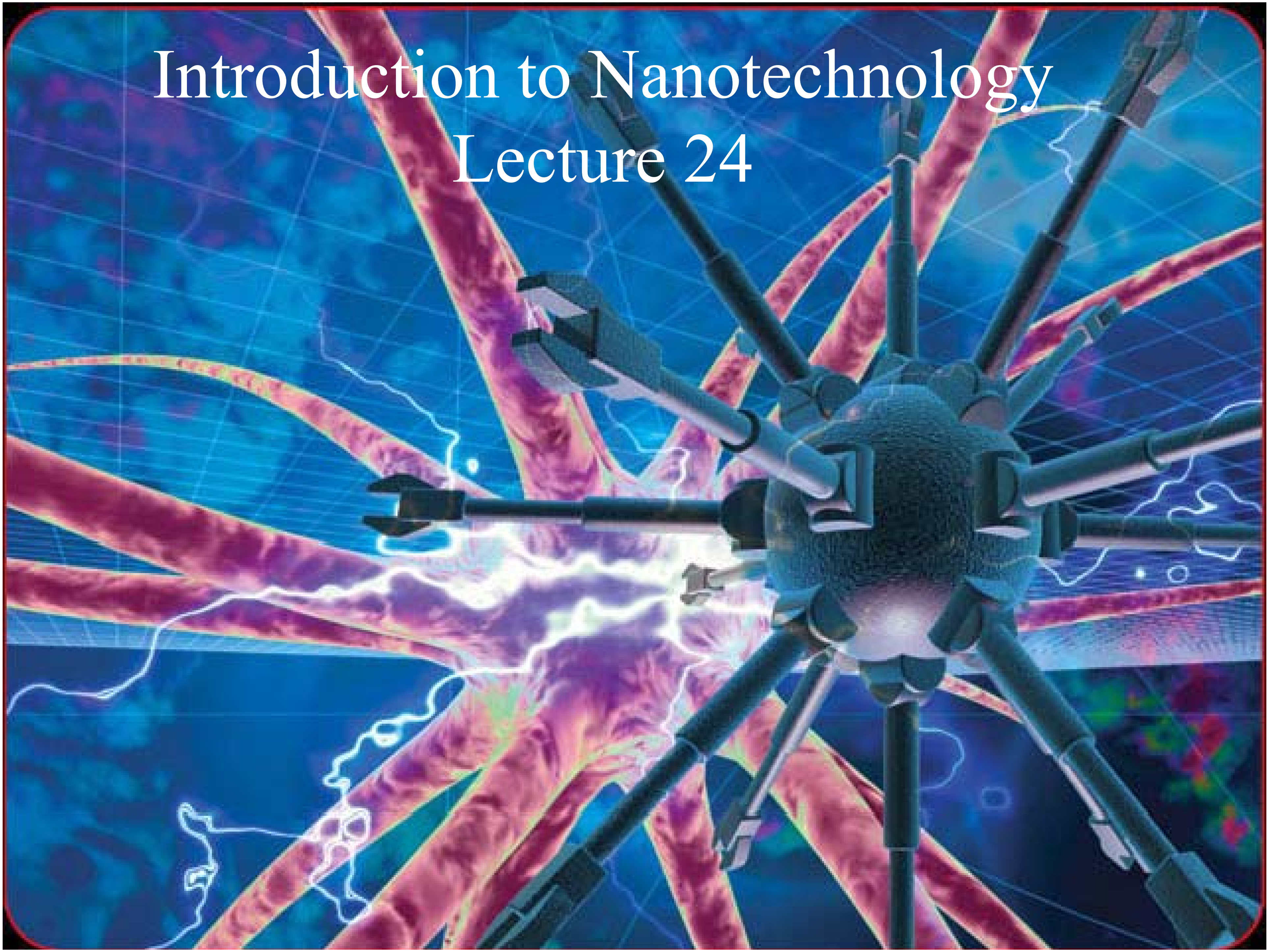
Introduction to Nanotechnology
Lecture 24



Nanotechnology
How small is nano?

100 meters

10 meters

How small is nano?

- Oak leaves

1 meter

100 millimeters

How small is nano?

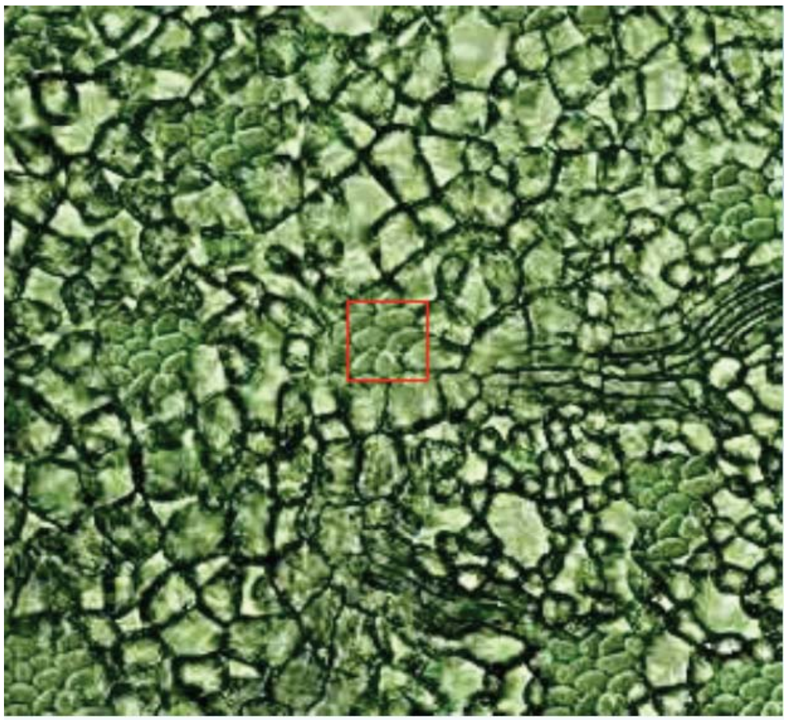
- Leaf surface

10 millimeters

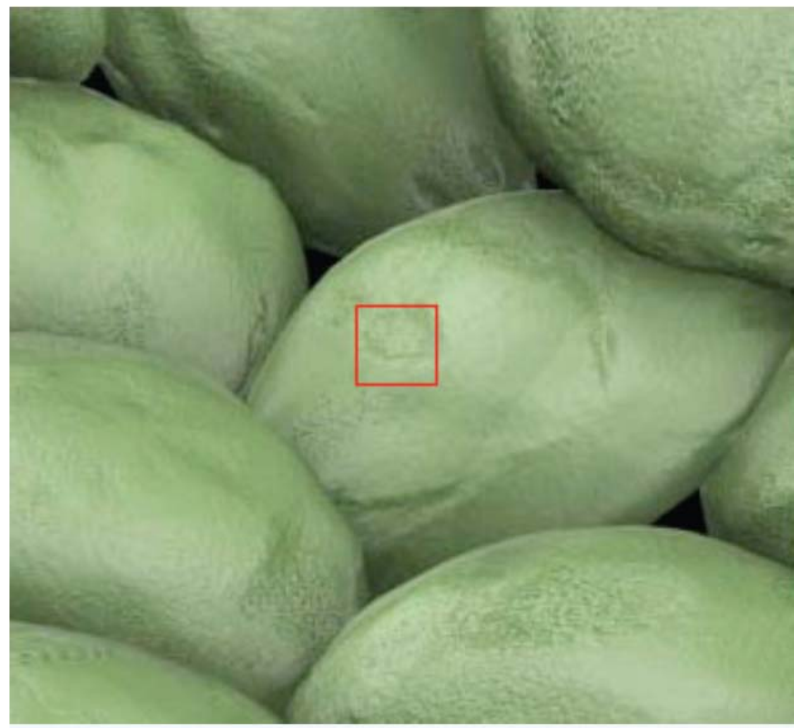
1 millimeter

How small is nano?

- Leaf cells



100 microns



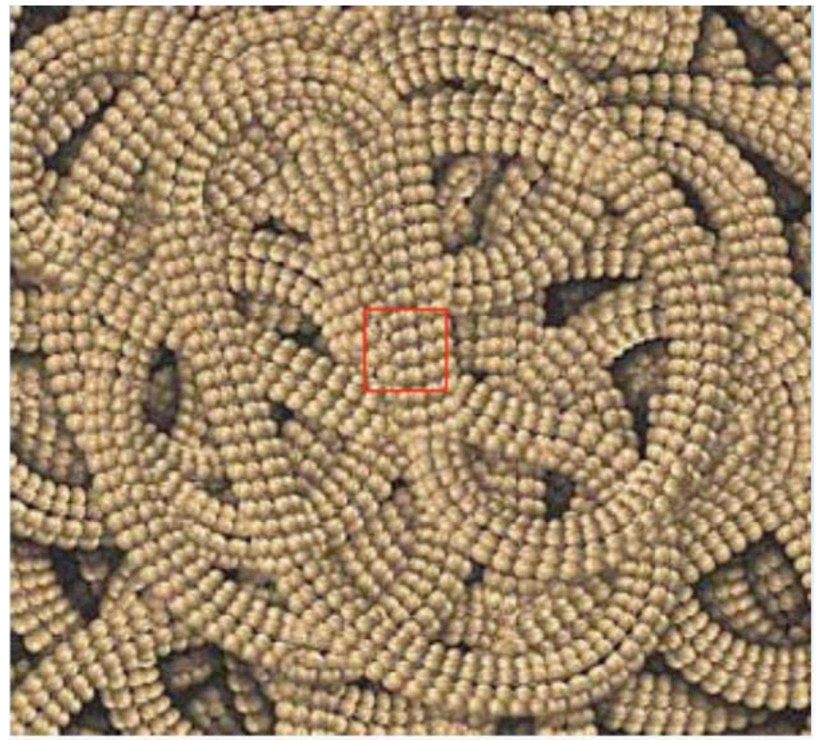
10 microns

How small is nano?

- Cell nucleus

1 micron

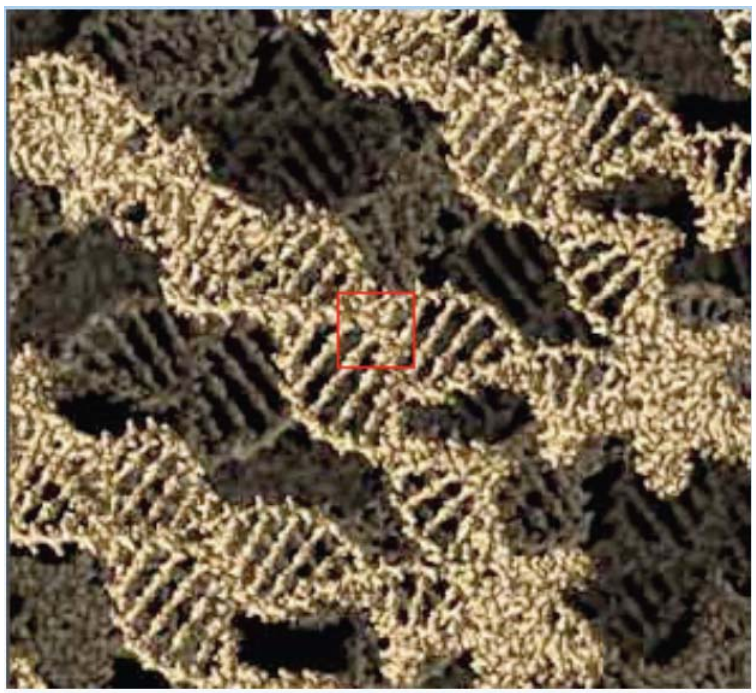
chromatin structure



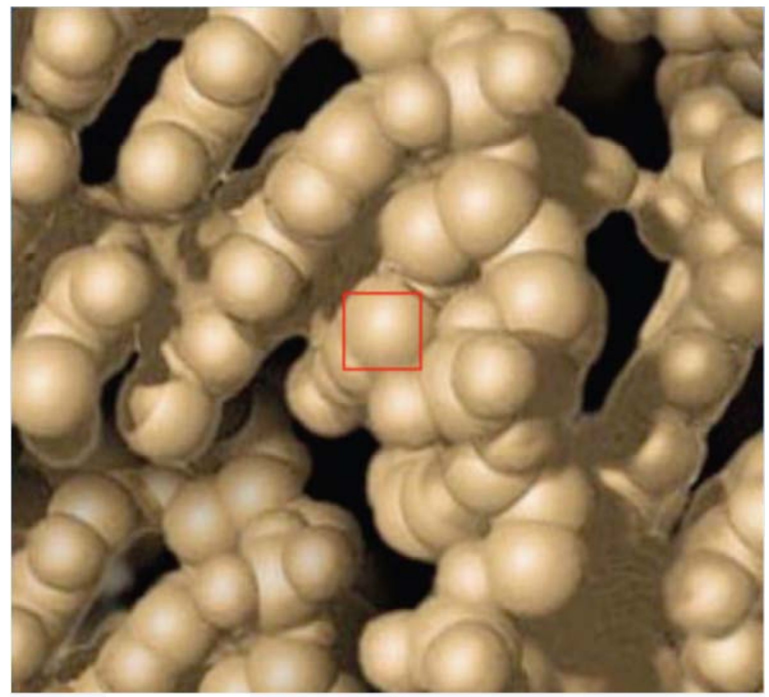
100 nanometers

How small is nano?

- DNA double strand individual molecules,
- atoms

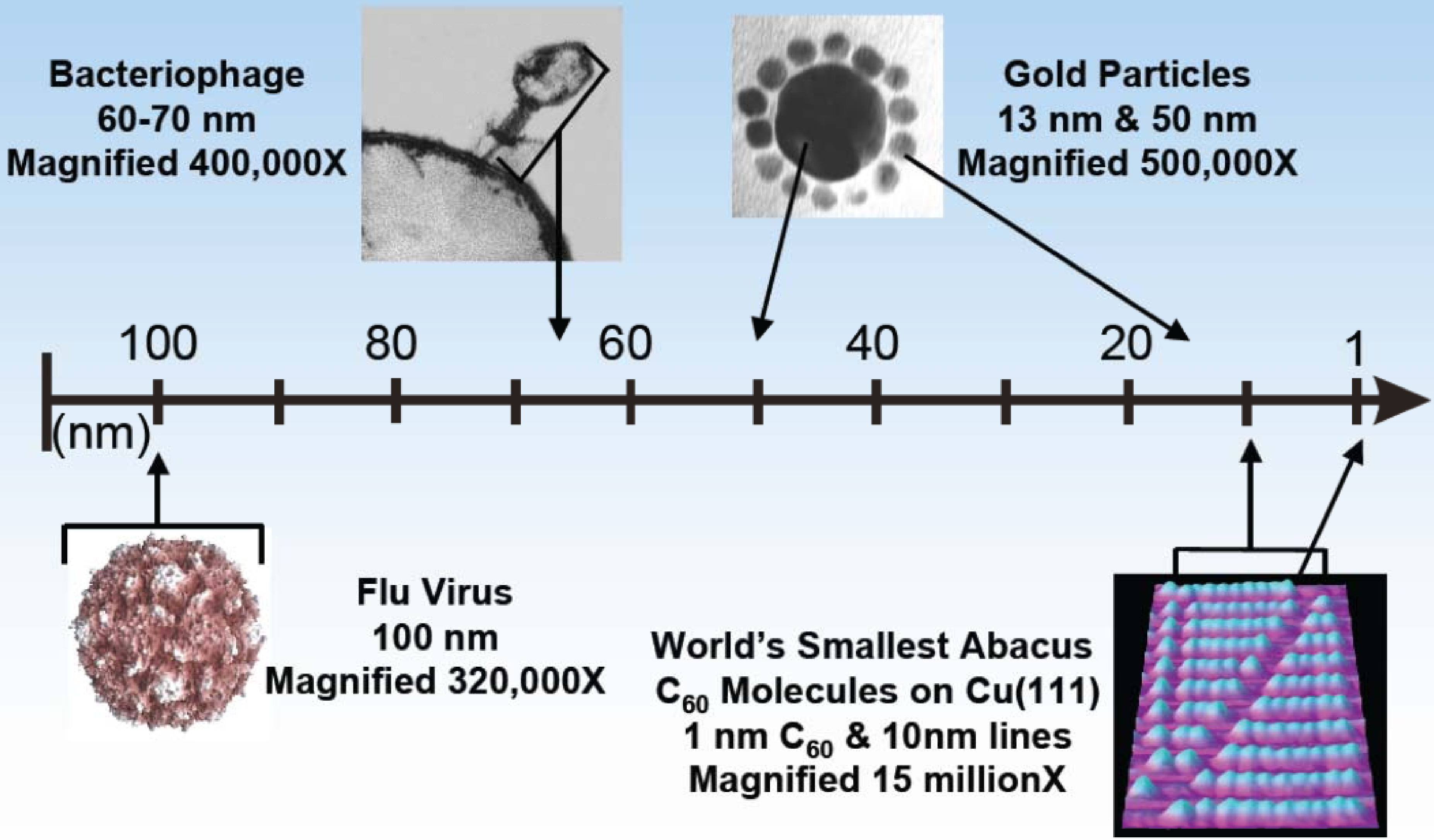


2 nanometers



0.1 nanometer

The Interesting Length Scale



Introduction

Nanotechnology

is the creation of functional materials, devices and systems through control of matter on the nanometer length scale and exploitation of novel phenomena and properties (physical, chemical, biological) at that length scale.

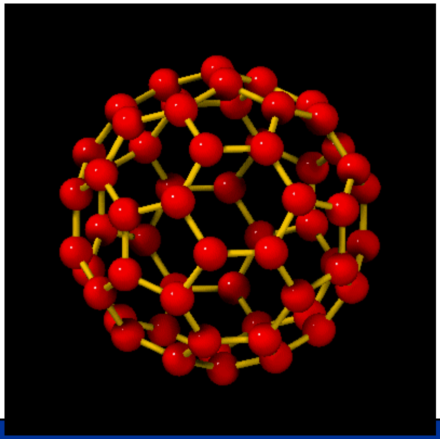
At length-scales comparable to atoms and molecules, **quantum effects** strongly modify properties of matter like "**color", reactivity, magnetic or dipolar moment.**

Origins of Nanotechnology

- Richard Feynman
  - 1959 speech
  - "There's plenty of room at the bottom"
- Eric Drexler
  - 1986 book
  - "Engines of Creation"
- SPM techniques 1981-1986

•Richard Smalley

•1996, Fullerene C_{60}



"There's Plenty of Room at the Bottom"

"The principles of physics do not speak against the possibility of maneuvering things atom by atom".

Richard P. Feynman

Nature engineering at nanoscale

Monomer molecules - amino acids, lipids

↓

Polymers - DNA, RNA, polysaccharides, proteins

↓

Assemblies - membranes, organelles

↓

Cells

↓

Organs

↓

Organisms

Living organisms are naturally-existing, fabulously complex systems of molecular nanotechnology.

Why nano is important for medicine?

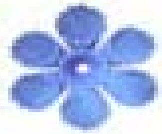
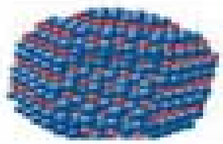
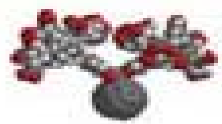
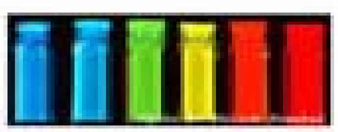
- Understanding molecular mechanism of disease – better targeting and treatment
- Analysis at the nanoscale (small samples)
- Detection and treatment at earlier stage, when disease progressed only at nanoscale
- Reduce side effects of medications, to attack only cancerous or other targeted cells.
- Development of neurological implants to repair people's vision and movement.

Using nanotechnology cancer can be detected and diagnosed much earlier giving a better chance of recovery for the patient.

Bio-Nanotechnology goals:

- Map living systems: particles – detection, sorting, imaging,
- Mimic living systems: biocompatible interfaces: screening, recognition, implants
- Control and manipulate living systems: direct manipulation (neuronal networks) destruction, treatment, surgery at the cellular level

Emerging nanomedicine technologies could dramatically transform medical science to address unmet medical needs and provide targeted therapy at cellular level

Modality		*Potential Applications*
Cantilevers		• High-throughput screening • Disease protein biomarker detection • DNA mutation detection (SNPs) • Gene expression detection
Carbon Nanotubes		• DNA mutation detection • Disease protein biomarker detection
Dendrimers		• Target sequestration • Controlled release drug delivery • Image contrast agents
Nanocrystals		• Improved formulation for poorly soluble drugs
Nanoparticles		• Multifunctional therapeutics • Targeted drug delivery, permeation enhancers • MRI and ultrasound image contrast agents • Reporters of apoptosis, angiogenesis, etc.
Nanoshells		• Deep tissue tumor cell thermal ablation • Tumor-specific imaging
Nanowires		• High-throughput screening • Disease protein biomarker detection • DNA mutation detection (SNPs) • Gene expression detection
Quantum Dots		• Optical detection of genes and proteins in animal models and cell assays • Tumor and lymph node visualization

Synthesis of Nanostructures

<u>Top-down</u>

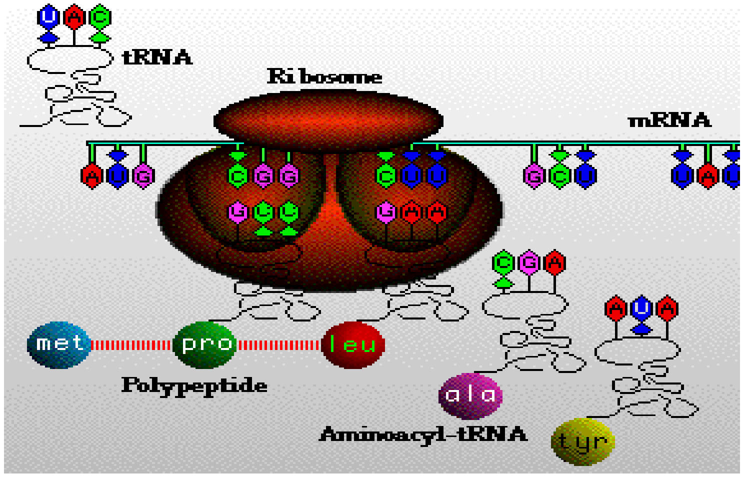
- Traditional approach
- Take away material until what is left is the product

eg. Sculpting

<u>Bottom-up</u>

- Nanotech approach
- Add material until the product has been created

eg. Biological systems



Nanomaterials, methods of synthesis:

Top-down

- Ball milling – crushing large crystals into small:
- nanocrystals,
- nanopowders

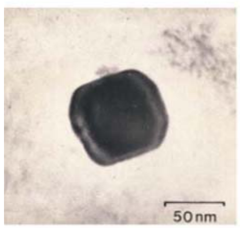
Bottom-up

- Plasma deposition (CNT)
- Vapor deposition (metal oxides)
- Vapor microwave plasma deposition (metal)
- Sol-gel (colloids)
- Electrodeposition
- Using porous templates:
- $[Al_{13}O_4(OH)_{24}]^{7+}$

Nanoparticles

a)

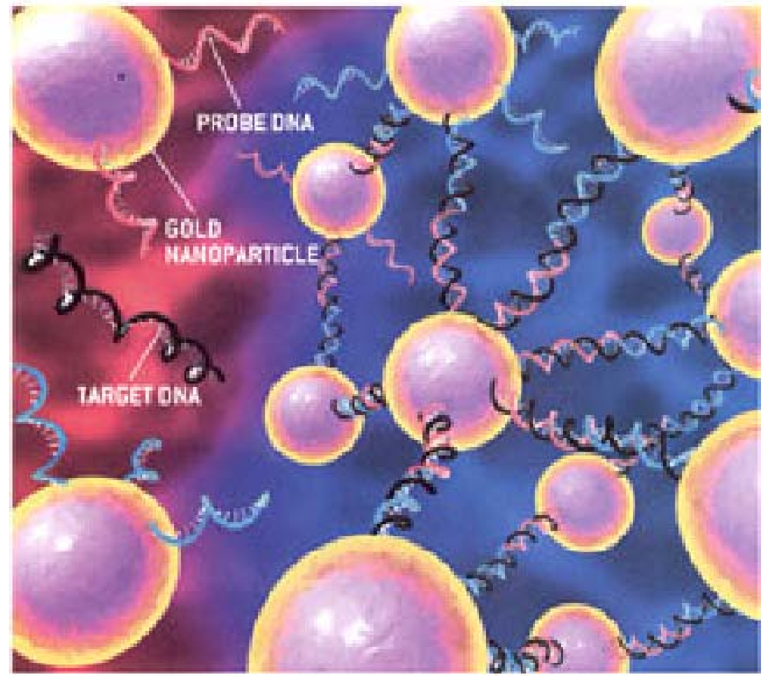
b)



c)

Nanoparticles

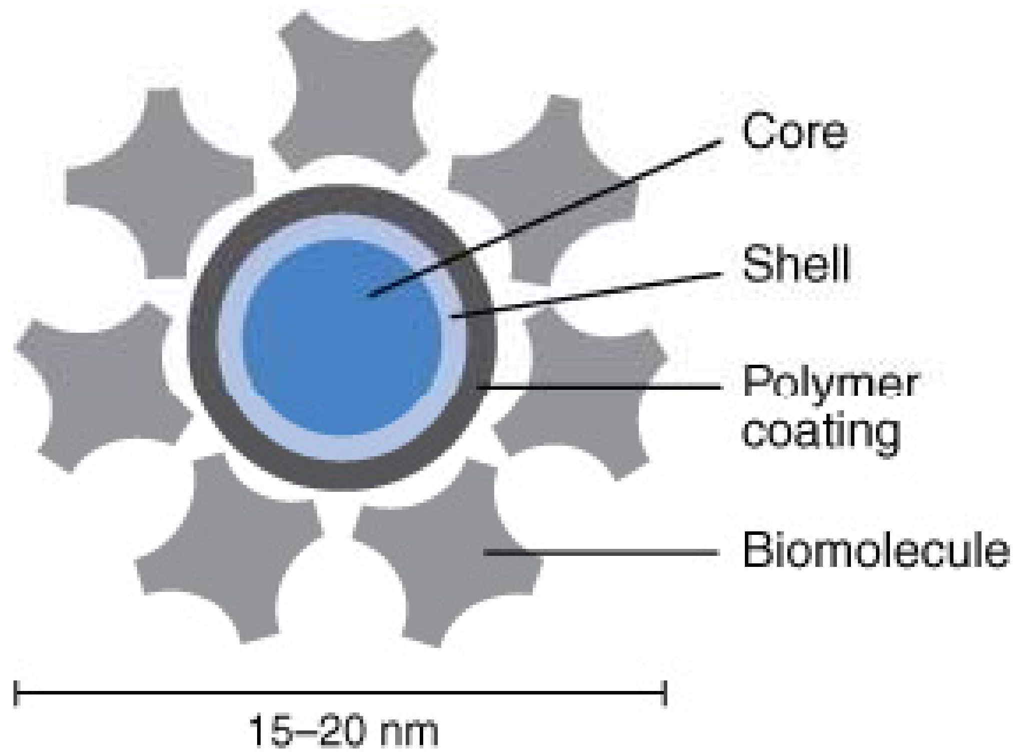
vary in color depending on size,
change color upon aggregation
emit light and can act as a fluorescent tag:
contrast agents for MRI,
positron emission tomography (PET),
molecular imaging in patients
fluorescent labels in optical microscopy
fade less quickly, less toxic to cells
can be used in combination to create almost
an infinite number of colors.



Robert L. Letsinger of Northwestern University testing the presence of a specific genetic sequence in solution.

Quantum Dots

- QD- Semiconductor heavy metal core cadmium selenide or cadmium telluride; semiconductor shell zinc sulfide; then biomolecule coating (heavy metal core responsible for fluorescent properties; nonemissive shell stabilizes core; organic coating miscibility and attachment to biomolecules)
- Nanometer scale size (i.e. 1-20nm)

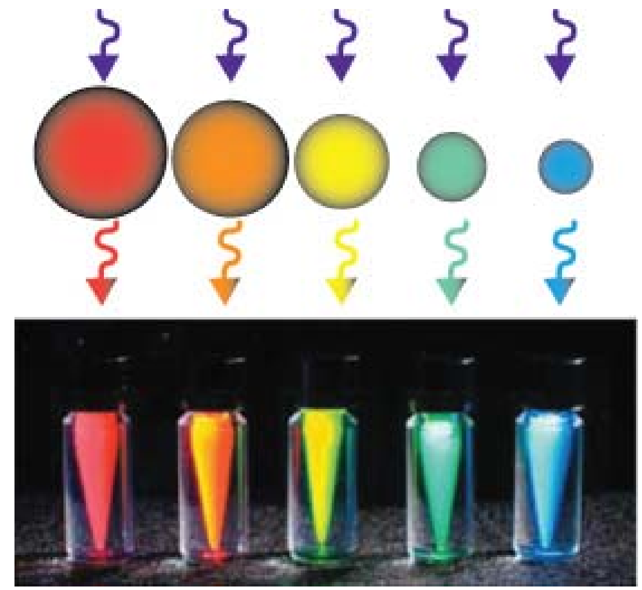


Quantum Dots

QD are fluorophores:

absorb photons of light then reemit

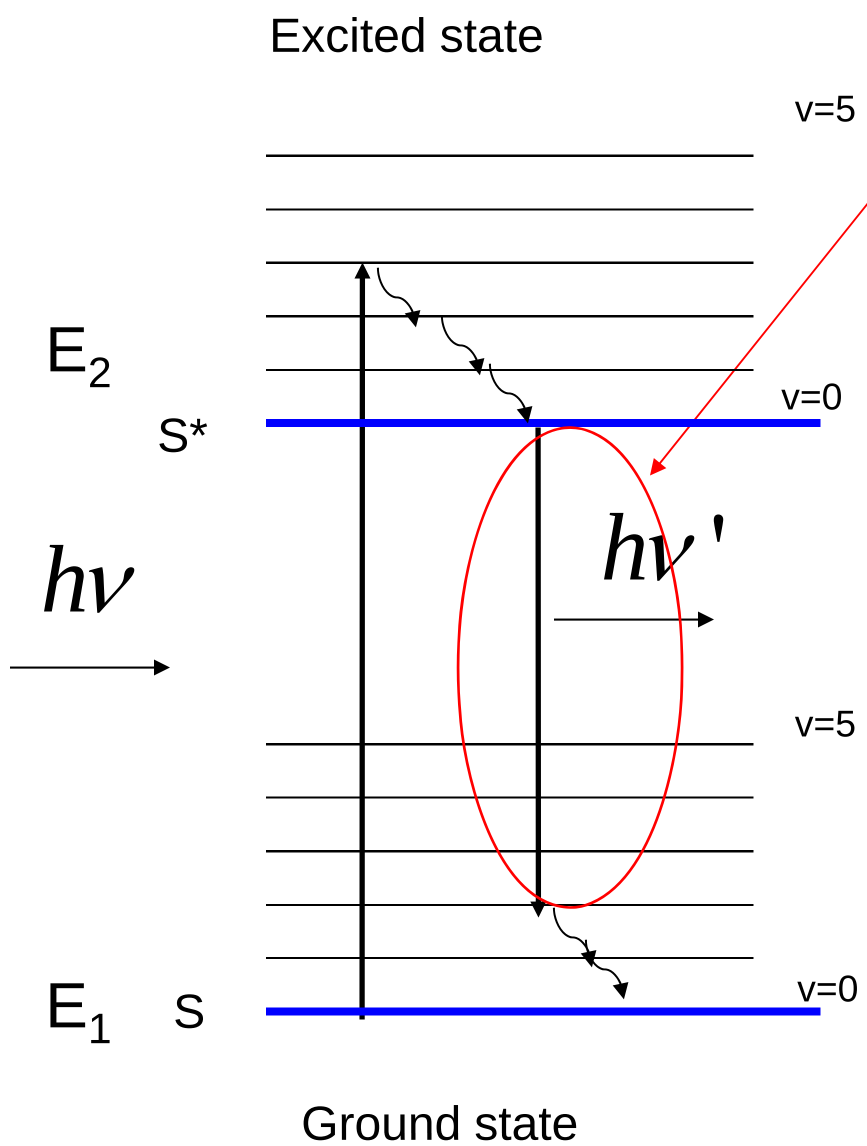
photons at different wavelength



Nanocrystal solutions containing differently sized nanocrystals are excited with the same long wavelength UV lamp; core size determines color

e.g. when excited by light of single wavelength, 3nm (core diameter) cadmium selenide particle radiates green light of 520nm, and 5.5nm particle of same material radiates red light at 630nm

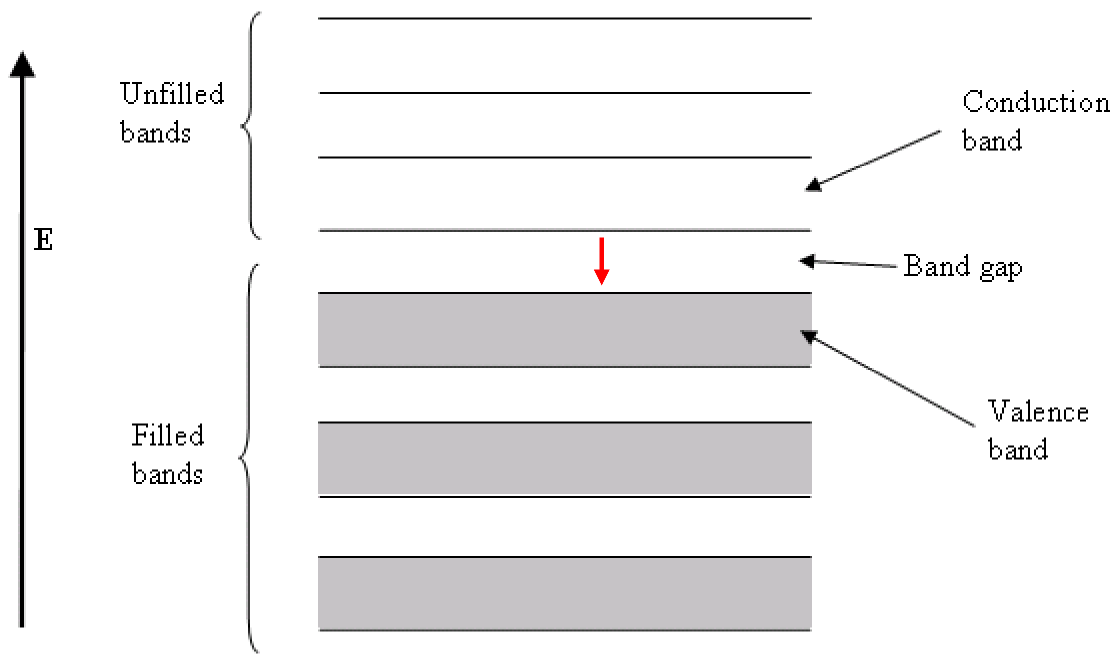
Fluorescence in molecules



Molecule absorbs light becomes excited

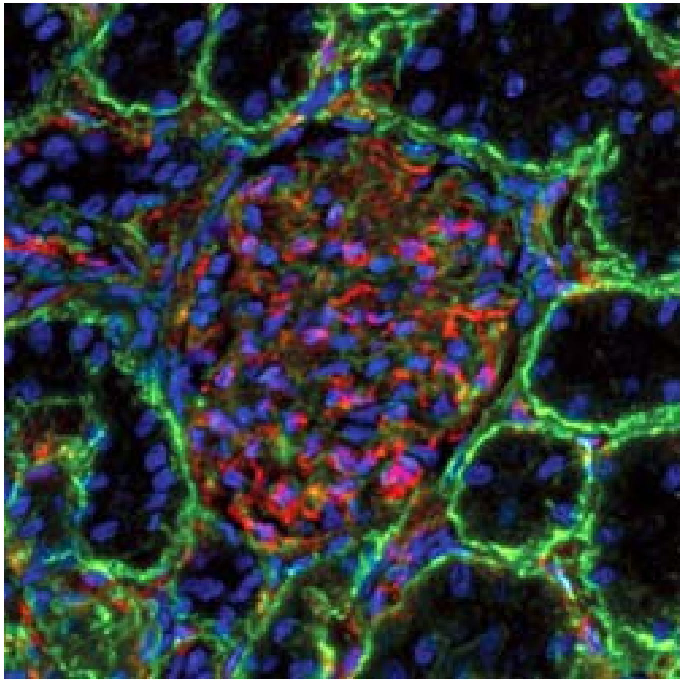
Molecule returns to the ground electronic state by radiating photon – **fluorescence,**

Quantum Dots



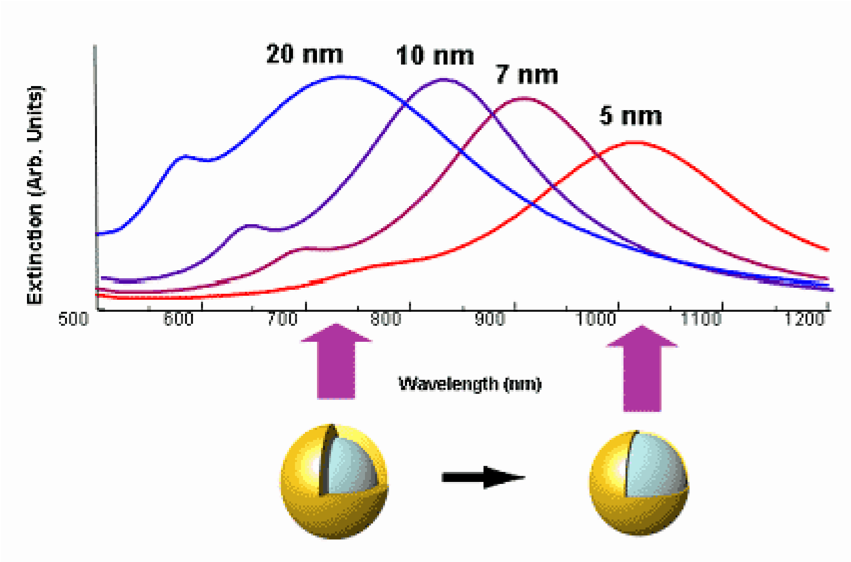
- the bandgap energy that decides emision energy, and color of emitted light is inversely proportional to the square of quantum dot size

Quantum Dots



- QD are used for fluorescence imaging

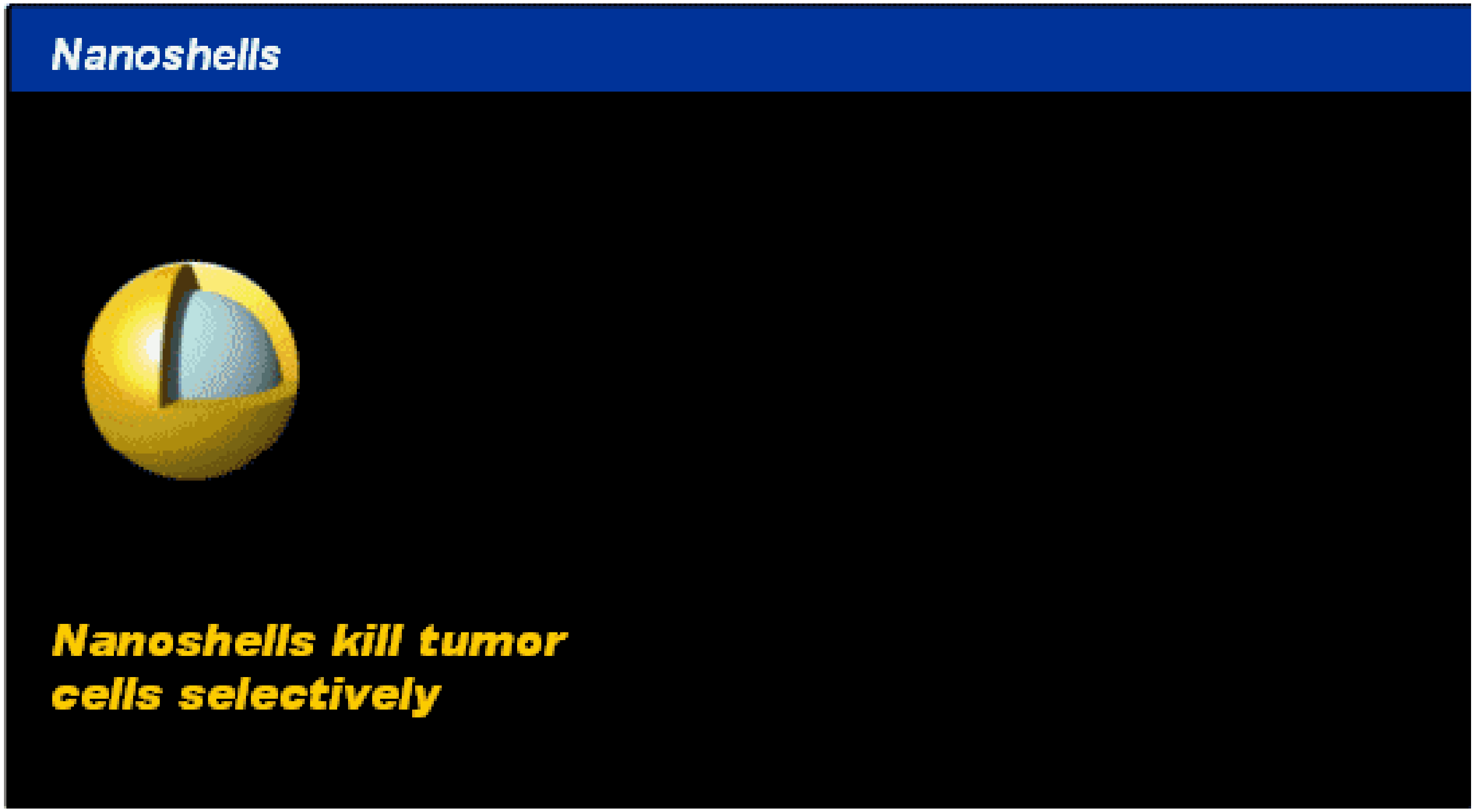
Nanoshells



core of silica and a metallic outer layer

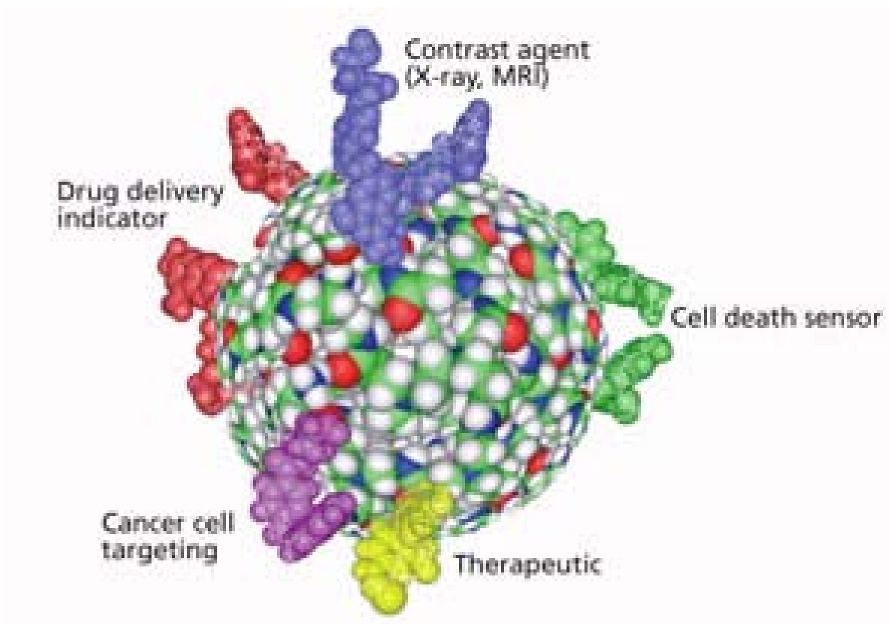
Because of their size concentrate in cancer lesion sites
Modified to bind to the tumor. Nanoshells adsorb external energy and create an intense heat that selectively kills the tumor cells.
The external energy - thermo, mechanical, radio frequency, optical
Greater efficacy and significantly reduced side effects.

Nanoshells



Reference: Jennifer West, Rice University

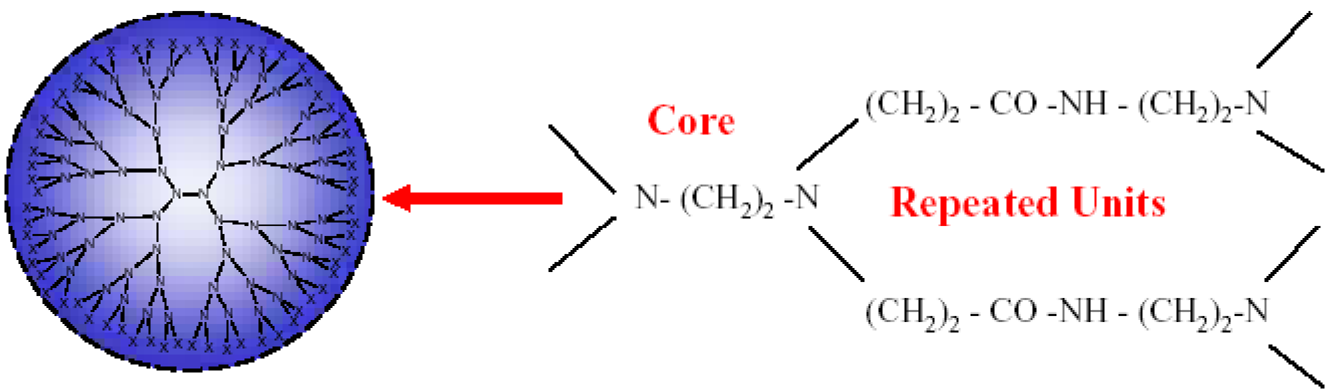
Dendrimers



Dendrimers are nanometer-sized, biocompatible polymers that can readily enter cells. They have been engineered to carry imaging agents and anti-cancer drugs in a single package.

Dendrimers structure

Starburst PAMAM Dendrimers



Dendrimers are 3d, highly branched, macromolecules with a core/repeat unit/terminal shell structure.

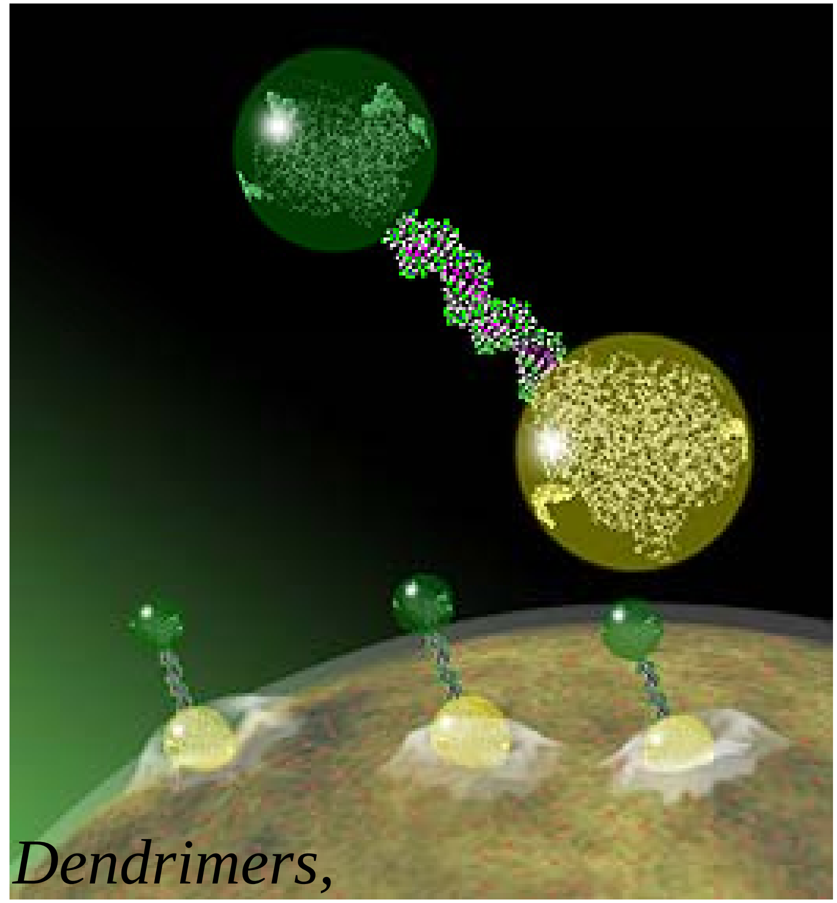
Cancer detection and treatment:

Complex contains:

tumor-targeting molecules
imaging agents
anti-cancer drugs

Binding modules via complementary DNA

Aim:
To target, image and kill tumor,



Dendrimers,
Michigan Center for Biologic Nanotechnology

Nanowires

- A **nanowire** is a nanostructure, with the diameter of the order of a nanometer (10^{-9} meters).

- Many different types of nanowires exist,
- Metallic (e.g., Ni, Pt, Au),
- Semiconducting (e.g., Si, InP, GaN, etc.),
- Insulating (e.g., SiO_2,TiO_2).
- Molecular nanowires are composed of repeating molecular units either organic (e.g. DNA) or inorganic (e.g. $Mo_6S_{9-x}I_x$).

The use of nanowires

- The nanowires could be used to link tiny components into extremely small electrical circuits –smaller electronics, computers.

- Nanowires, nanoparticles and other nanostructures are prospective and are used in sensing, as conductivity is very sensitive to adsorbed material

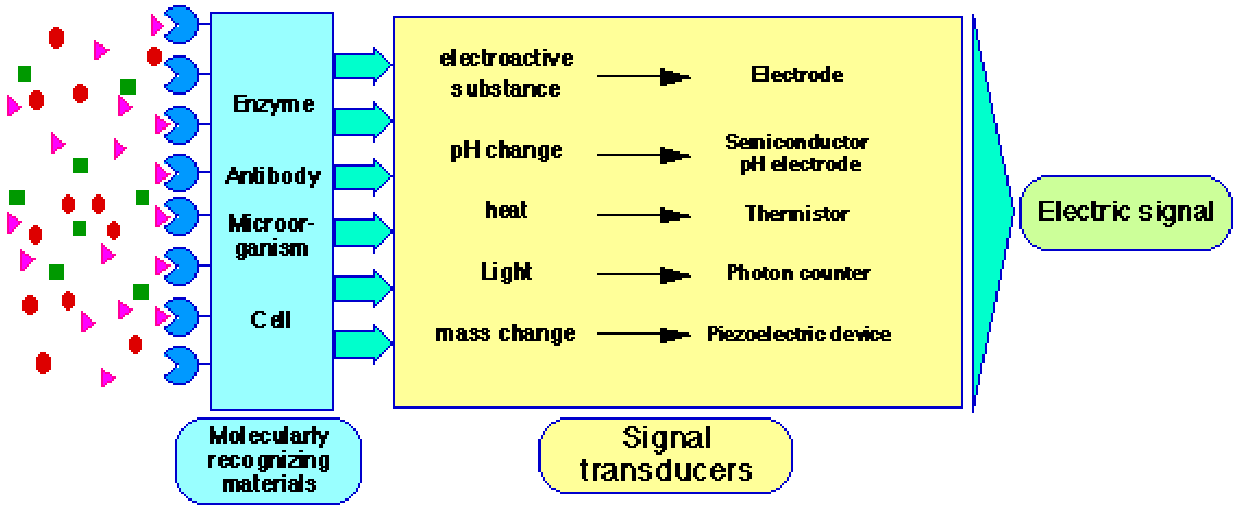
Detection - biosensors

Bio-recognition systems:

enzymes and antibodies, nucleic acids, bacteria, single cell, hole tissue of organism

Transducer:

electrochemical, pH changes, optical, mass and thermal changes.



Nanosensor- works at nanoscale, involves single molecule interaction, recognition and signal transfer

specific interactions – physico-chemical change – transducer – electric signal

Nanowires are used in sensing

- The surface atoms are sensitive to the adsorption of other atoms - nanowire-based sensing.
- Single molecule sensitivity
- Detecting biowarfare agents
- Testing toxicity

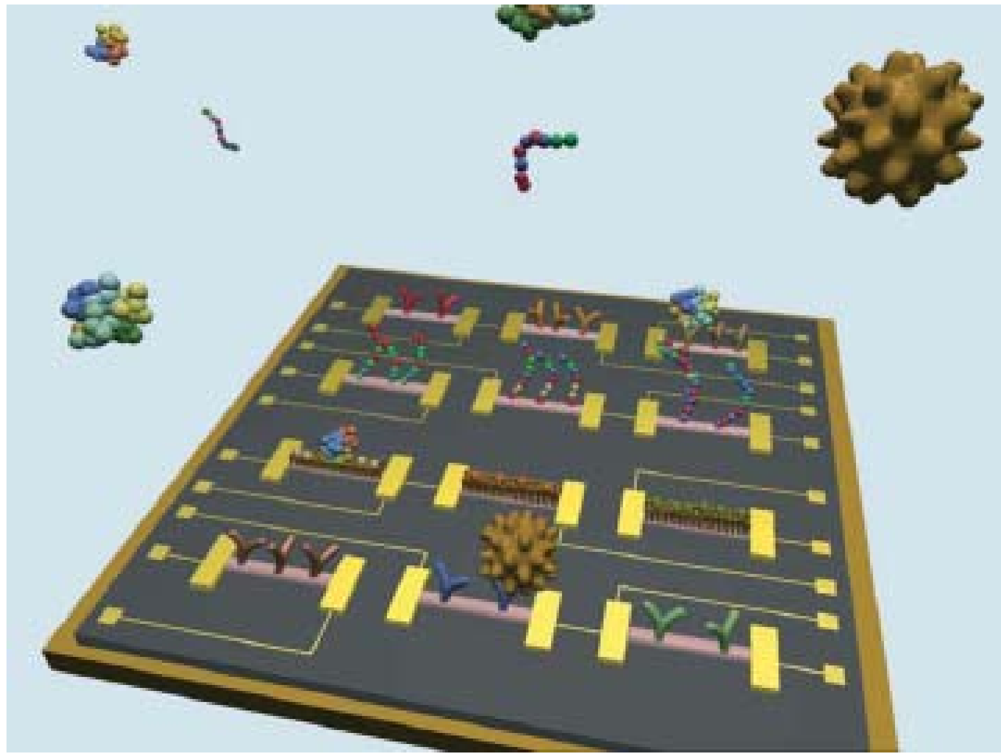
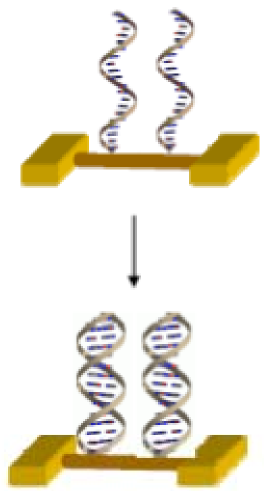
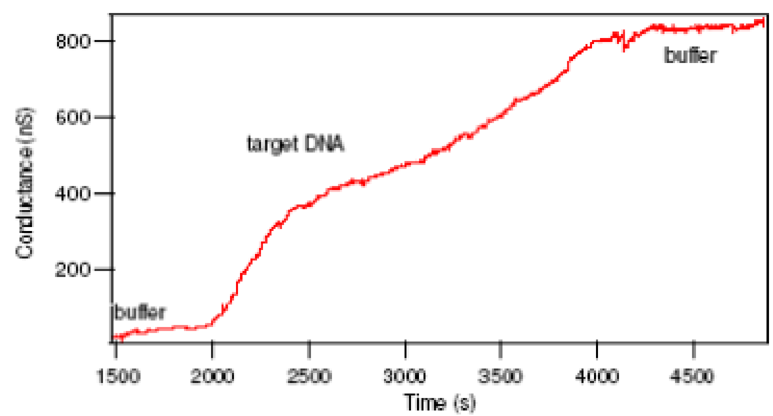


Illustration of a nanowire-based sensing concept as envisioned by F. Patolsky, C.M. Lieber et al. (2007) MRS Bulliten 32



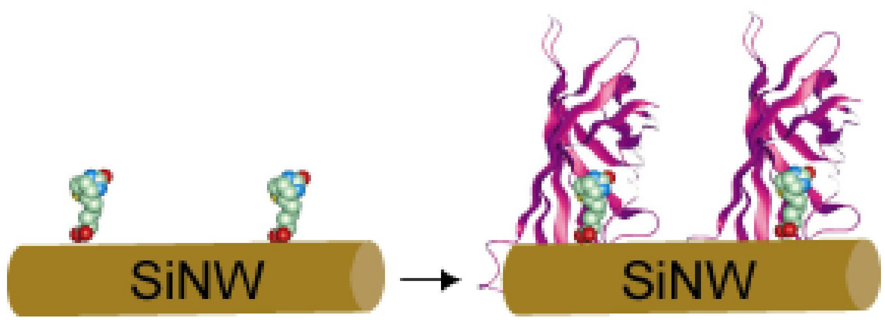


Yi Cui,

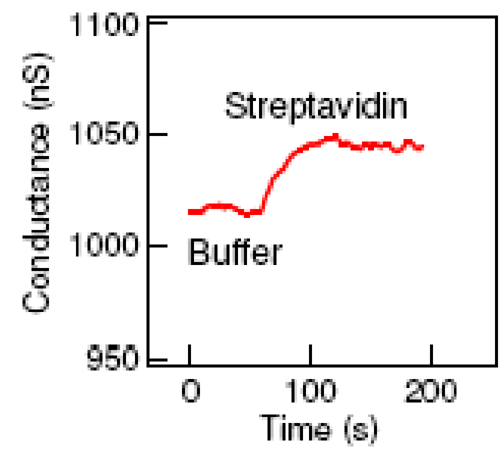
Dept of Material Science and Engineering,

Stanford University

DNA: highly negatively charged



25 pM streptavidin on biotin-nanowires



C60 and Carbon nanotubes

CNT is a tubular form of carbon with diameter as small as 1 nm.
Length: few nm to microns.

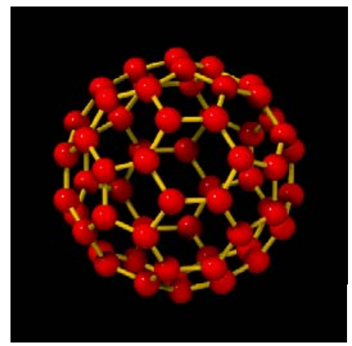
CNT is configurationally equivalent to a two dimensional graphene sheet rolled into a tube.

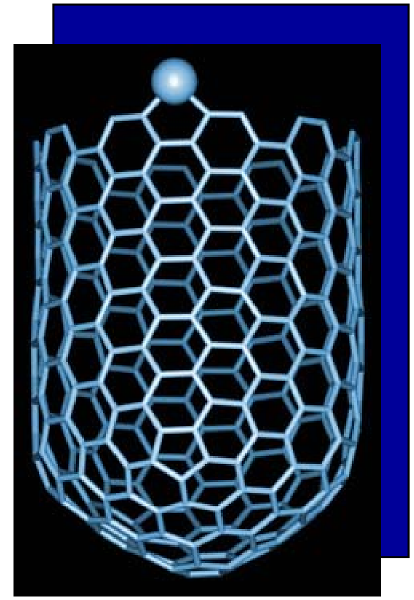
The strongest and most flexible molecular material

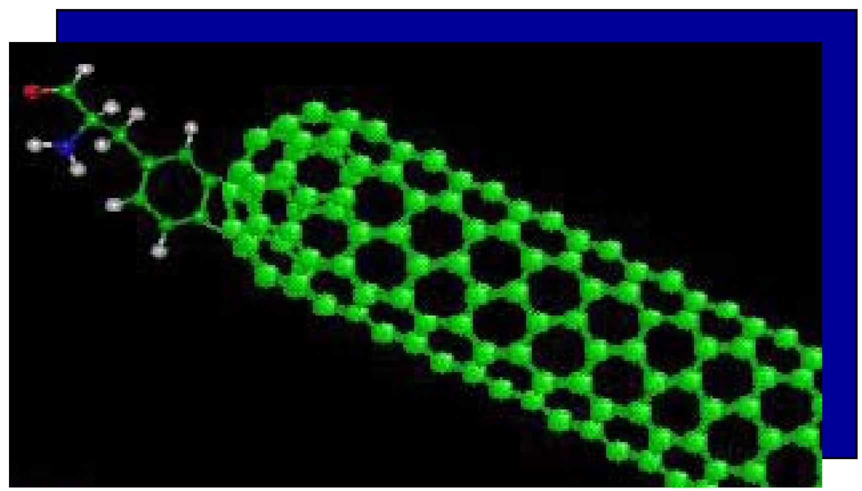
CNT can be metallic or semiconducting, depending on chirality.
Electrical conductivity six orders of magnitude higher than copper

Can be functionalized and filled with biomolecules and drugs

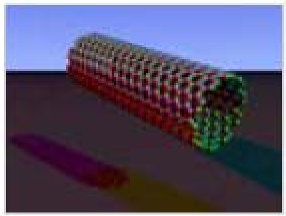
Fullerene



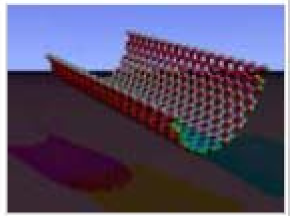




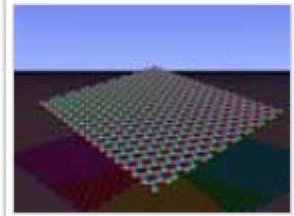
Single –walled CNT



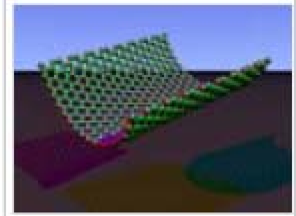
armchair (n, n)



the chiral vector is bent, while the translation vector stays straight



graphene nanoribbon



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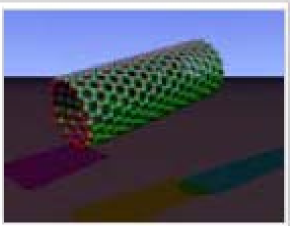
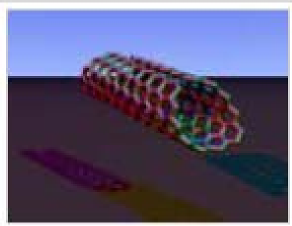
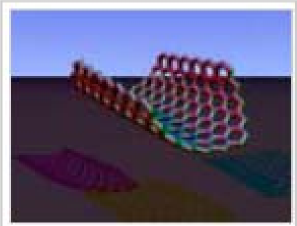


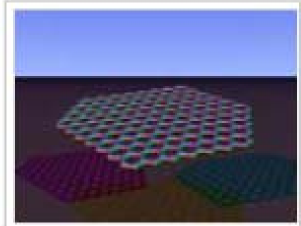
zigzag (n,0)



chiral (n, m)



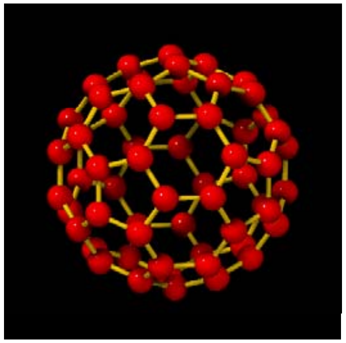
n and m can be counted at the end of the tube

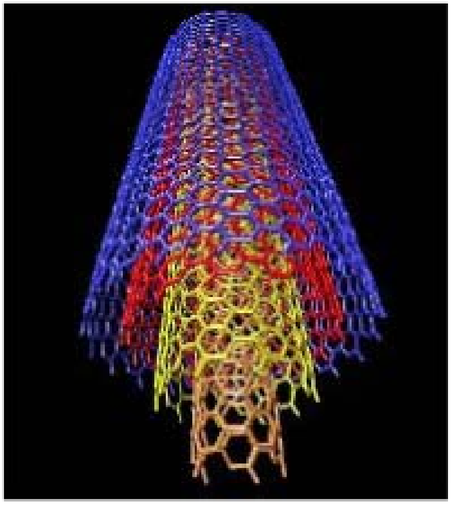


graphene nanoribbon

Other CNT

- Fullerene
- Multi-walled CNT
- Nanobud
- nanogear





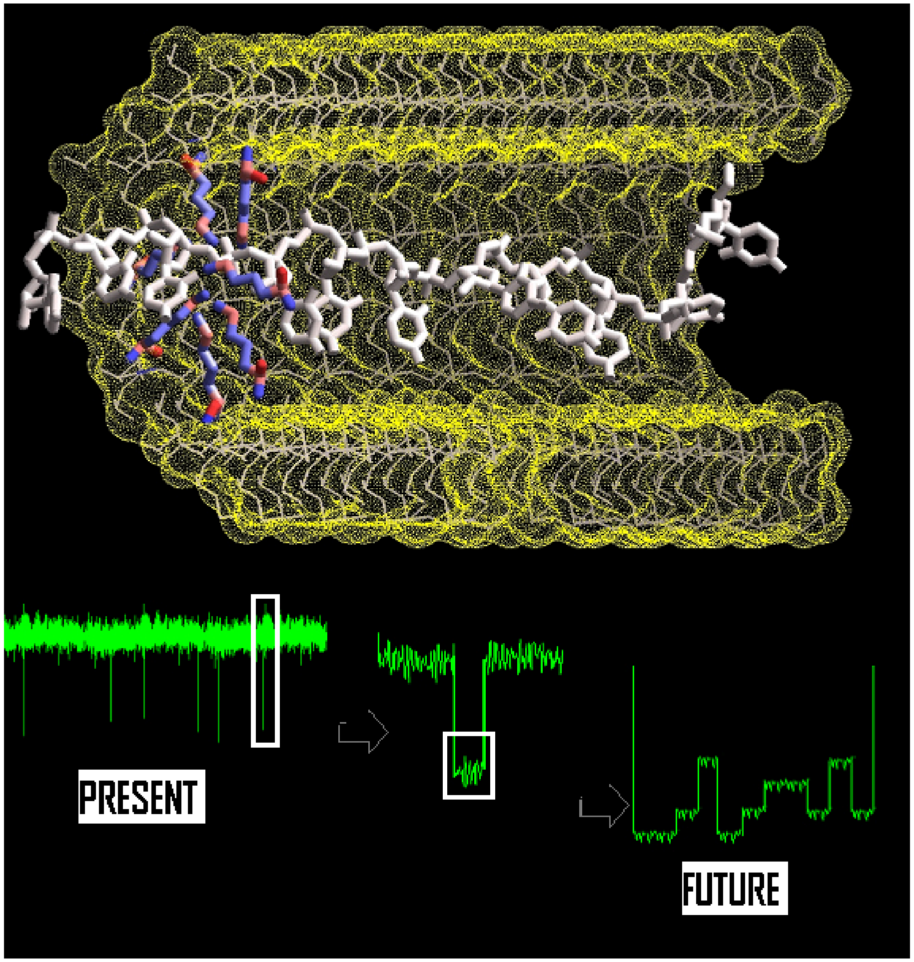
CNT applications

- Nanotubes, depending on their structure, can be metals or semiconductors.
- They are also extremely strong materials and have good thermal conductivity.
- The above characteristics have generated strong interest in their possible use in nano-electronic and nano-mechanical devices.
- For example, they can be used as nano-wires or as active components in electronic devices such as the field-effect transistor shown in this site.

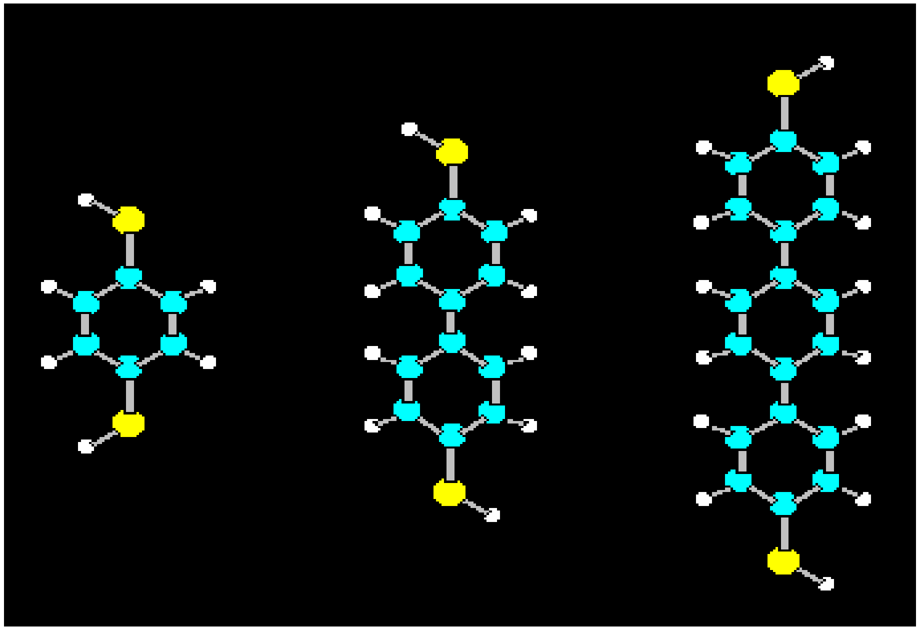
Use in bionanotechnology

- **As a vessel for drug delivery**
- The nanotube commonly carries the drug one of two ways: the drug can be attached to the side or trailed behind, or the drug can actually be placed inside the nanotube. Both of these methods are effective for the delivery and distribution of drugs inside of the body.

DNA analysis - nanopore



Molecular wires



R.P. Andres, S. Datta, D.B. Janes, C.P. Kubiak, R. Reifenberger
The design, fabrication, and electronic properties of self-assembled molecular nanostructures
in *Handbook of Nanostructured Materials and Nanotechnology*, edited by H.S. Nalwa, Vol. 3, pp. 179-231 (Academic Press, San Diego, 2000).

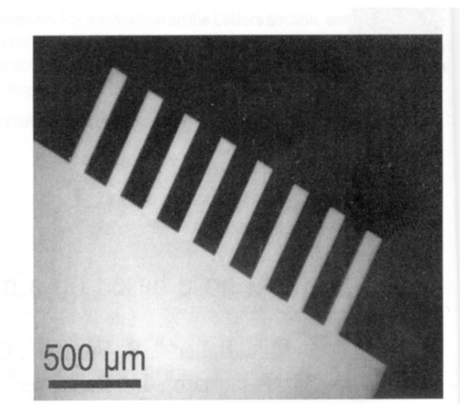
- Composition : Carbon(blue), Sulfur(yellow), Hydrogen(white)
- Length : 0.6 nm, 1.1 nm, 1.5 nm respectively
- They stick to gold surface using sulfur-gold bond and form intimate electric contact.
- Resistance is expected to be a few mega-ohms.
- On gold (111), they form a nice ordered self-assembly monolayer (SAM).

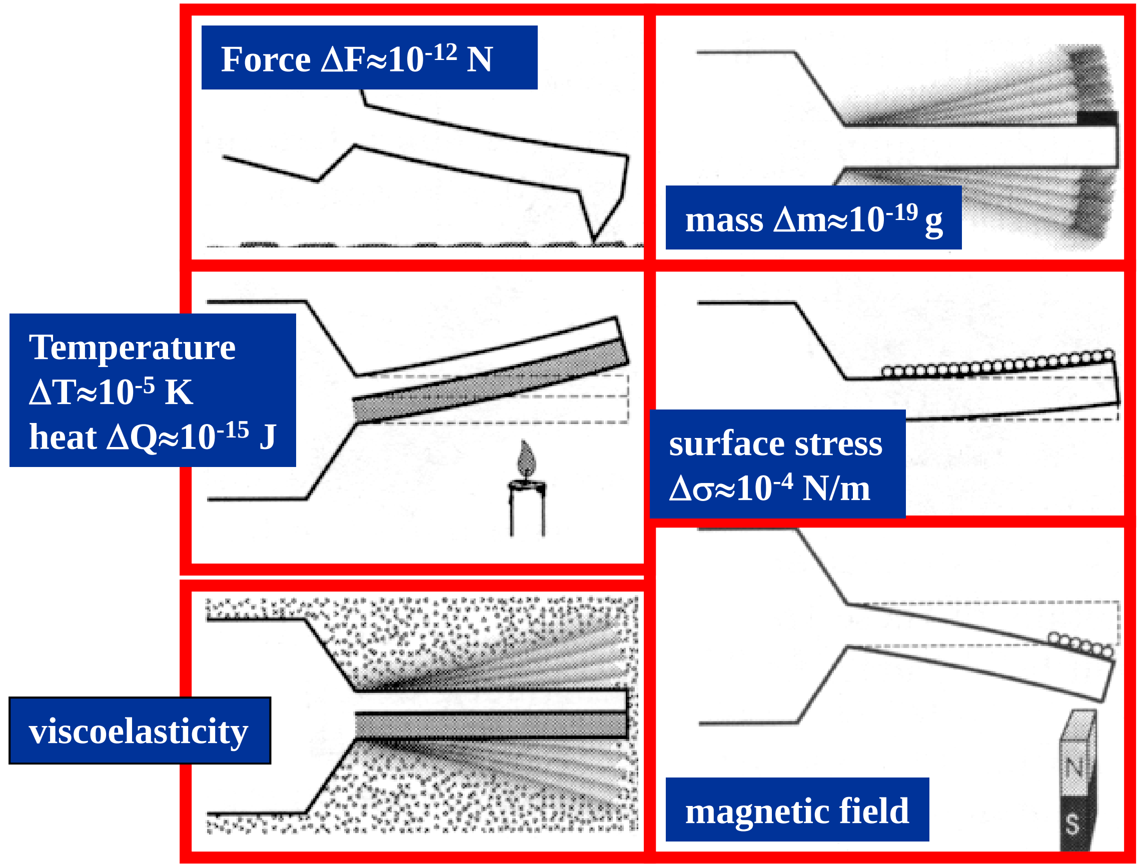
Actuators

- Machines which convert electrical motion to mechanical energy and visa versa.
- Example cantilevers

Cantilever based sensing

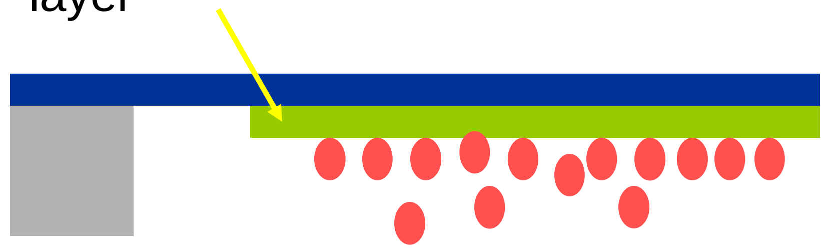
Frequency or
Deflection change





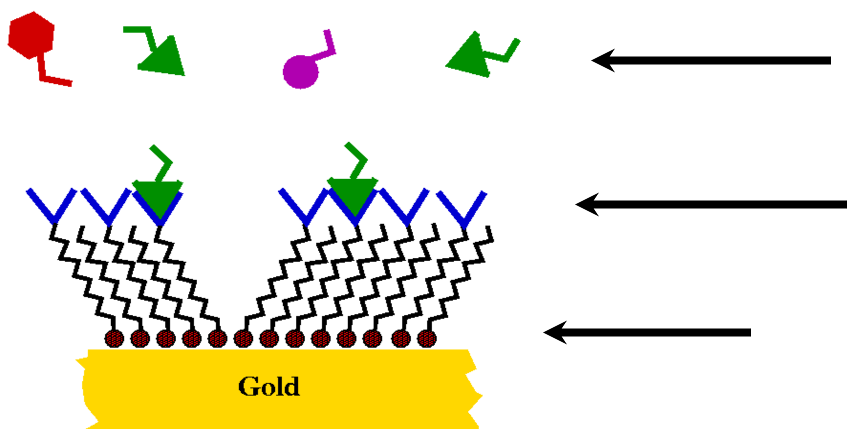
Cantilever based sensing

Molecule recognition layer



Analyte molecules

Making a Surface
Selective and Responsive



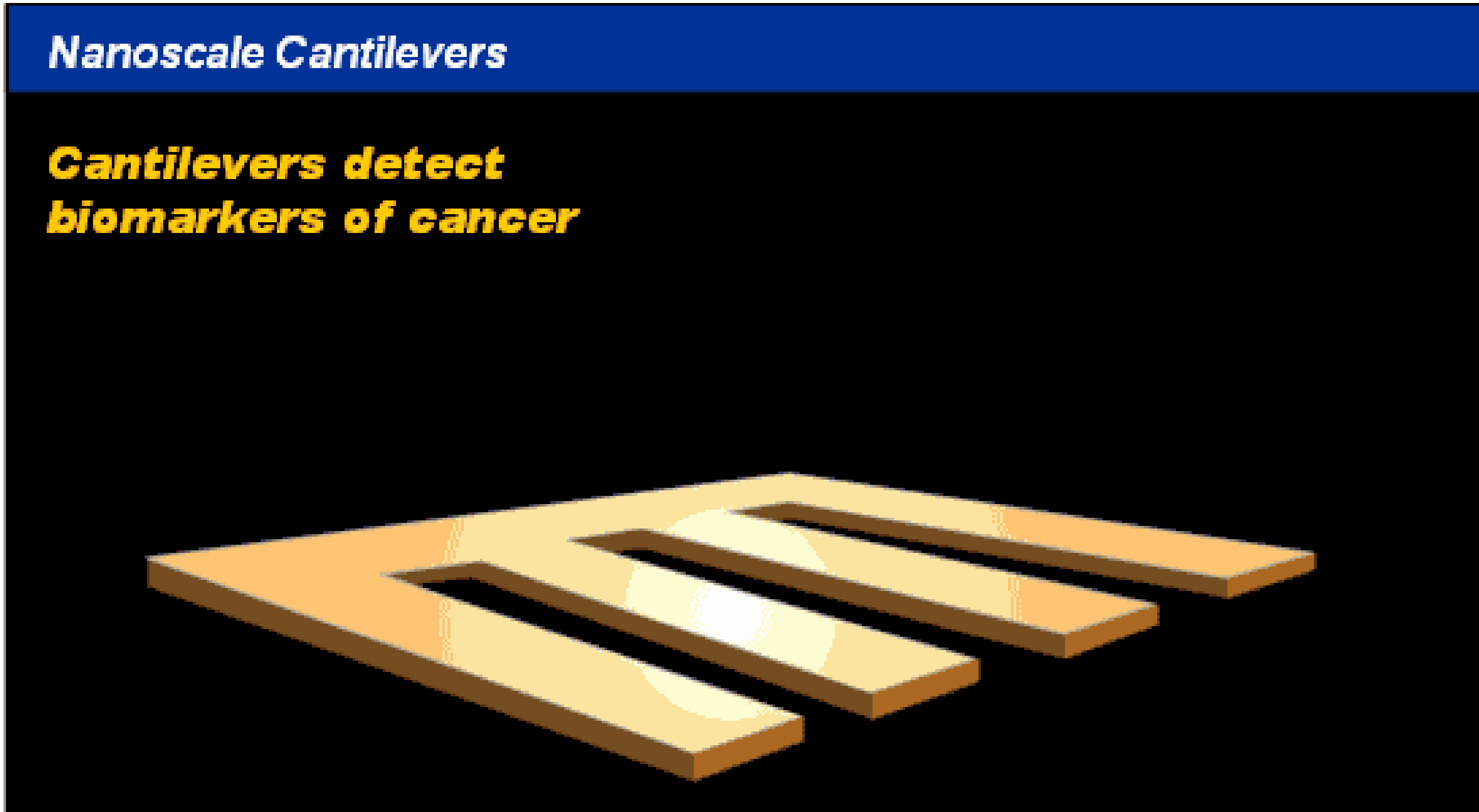
analytes

immobilized
Receptors

thiol SAMs,

Cancer detection

Cantilever based sensing



Reference: Arun Majumdar, University of California at Berkeley

Biological nanostructures

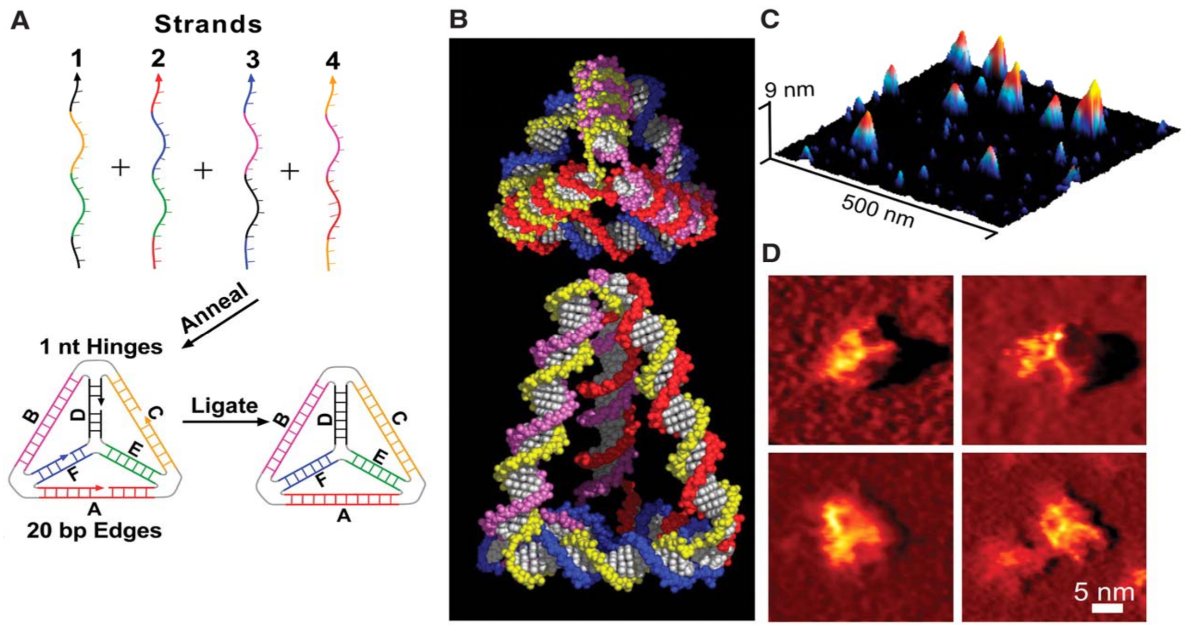
Include biomaterials such as amino acids, lipids, DNA, RNA, proteins, antibodies, membranes, cells, ect.

Desirable chemical, physical, electrical, optical, mechanical properties,

Specificity- Molecular recognition!

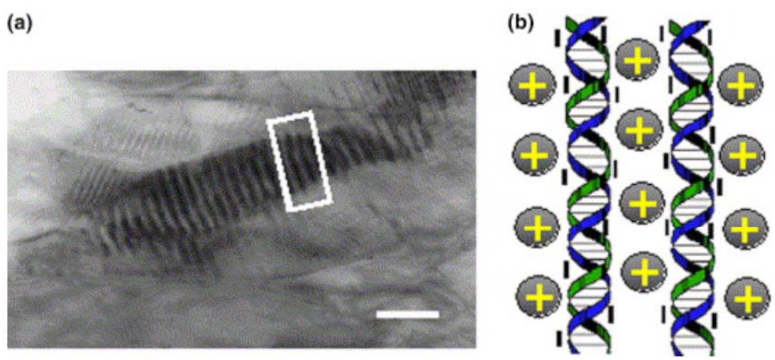
Potential applications in medical diagnostics, sensors, molecular electronics,
when combined with inorganic nanostructures

DNA is A NANOTECH SYSTEM



DNA templating gold particles

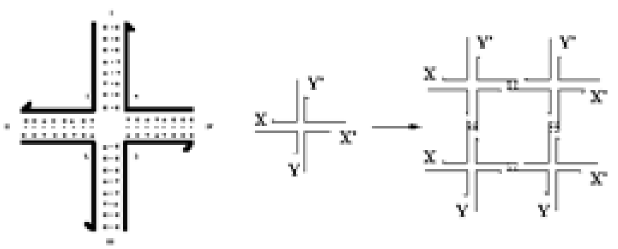
Curr. Appl. Phys. 5, 102 (2005)



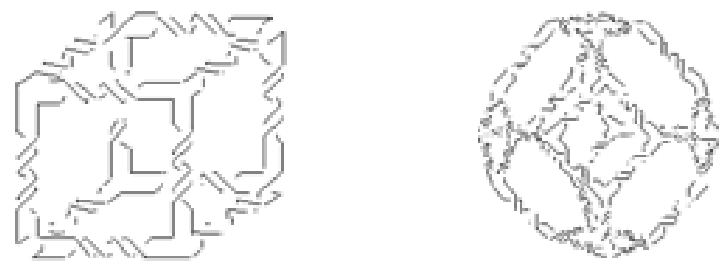
DNA Building Blocks for Molecular Nanofabrication

Science 310, 1661 (2005)

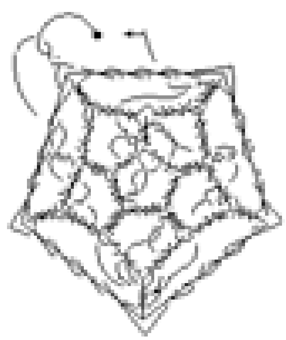
DNA Constructed Shapes



Left *-stable branched DNA molecule* ***Right****- a molecule with sticky ends*
Four of these sticky-ended molecules are shown assembled into a quadrilateral.



Cube and truncated octahedron



Schlegel diagram of a pentagonal dodecahedron

Borromean rings constructed from DNA.

Source: http://itri.loyola.edu/nano/us_r_n_d/09_04.htm

DNA Templating – Mirkin Group

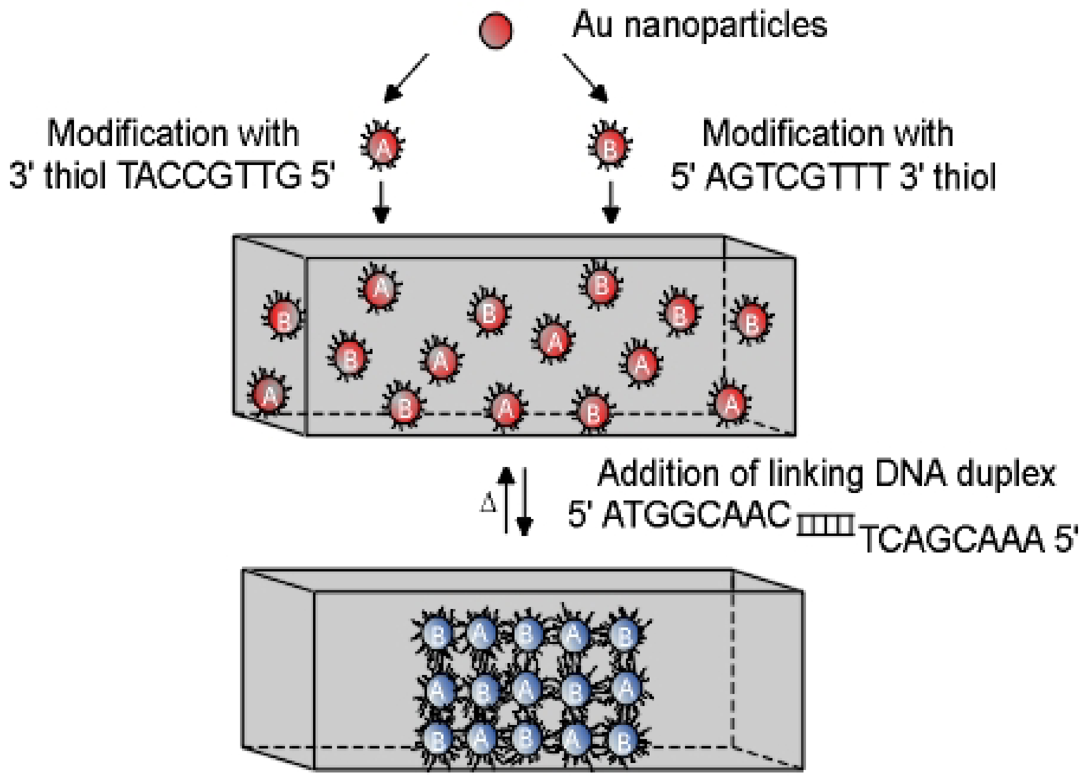
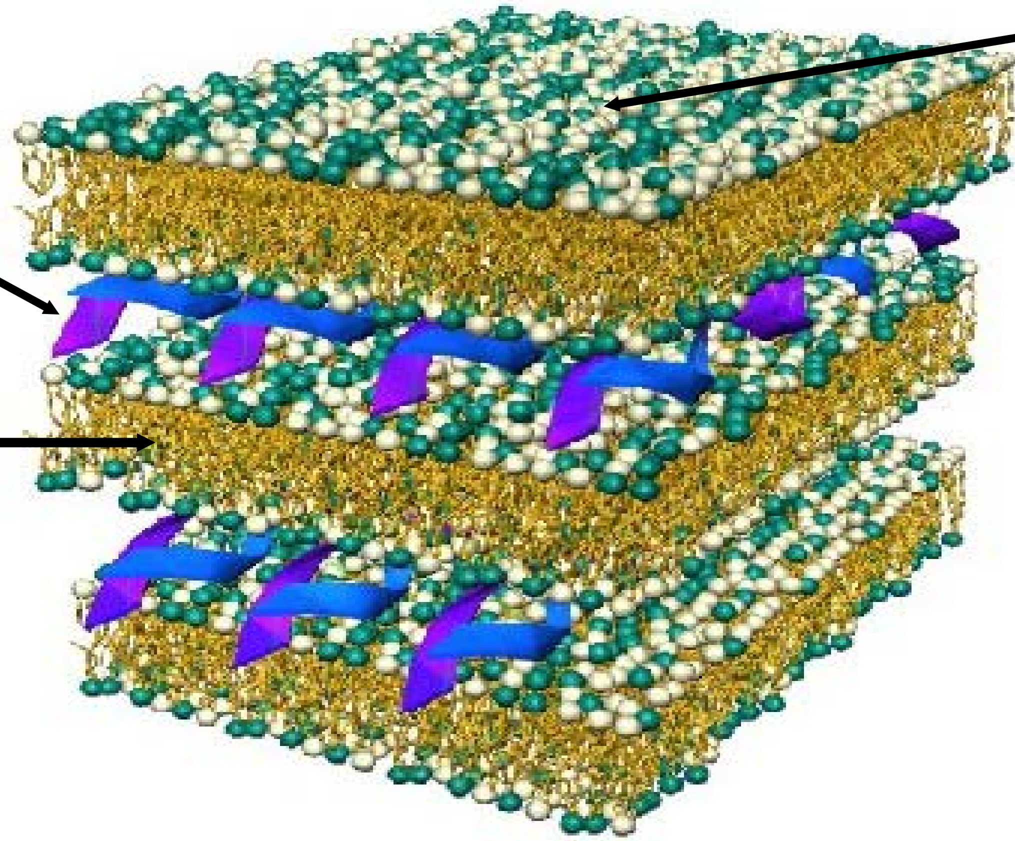


Figure 1. Scheme showing DNA-based nanoparticle assembly strategy.

Source: http://www.chem.nwu.edu/~mkngrp/nano/nano2.html

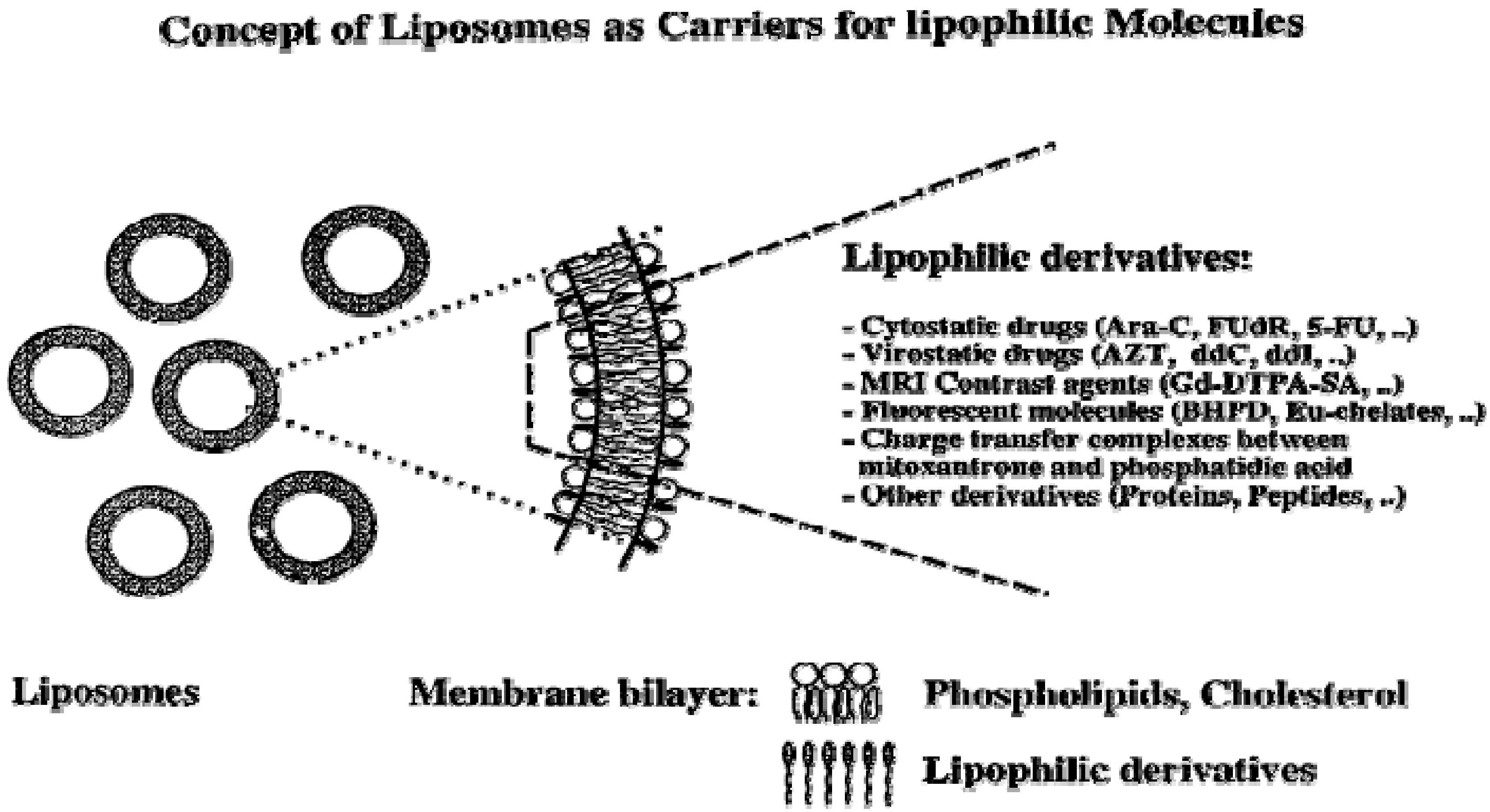
DNA Membrane Self Assembly



Source: http://www.aip.org/physnews/graphics/html/dna_memb.htm

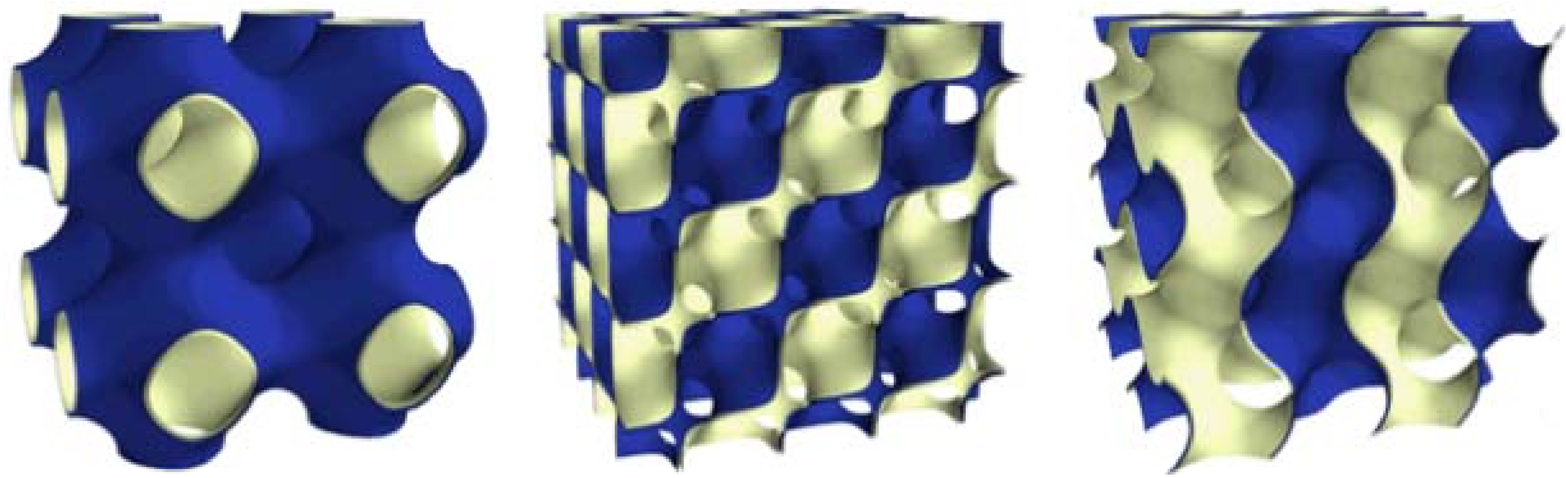
Applications of Liposomes

include drug delivery and carrier for molecules such as proteins, nucleotides, plasmids

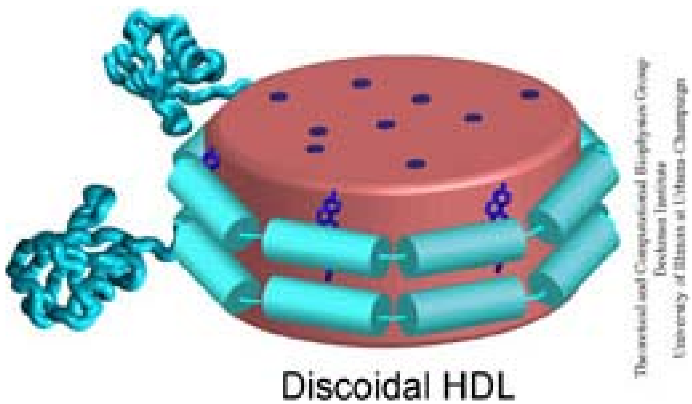


Source: http://www.unizh.ch/onkwww/lipos.htm

Lipid cubic phases as nano-carriers



Lipid nanodiscs

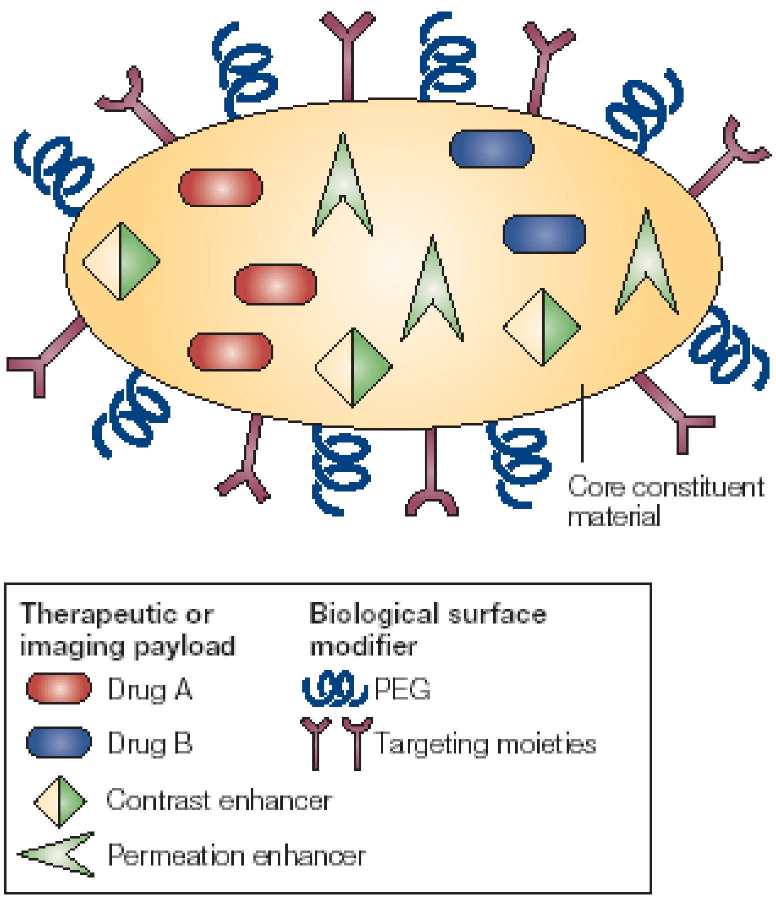


- Lipoproteins are protein-lipid particles which circulate in the blood collecting cholesterol, fatty acids and lipids. One such lipoprotein particle is called high-density lipoproteins (HDL) and is often regarded as "good cholesterol" due to its ability to remove cholesterol from artery walls and transport them to the liver for degradation.

Nanodiscs are an engineered rHDL mimic are being developed as platforms in which to embed membrane proteins in a native phospholipid bilayer environment. Various membrane proteins, such as cytochrome P450s, bacteriorhodopsin, rhodopsin, translocon, blood clotting factors, and bacterial chemotaxis receptors, have already been successfully incorporated into nanodiscs.

K Schulten, Beckman Institute Urbana, IL, Stephen Sligar, U. Illinois at Urbana-Champaign , http://www.ks.uiuc.edu/Research/Lipoproteins/

Multifunctional nanoparticles



carry therapeutic agents;

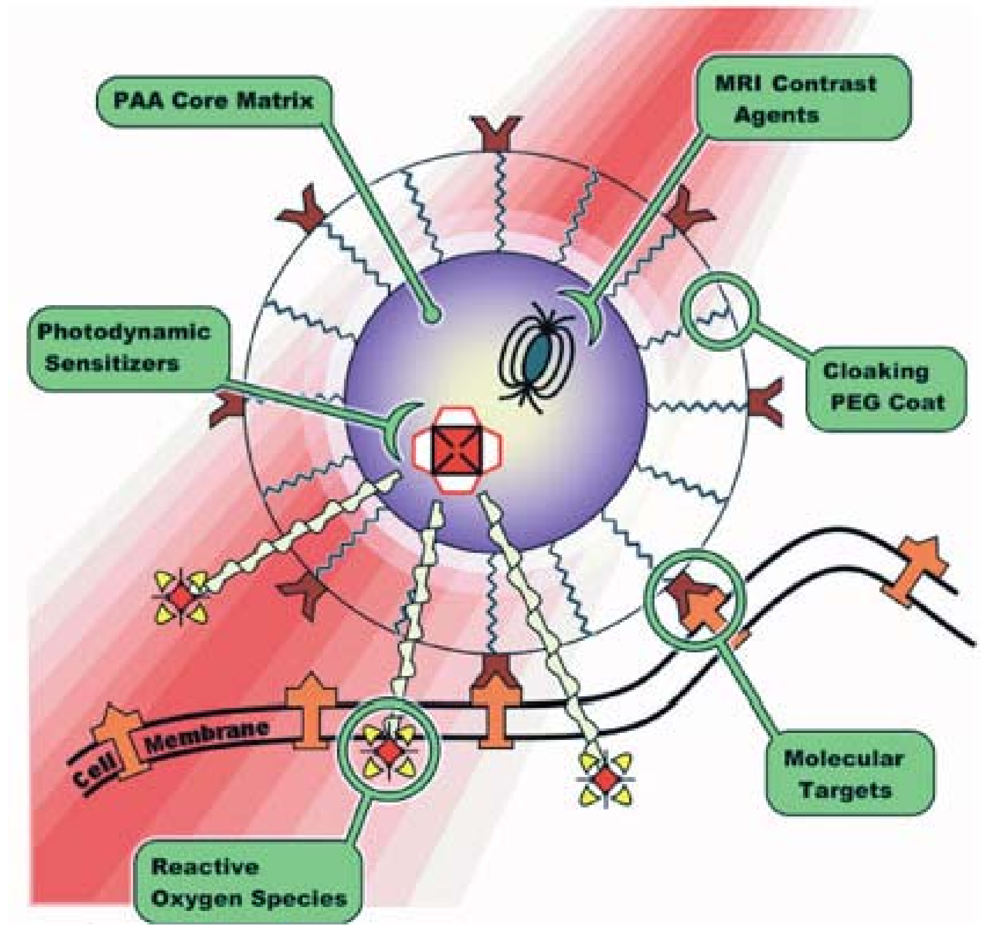
biomolecular targeting through recognition agents (antibodies);

imaging signal amplification, by way of co-encapsulated contrast agents;

biobarrier avoidance, polyethylene glycol (PEG)

Nanoplatforms, nanomachines

Combination of various nanostructures to create complex multipurpose, multifunctional, Nano-machines



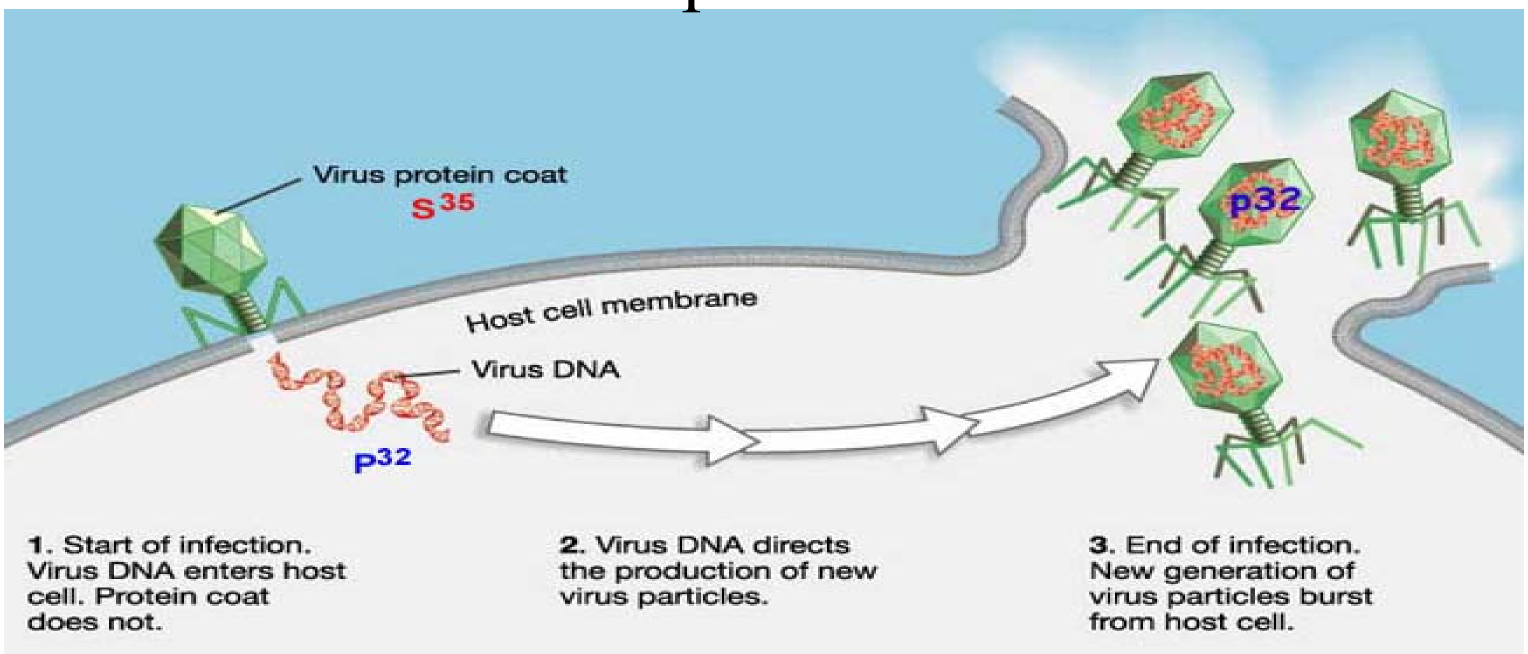
Raoul Kopelman, Ph.D., University of Michigan

The Nanotechnology Workforce

- Assemblers
  - Nanomachines that manipulate matter one atom at a time
  - Replicate at least once
- Replicators
  - Nanomachines that make copies of themselves
  - Function to increase the work-force

Examples from nature

Viral Self-replication



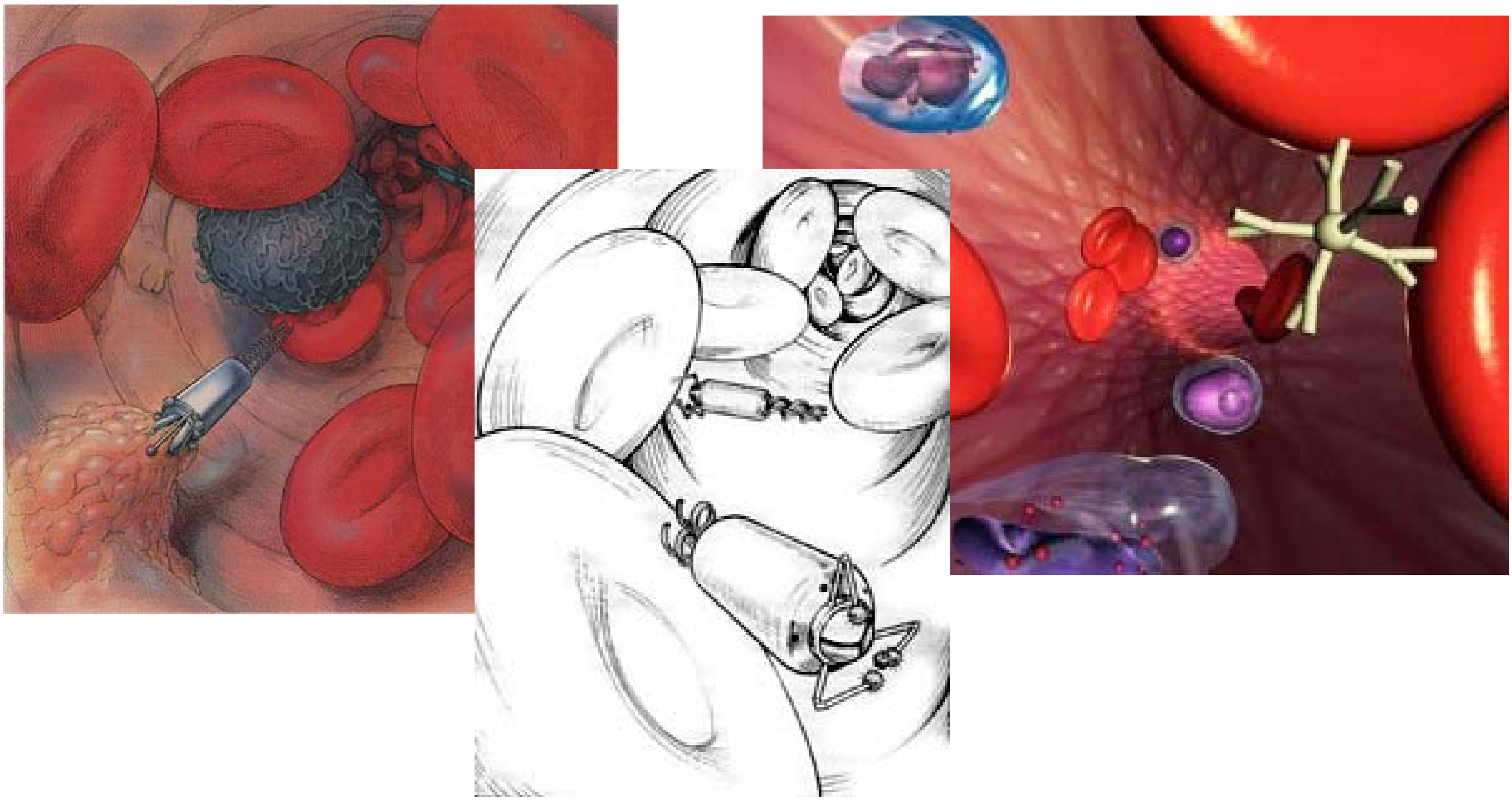
- Use their environment to replicate more identical virions
- Regulated by environmental conditions

nanotechnology – nanomanufacturing

- Create assemblers and disassemblers
- Nanomachines and nanoengines

- http://www.youtube.com/watch?v=vEYN18d7gHg&feature=related

Visions for the Future: Biomedical Nanotechnology



Questions/problems

- Uncertainty principle?
- Molecular vibrations?
- Radiation?
- Evolution has failed to create assemblers-is it impossible?
- Is there special magic in the cell?
- Should we just wait for them to be created?

Road Ahead..

We should close this office.. Everything that needs to be invented, is already..
Director, US Patent Office, 1929

A few computers should be enough for the society!
Watson (IBM Watson Center fame)

640k should be enough for everyone!
Bill Gates, 1982

Infectious diseases is now history..
Surgeon General, 1959

Graduate Program in Nanotechnology

- The University of Waterloo offers the first MS and PhD programs in Nanotechnology of its kind in Canada. The interdisciplinary research program, jointly offered by three departments in the Faculty of Science and four in the Faculty of Engineering, provide students with a stimulating educational environment that spans from basic research through to application. The goal of the collaborative program is to allow students to gain perspectives on nanotechnology from a wide community of scholars within and outside their disciplines in both course and thesis work.
- The MS collaborative program provides a strong foundation in the emerging areas of nano-engineering in preparation for the workforce or for further graduate study and research leading to a doctoral degree. Four key areas of research strengths have been identified: nanomaterials, nano-electronics design and fabrication, nano-instruments and devices, and nano-biosystems. The objective of the PhD program is to prepare students for careers in academia, industrial research and development, and government research labs.

- Waterloo Institute for nanotechnology (WIN)
- https://uwaterloo.ca/institute-nanotechnology/