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Principles and Applications of Nanobiotechnology

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Focus on Nanobiotechnology

This issue looks at some of the emerging life science applications of nanotechnology and nanoscience, a field that has been loosely termed nanobiotechnology. Nanobiotechnology integrates the design of new materials and devices with the exquisite specificity of biological molecules, enzymes and cells. Applications include new types of biomaterials, sensors relying on conformational changes in biomolecules, molecules for use in imaging and tagging macromolecules and cells, and devices, materials and particles for use in drug delivery or directly as therapeutics.

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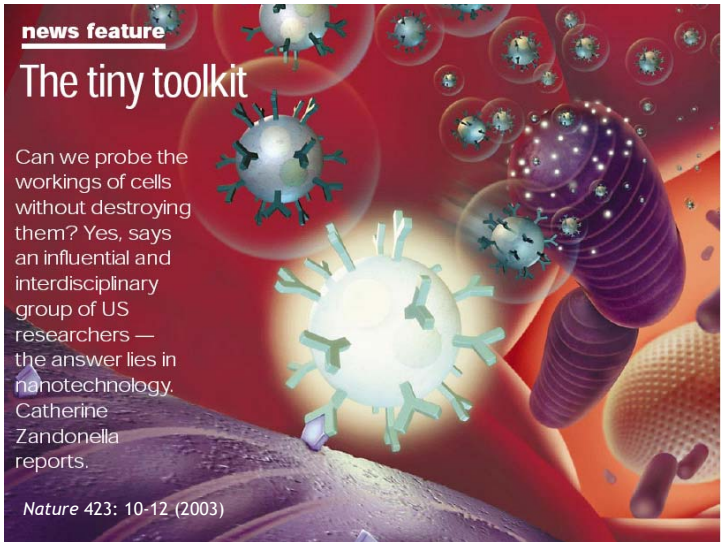
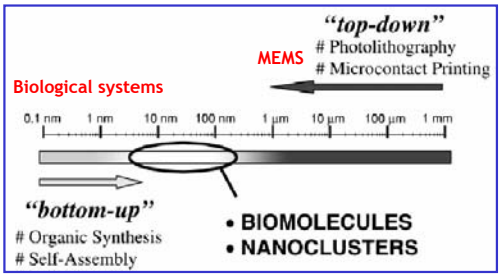


Definition and Scope of Nanotechnology

- Science for exploring the materials and phenomena in the nanometer (atomic, molecular) scale
- Technology for manipulating and controlling the structure and components in the nanometer scale, thus inventing new materials, devices and systems



What is Nanobiotechnology?

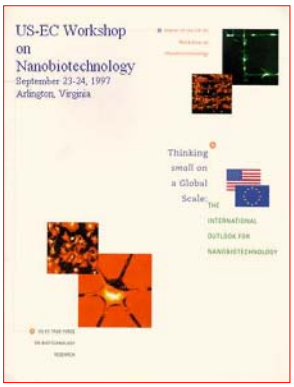
Nanobiotechnology

- Nanobiotechnology is the application of nanotechnology to the life sciences. This research field includes two approaches. One is the application of nano-scaled tools to biological systems and the other is the use of biological systems as templates in the development of novel nano-scaled products.
- Nanobiotechnology is the intersection of inorganic and organic engineering to solve critical problems in biology. These problems can be the creation of new drugs, drug delivery vehicles, diagnostics, sensors, assays, tools such as fluidics, and manufacturing processes for all of the above.

  (Source) Ian J. Mehr, "Nanobiotechnology, Commercial Opportunities from Innovative Concepts," D&MD Reports #9072 (2002. 4)
- A continuum of opportunity for nanotechnology in the life sciences Nature Biotechnology 21: 1137-1143 (2003)

Why Nanobiotechnology?

- Mother Nature did it first. Nature has built nanomachines for millennia.
  - *Nature applies nanotechnology daily to grow the multifunctional cells and tissues of plants and animals from a single biological cell*
  - *A cell is a warehouse of nanoscale machines.*
- Biology can teach the physical world of electronics, computing, materials science and manufacturing
  - *There exist biomolecular analogues of conventional functional devices*



An Animal's Senses Guide Its Movements

- **Nostrils** on each side of the head of the salmon allow water to flow into one and out the other
  - Sensory cells in the nostrils detect specific chemicals in the water
  - These cells aid the salmon in its homing ability
- Salmon have a **lateral line system**, seen here as a blue line along the sides of the fish
  - This enables the salmon to sense the direction and velocity of water currents and thus distinguish which direction is upstream

Capillary-force Actuators

- Surface tension and capillary forces can be controlled actively or passively using different effects: electrocapillary, thermocapillary, and passive capillary.

Electrocapillary Effect (known as Electrowetting)

Changes the surface tension between two immiscible, conductive liquids or between a solid surface and a liquid by varying their potential difference.

Machines & Molecular Machines

Machines	Molecular machines
Vehicles	Hemoglobin
Assembly lines	Ribosomes
Motors, generators	ATP synthases
Train tracks	Actin filament network
Train controlling center	Centrosome
Digital databases	Nucleosomes
Copy machines	Polymerases
Chain couplers	Ligases
Bulldozer, destroyer	Proteases, proteosomes
Mail-sorting machines	Protein sorting mechanisms
Electric fences	Membranes
Gates, keys, passes	Ion channels
Internet nodes	Neuron synapses

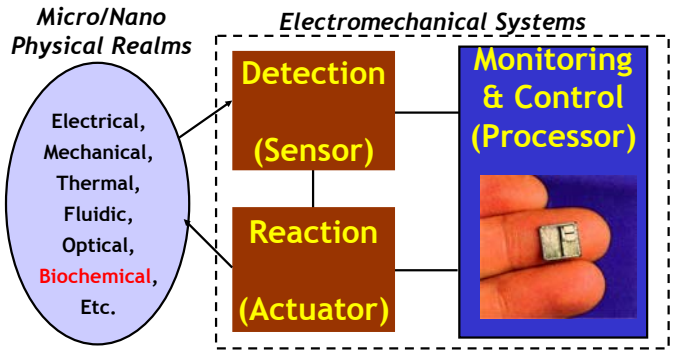
Nanotechnology Impacts on Biology

- Nanotechnology also offers researchers the chance to detect rare events or molecules that are present only at low concentrations.
- As nanotechnology brings more tools to the biologist's bench, the divisions between the fields of science will begin to break down.
- *"The combination of microfluidics and nanotechnology will transform how biologists do everything."*

Nanofabrications

MEMS/ NEMS
Self-Assembly
Dip-Pen Nanolithography
Soft-Lithography
PDMS Molding
Nanoparticles, Nanowires, Nanotubes

Electro Mechanical Systems



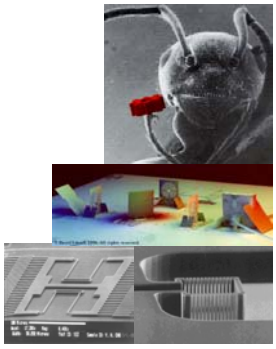
What is MEMS/ NEMS?

- Integrated micro devices or systems combining electrical and mechanical components fabricated using integrated circuit (IC) compatible batch-processing techniques and range in size from micrometers to millimeters

  In US: MEMS, Micromachining
  In Europe: Micro Systems Technology (MST)
  In Japan: Micromachines,MicroRobots

- Miniaturization of non-electrical (optical· thermofluidic· biochemical) components

- *MEMS: Micro Electro Mechanical Systems*
- *NEMS: Nano Electro Mechanical Systems*



What is BioMEMS/NEMS?

- A Paradim Shift in the Making
  "MEMS become BioMEMS" (BioPhotonics 2000.6)

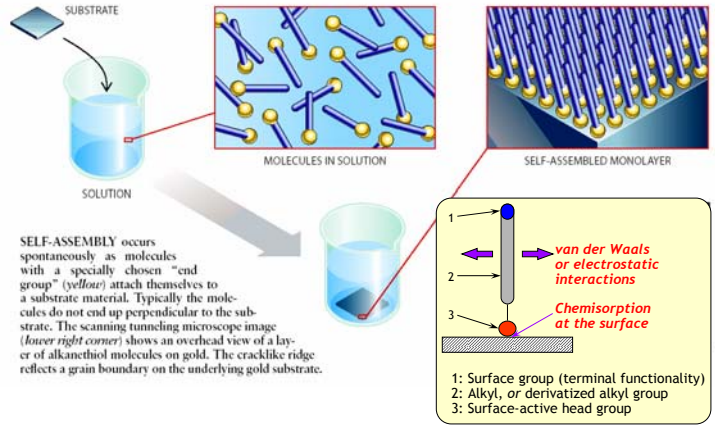
- *Implementation of MEMS/NEMS to Bio-related areas (Bio Micro/Nano Electro Mechanical Systems)*

- *Needs*
  - Lower chip cost *(Glass or plastic chips)*
  - Reduction of expensive reagents & test compound used
  - Integration of multiple functions onto a single chip *(Micro total analysis system (μ-TAS), Lab-on-a-chip)*
  - Point-of-care (POC) diagnostics *(Easy sample preparation)*
  - High throughput *(Microfluidic HTS disposables)*

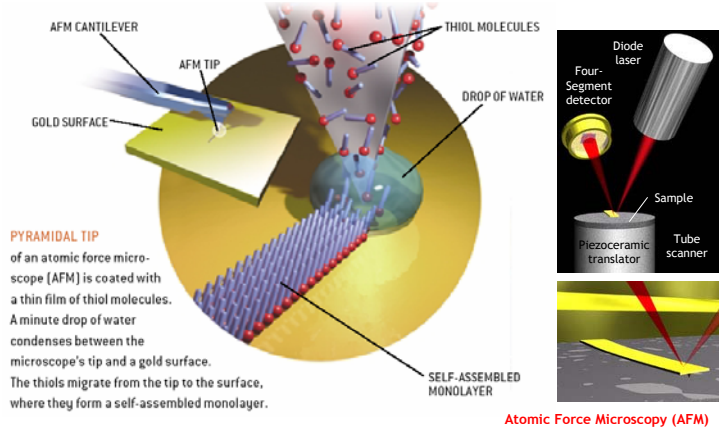
Biotechnological & Biomedical Microsystems

- Tools for Chemistry, Molecular Biology and Biochemistry
  - Sample preparation, Molecular separation
  - Small-scale organic synthesis
  - Amplification of nucleic acids/ Sequences
- Tools for Cell Biology
  - Cell mechanics & dynamics, Cell culture devices
  - Dielectrophoresis, Flow cytometry, Cell sorting
- Tools for Medicine, Biomedical Devices
  - Minimally invasive surgery
  - Neural prosthesis
  - Implantable devices, DDS
- Miniaturized analytical systems
  - Genomics and proteomics
  - Clinical analysis, Environmental testing, and Warefare defense
  - High throughput screening

Self-Assembly

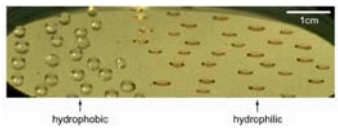


Dip-Pen Nanolithography

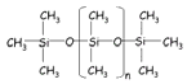


Atomic Force Microscopy (AFM)

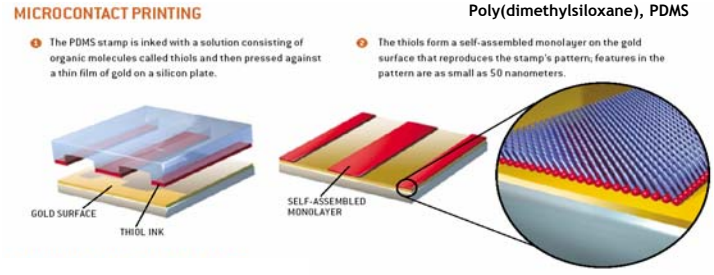
Soft lithography



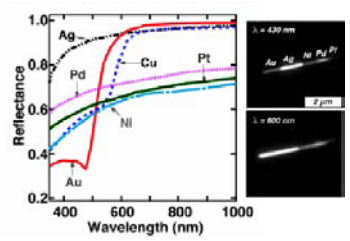
- Self-Assembled Monolayers (SAMs)
- Contact Printing, Replica Molding, and Embossing
- Elastomeric Stamps and Molds
- Masters and Rapid Prototyping



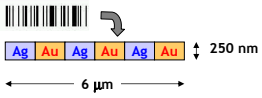
Poly(dimethylsiloxane), PDMS

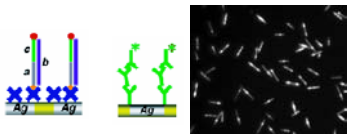


Nanobarcodes™ Particles



- Cylindrically-shaped, striped metal particles, readout based on differential reflectivity using an optical microscope





Multiplexed DNA assays

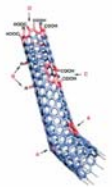
Multiplexed Oligo Titrations

Multiplexed Sandwich immunoassays

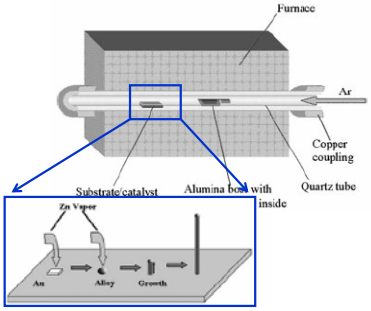
Proximity-based Bioassays

www.nanoplextech.com

Synthetic Methods for 1-Dimentional Nanostructures

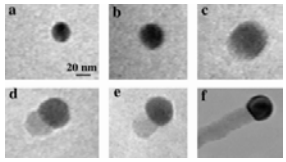


Thermal chemical vapor deposition(CVD)



One-Dimentional Nanostructures are grown on the Au-coated substrate

Adv. Funct. Mater. **2002**, *12*, 323
Adv. Mater. **2003**, *15*, 353
J. Am. Chem. Soc. **2001**, *123*, 3165

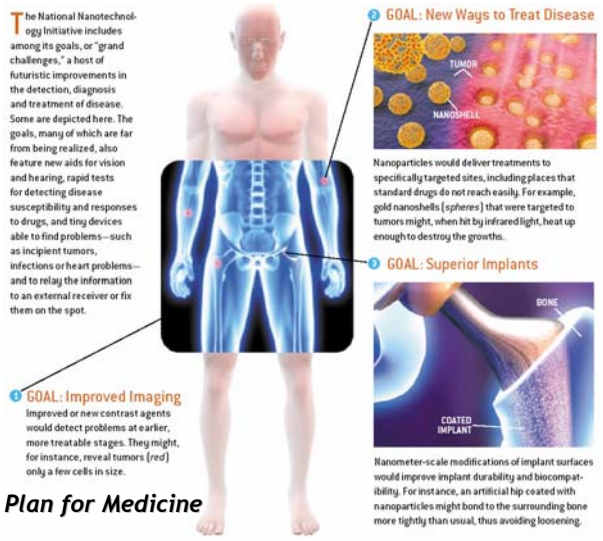


Real observation :
In-situ Nanowire growth by TEM

Nanobiotechnology Applications

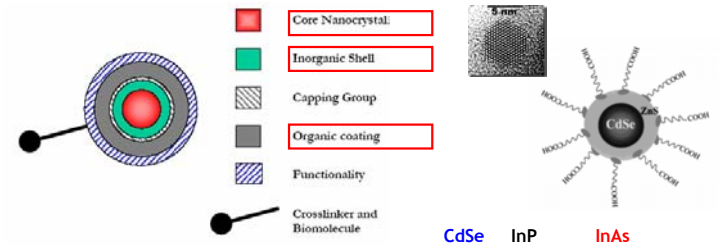
Nanomedicine

Nanobiosensor (biochip)
Nano Fluidics (LOC, Biofluidic devices)
Molecular Self-Assembly
Intelligent Drug Delivery Systems (DDS)
Nanomachine
Other Nano-Bio Devices & Systems



A Grand Plan for Medicine

Quantum Dot Nanocrystals



Size- and material-dependent optical properties

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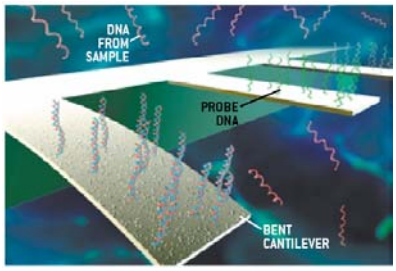
Translating Biomolecular Recognition into Nanomechanics

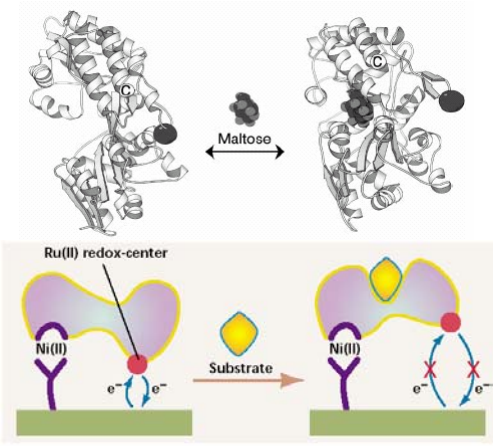


Biological samples can be screened for the presence of particular genetic sequences using small beams (cantilevers) of the type employed in atomic force microscopes.

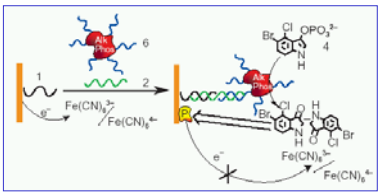
The surface of each cantilever is coated with DNA able to bind to one particular target sequence.

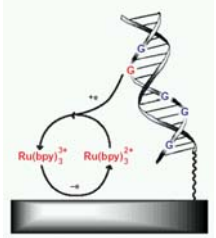
Bioelectronic Sensor

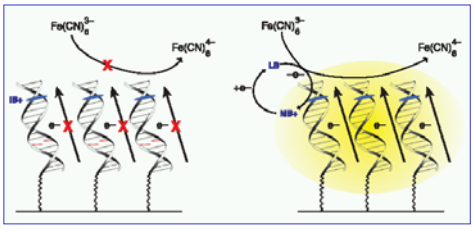
Science 293:1641-1644 (2001)



Electrochemical DNA Sensors







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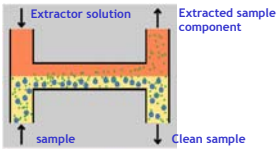
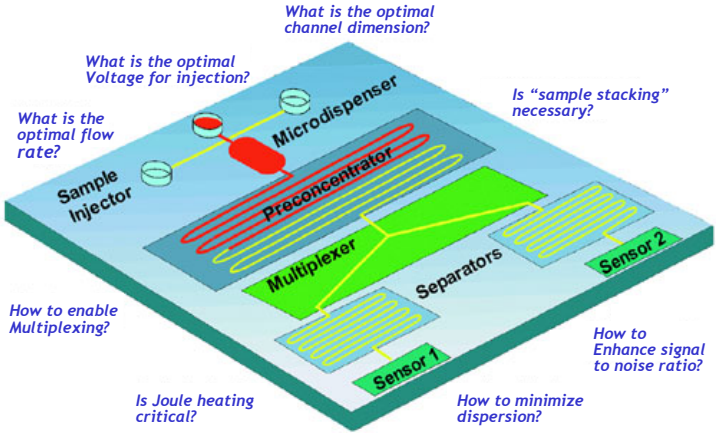
Other Nano-Bio Devices & Systems

In microchannels in which either width or height is less than ~200 μm,

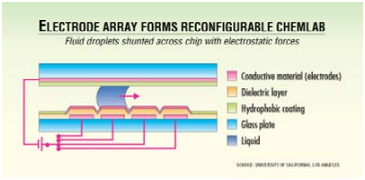
- Aqueous flow is generally laminar, not turbulent
- Diffusion is an efficient process for mixing the dissolved contents of two or more fluids
  - Diffusion-based Separation: H-Filter
- Particles can also be separated by diffusion according to their size



How does one successfully build a lab-on-a-chip?



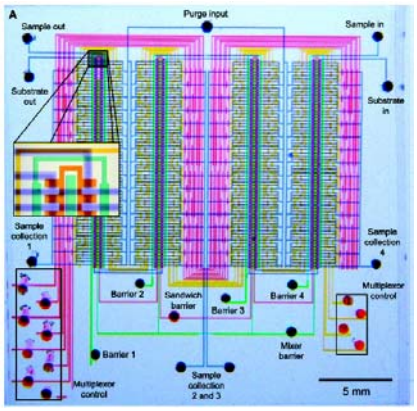
Lab-on-a-chip tech goes reconfigurable

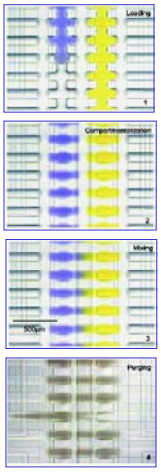


http://www.eetimes.com/story/OEG20030407S0049

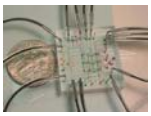
http://cjmems.seas.ucla.edu/

Microfluidic Comparator Chip

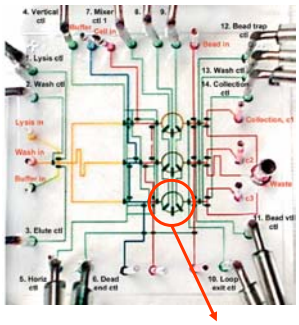


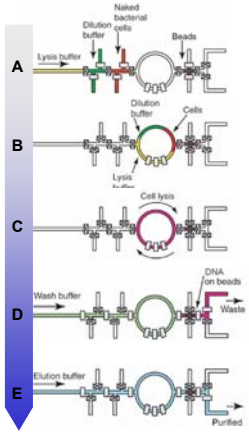


Science 298: 580-584 (2002)



Nanoliter-Scale Nucleic Acid Processor





Nature Biotechnology 21: 1179-1183 (2003)

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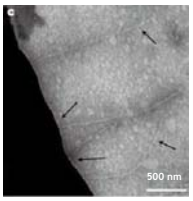
Biomolecular Recognition of Semiconductor Quantum Dots and Magnetic Materials

Peptide combinatorial approach

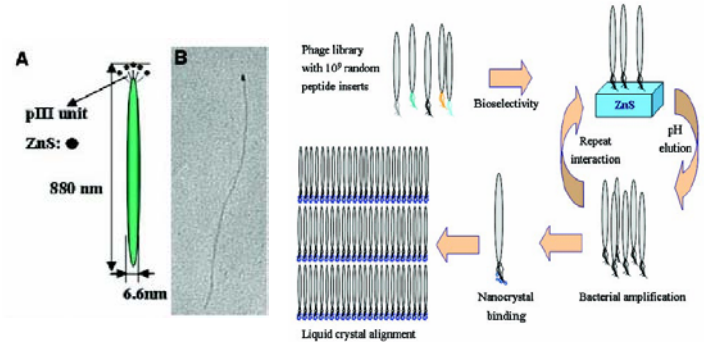
- Select peptides with high affinity for specific semiconductor structures and crystal orientations using molecular recognition
  - Phage display and bacterial display
- Rationally design peptides and polymers to assemble nanoparticles in 2D and 3D structures



TEM image of G1-3 phage recognition of GaAs. Individual phage particles are indicated with arrows.

Nature 405: 665-668 (2000)

Ordering of Quantum Dots Using Genetically Engineered Viruses



Science (2002) 296: 892-895

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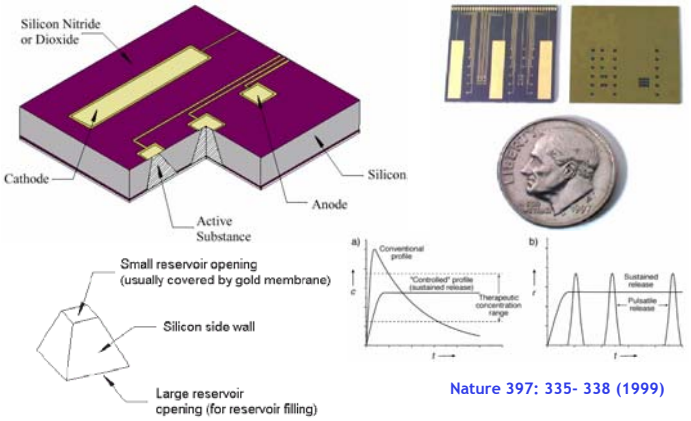
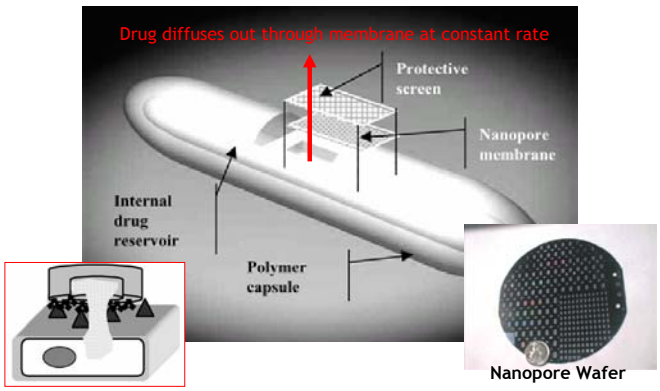
A Controlled-Release Microchip for Drug Delivery



Nature 397: 335- 338 (1999)

NanoGate Implant, iMEDD, Inc.

intelligent MicroEngineered Drug Delivery



Nanopore Wafer

Nanobiotechnology Applications

Nanomedicine
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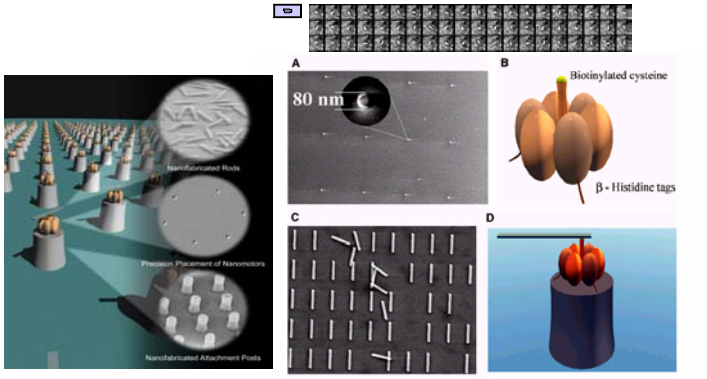
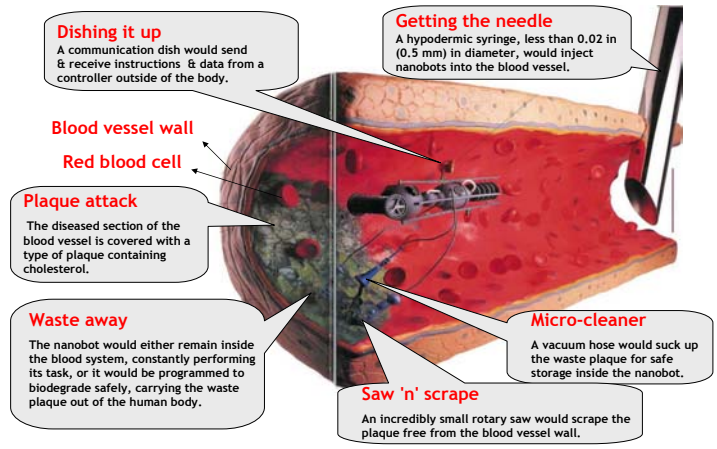
Biomoelcular Motor



Science
290:1555-1558
(2000)

Fig. 1. Schematic diagram of the F_1-ATPase biomolecular motor–powered nanomechanical device. The device consisted of (**A**) a Ni post (height 200 nm, diameter 80 nm), (**B**) the F_1-ATPase biomolecular motor, and (**C**) a nanopropeller (length 750 to 1400 nm, diameter 150 nm). The device (**D**) was assembled using sequential additions of individual components and differential attachment chemistries.

What are Nanomachines?



Nanobiotechnology Applications

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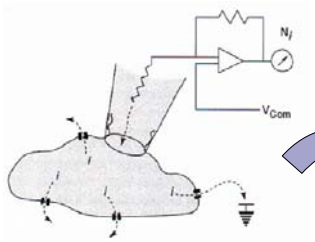
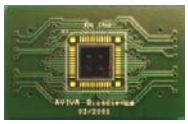
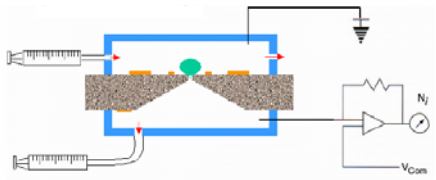
Conventional Patch Clamp *vs*. Microchip





- Operator
- Micromanipulator
- Microscope
- Pipette puller
- Microforge
- Faraday cage
- Air table
- Perfusion system



Future Visions

- Engineers of the future will have expertise in both biology and technology.
- Biology already has nanomachines.

➡ *Take lessons from Mother Nature*

- Engineered biomolecular machines
- Nanomedical surgical implements
- Molecular healing and repair of injury and disease
- Smart drugs
- NEMS
- Mobile nanopharmacies, nanomachines, …