-Complementary) DNA Sequences



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

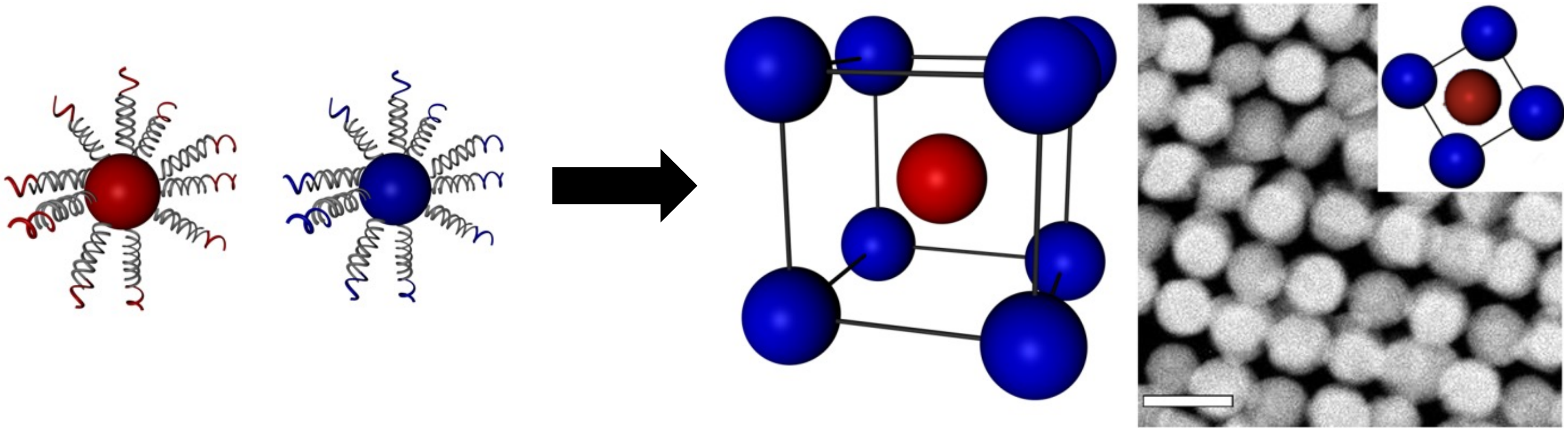
- **Pauling's Rules predict ionic crystal structures with two-component systems as well.**
  - For Pauling's Rules, they are cations and anions. Only cations were attracted to anions.

Radius Ratio	Cation Coordination	Anion Geometry
$0.225 < r_c/r_a < 0.414$	4	Tetrahedron
$0.414 < r_c/r_a < 0.732$	6	Octahedron
$0.732 < r_c/r_a < 1$	8	Cube

- **For particles with similar size, the greatest number of nearest neighbors is 8.**

DNA-Mediated Assembly of Gold Nanoparticles

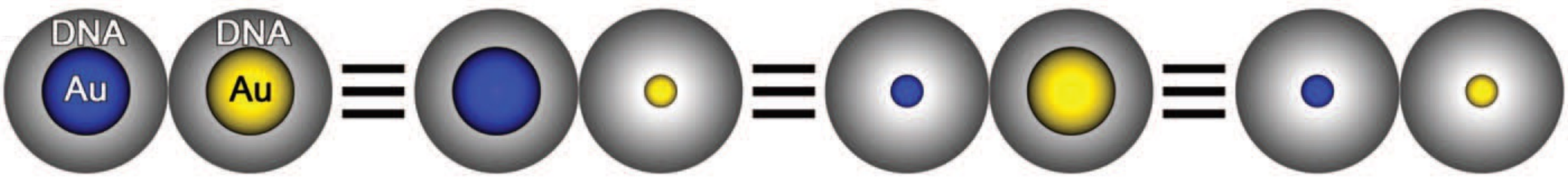
- **Pauling's Rules predicted a BCC crystal structure for ions with approximately equal radii. This occurs for nanoparticles as well.**



- **Remember: Pauling's rules depend on fixed cation and anion ratios.**

DNA-Mediated Assembly of Gold Nanoparticles

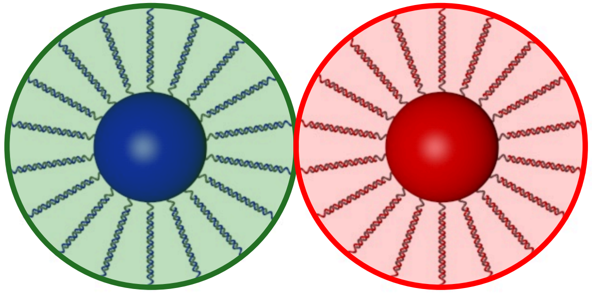
- **With DNA and gold nanoparticles, the crystal structure can be maintained, while the sizes of the building blocks are varied.**
  - Decrease in nanoparticle size compensated by increase in DNA length.

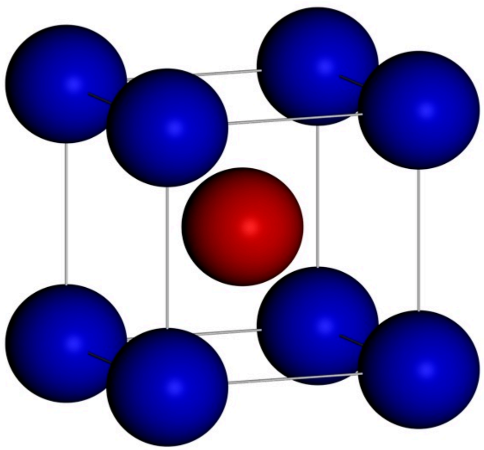


  - For each set of nanoparticles, a BCC-like crystal structure will form.

Design Rules for DNA-Mediated Nanoparticle Assembly

Rule 2: The overall hydrodynamic radius of a DNA-NP dictates its assembly and packing behavior

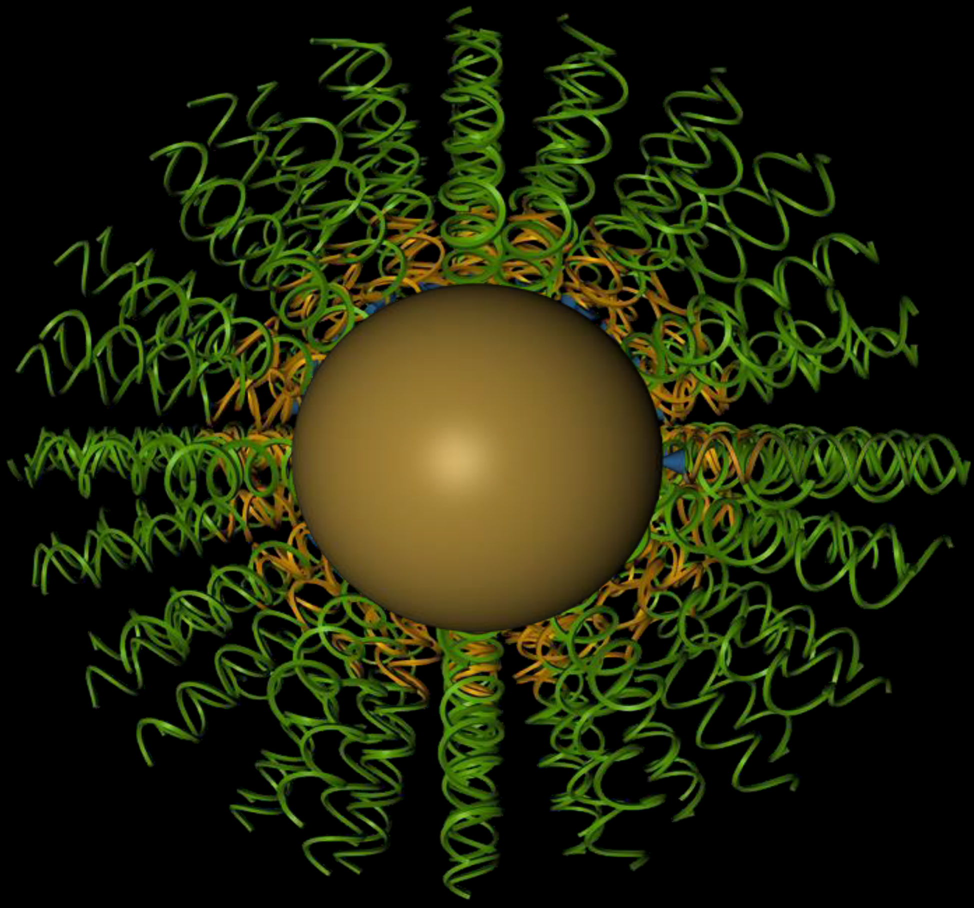


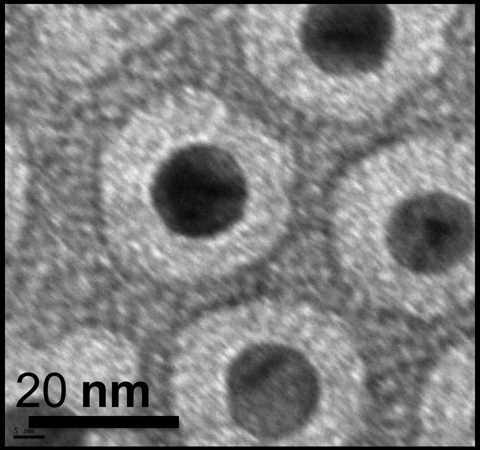


Body-Centered Cubic Lattice

Science 2011, *334*, 204.
Chad A. Mirkin

The Final Application: Spherical Nucleic Acids (SNAs) – A New Form of DNA



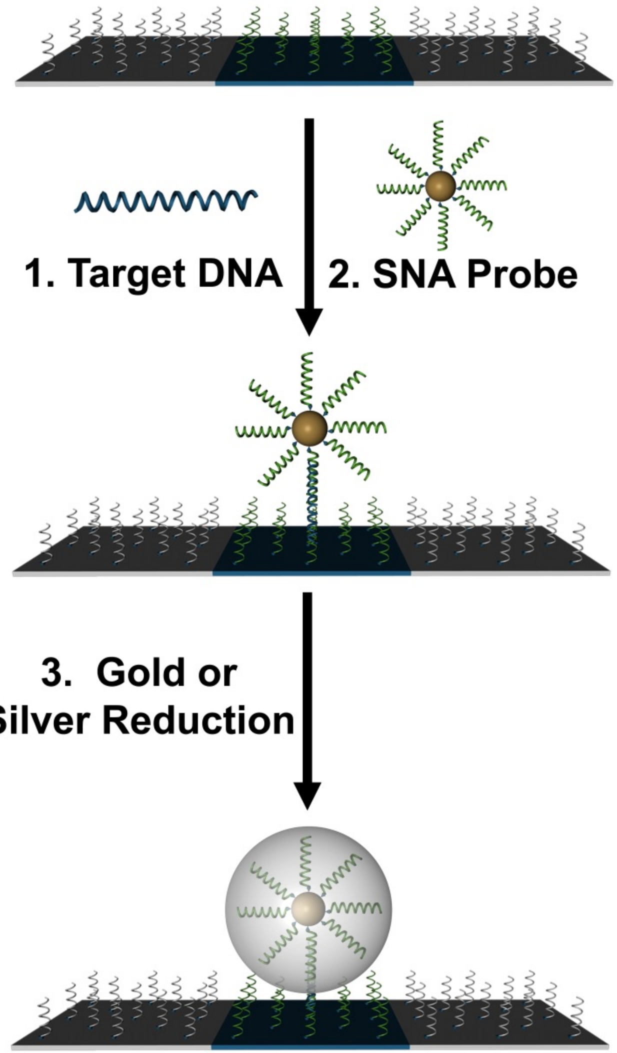


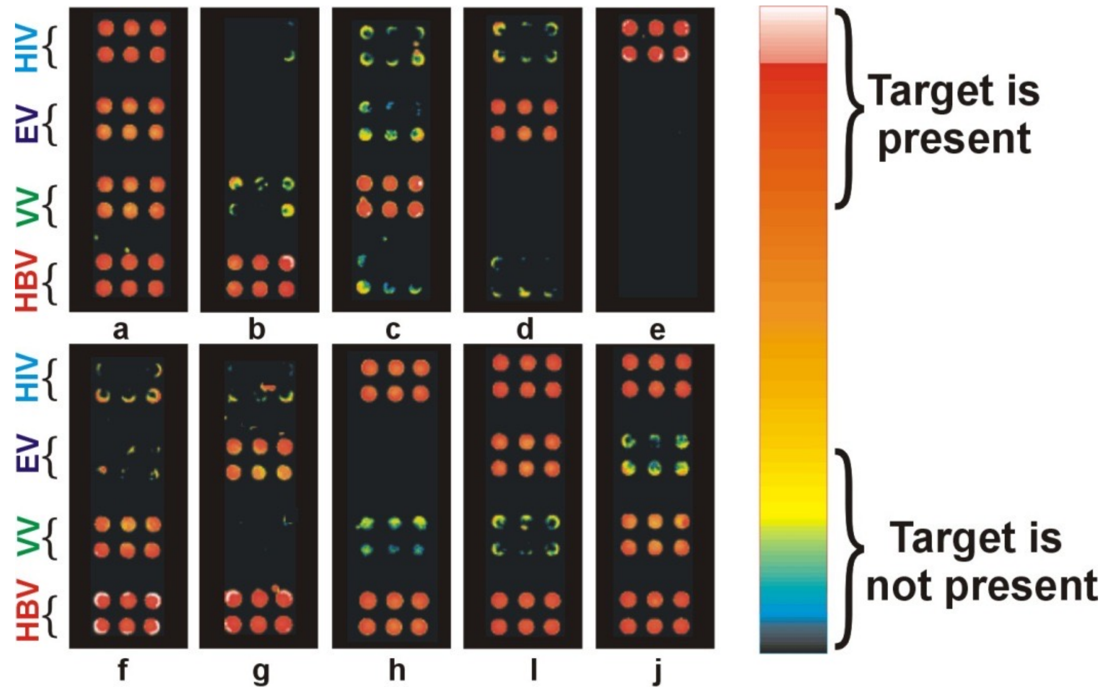
40-mer Oligo-Nucleotide 1,400 atoms

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

13-nm Au NP
~67,500 atoms

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





Science, **2000,** *289*, 1757; *Angew. Chem. Int. Ed.* 2006, 45, 3303.

Chad A. Mirkin

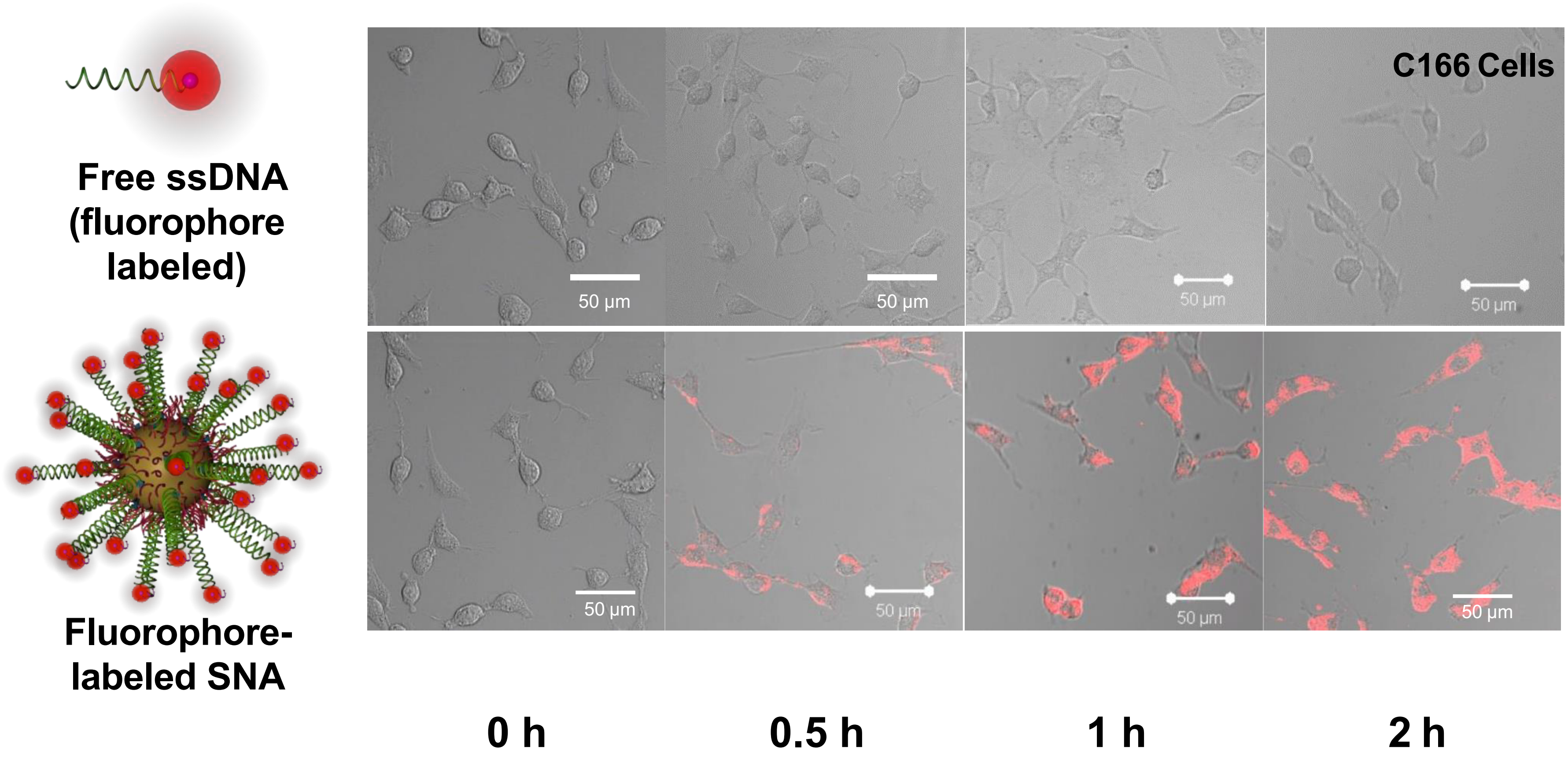
Verigene^{TM} System

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

FDA-Cleared Hypercoagulation, Warfrin Metabolism, Cystic Fibrosis, Influenza and Blood Stream Infection Assays

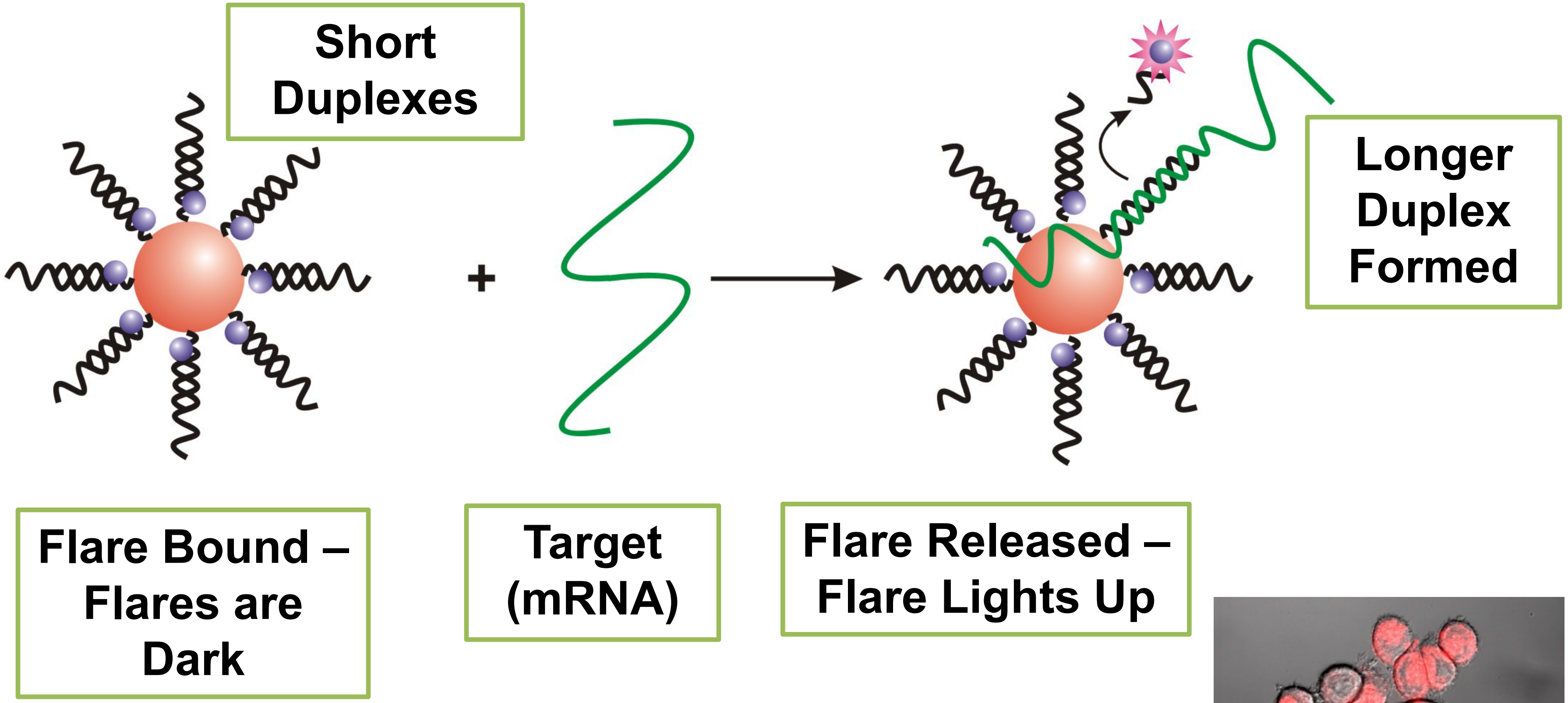
- **Direct genomic detection**
- **~100 aM (10^{-18}) LOD**
- **Multiplexed targets**
- **Automated assay process**
- **Ease of use**
  - **Minimal training required**
  - **Automated data tracking**
  - **No interpretation required**
  - **Fast (less than 2 h)**

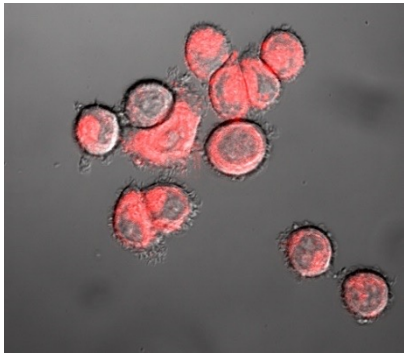
SNAs Enter Cells Rapidly And Efficiently



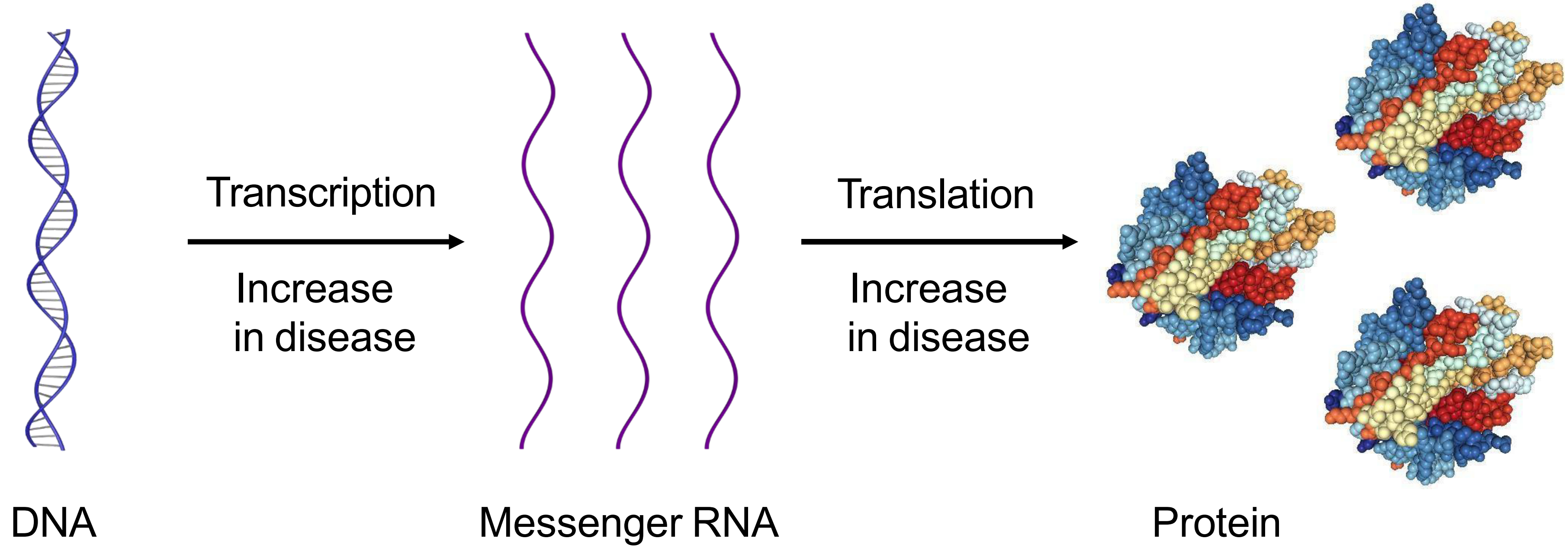
Proc. Natl. Acad. Sci. U.S.A. 2013, *110*, 7625.
Chad A. Mirkin

Nano-Flares for mRNA Detection

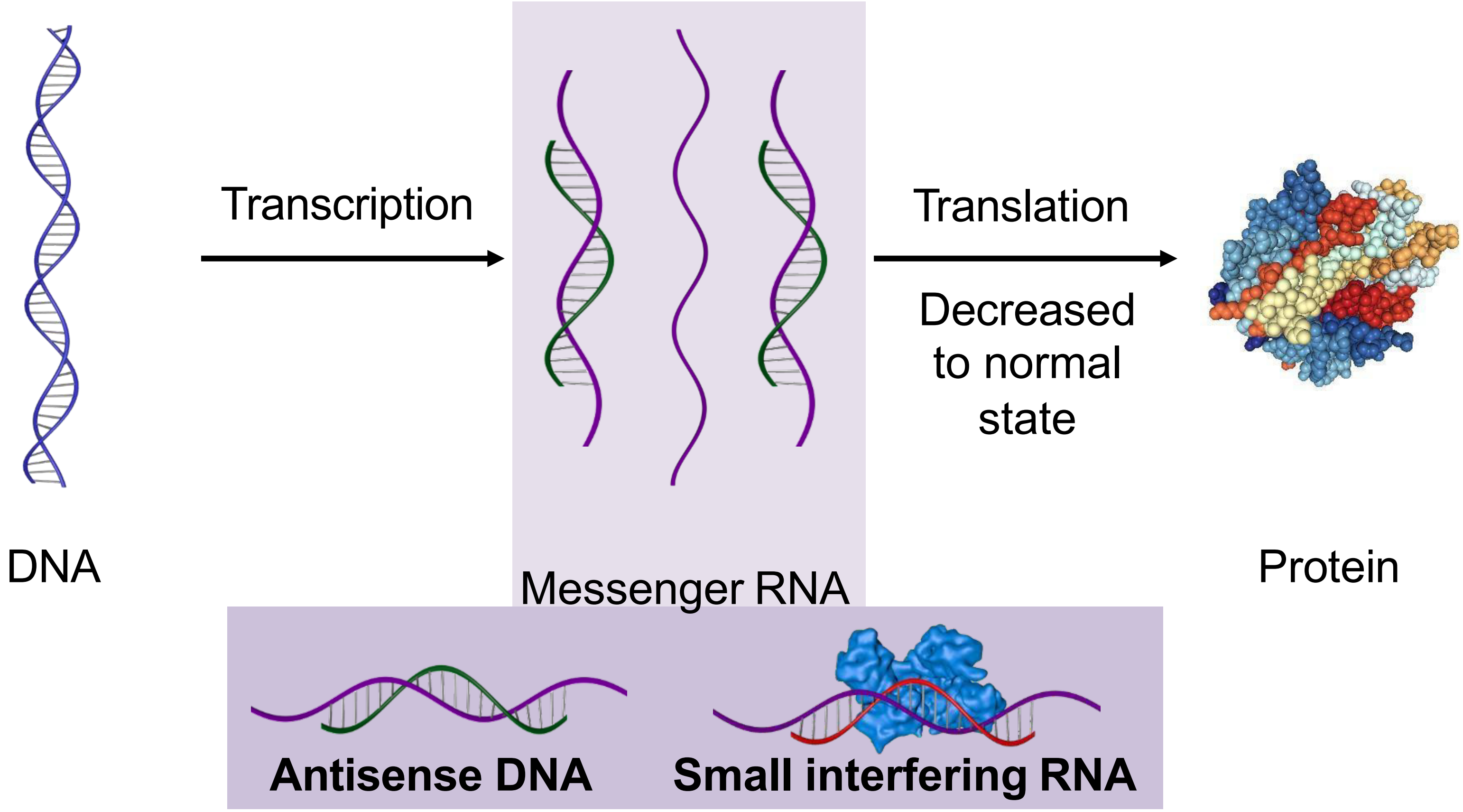




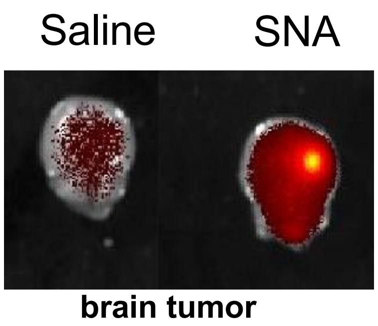
The Promise of Gene Regulatory Oligonucleotides

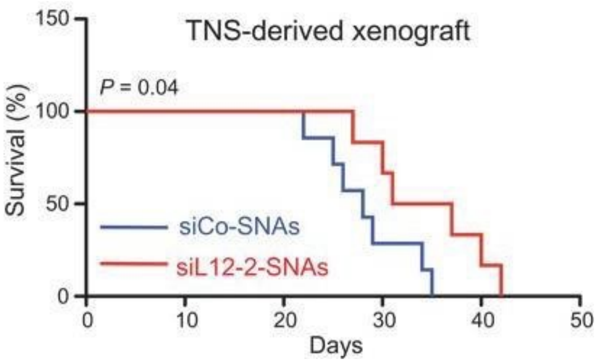


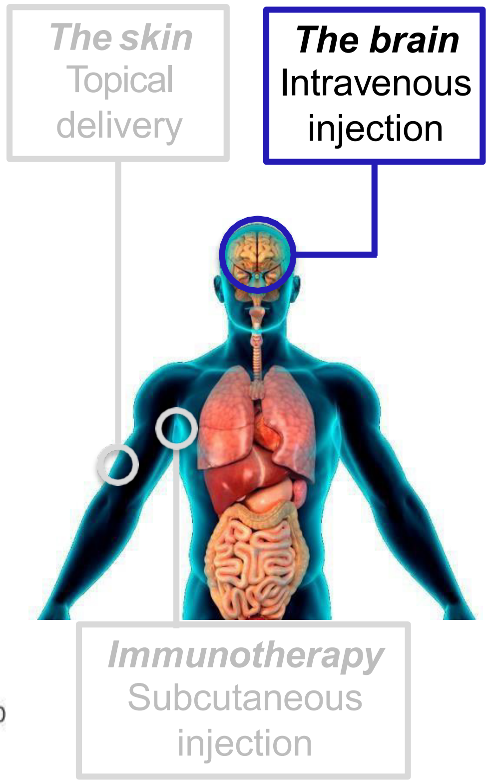
The Promise of Gene Regulatory Oligonucleotides



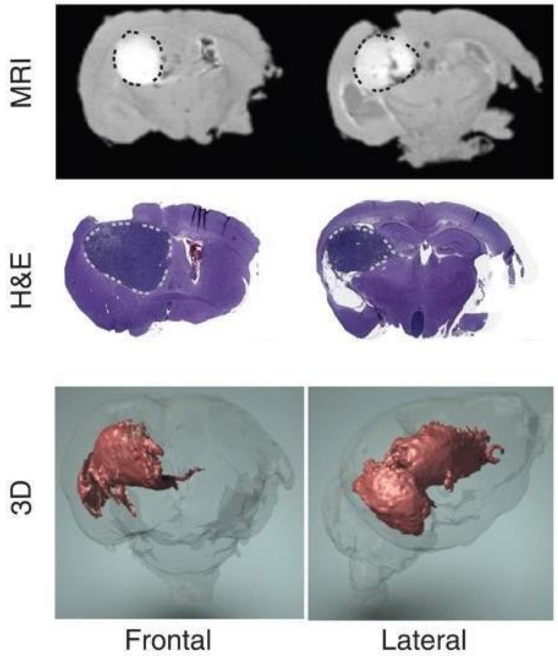
Spherical Nucleic Acids for GBM Brain Tumors: New Treatments for Cancer







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)

Sci. Transl. Med. 2013, *5*, 209ra152.
Sci. Transl. Med. 2021, *13*, eabb3945.
Chad A. Mirkin

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