Nanotechnology in the life sciences

A FRONTIS LECTURE SERIES

organized by

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Nanotechnology in the life sciences

February 13	13:30	Pieter Stroeve (UC Davis)- Size, measurement and sensing
	14:30	Mieke Kleijn (WUR)- Surface forces using AFM
February 20	13:30	Pieter Stroeve- (Bio)materials
	14:30	Ernst Sudholter (WUR)- Hybrid organic semiconductor FETs
February 27	13:30	Pieter Stroeve- Self assembling molecular structures
	14:30	Richard Schasfoort (U Twente)- Surface modification and microfabrication strategies
Friday, March 5	13:30	Pieter Stroeve- Environment
	14:30	Keurentje (TU Eindhoven)- Micellar systems for nanoscale engineering of reaction and separation processes
Friday, March 12	13:30	Pieter Stroeve- Life sciences and medicine
	14:30	Ton Visser (WUR)- Single-molecule fluorescence in microfluidic devices

Nanotechnology in the life sciences

- What is nanotechnology?
- What are its origins?
- If things are small, how do we measure it?
- What type of research is going on?
- Where is nanotechnology going?
- Relation to the life sciences?

Nanotechnology in the life sciences

Size, measurement and sensing

with an introduction to nanotechnology

Size Matters

- 10 centimeters

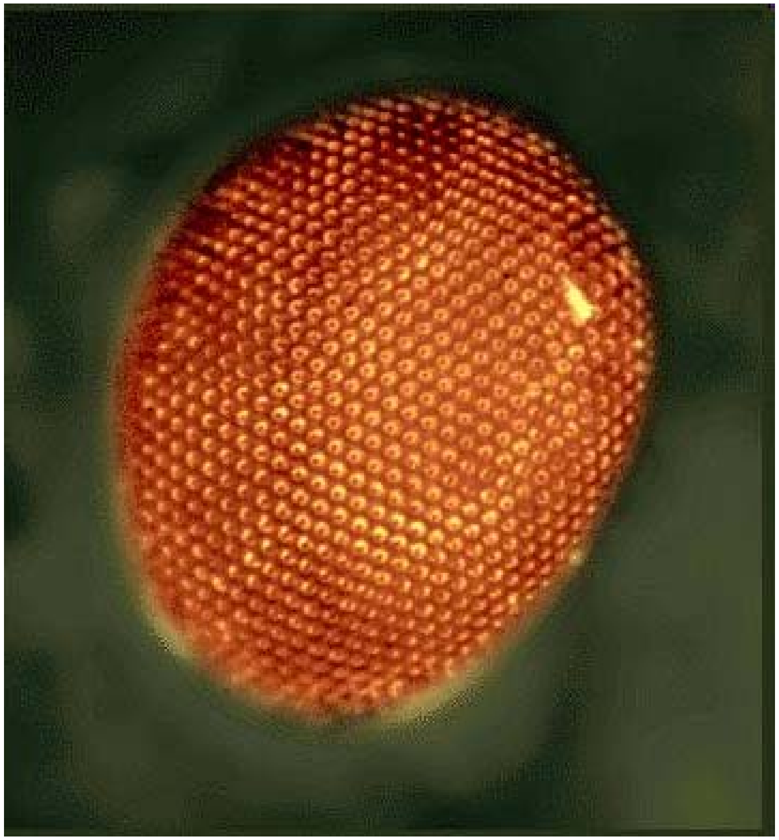
source: CERN http://microcosm.web.cern.ch/microcosm

Size Matters

- 1 centimeter

source: CERN http://microcosm.web.cern.ch/microcosm

Size Matters



- 100 micrometers
- The fly's eye is made of hundreds of tiny facets, resembling a honeycomb.

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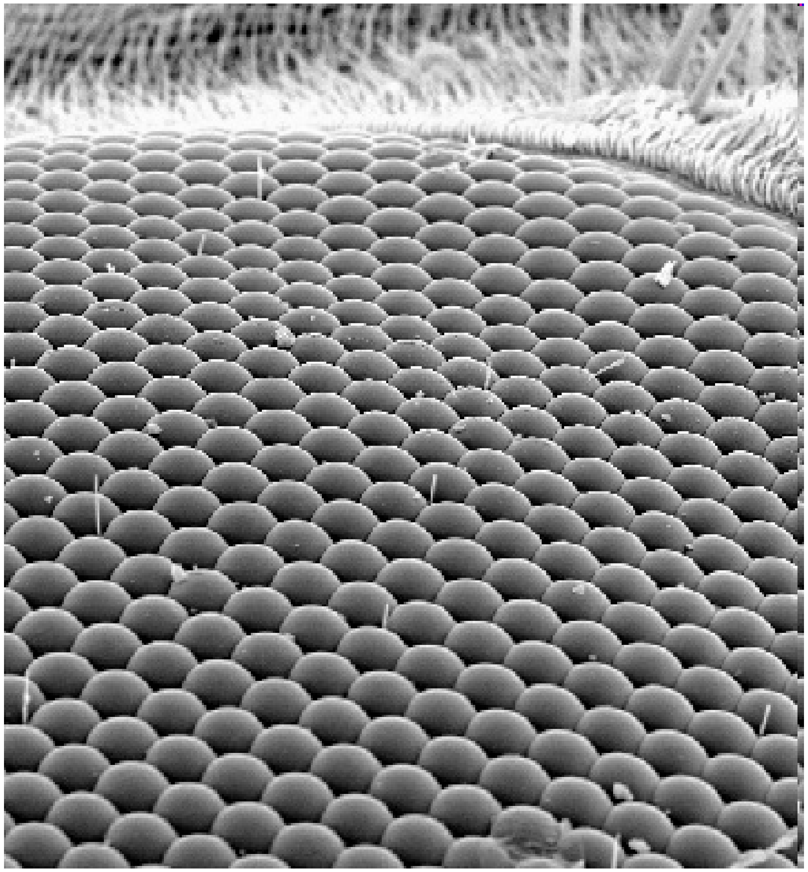
source: CERN http://microcosm.web.cern.ch/microcosm

Size Matters



- 10 micrometers
- The fly's eye is made of hundreds of smaller eyes. Each facet is a small lens with light sensitive cells underneath.

source: CERN
http://microcosm.web.cern.ch/microcosm

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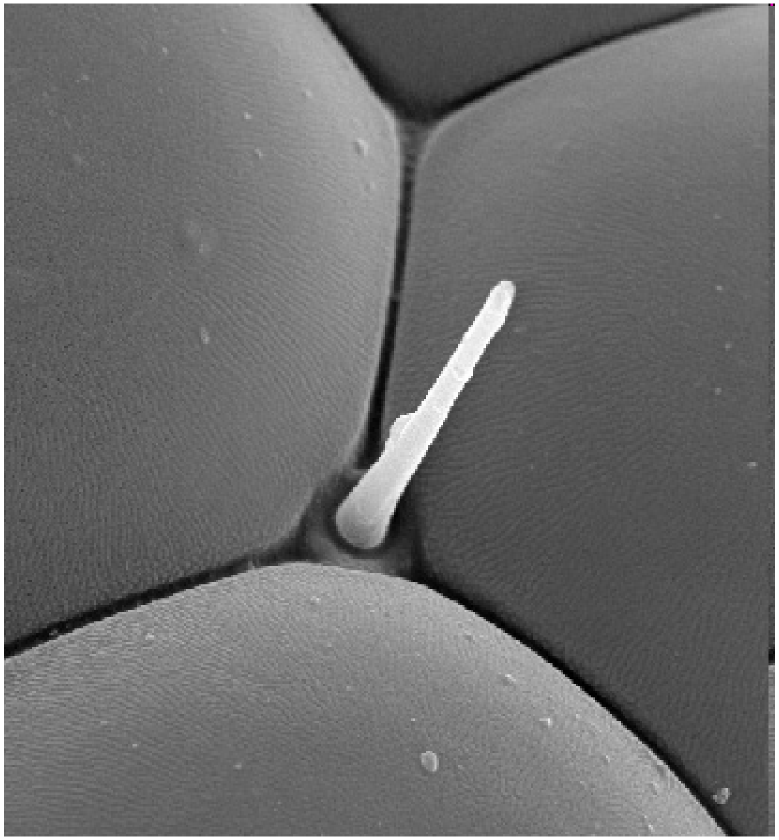
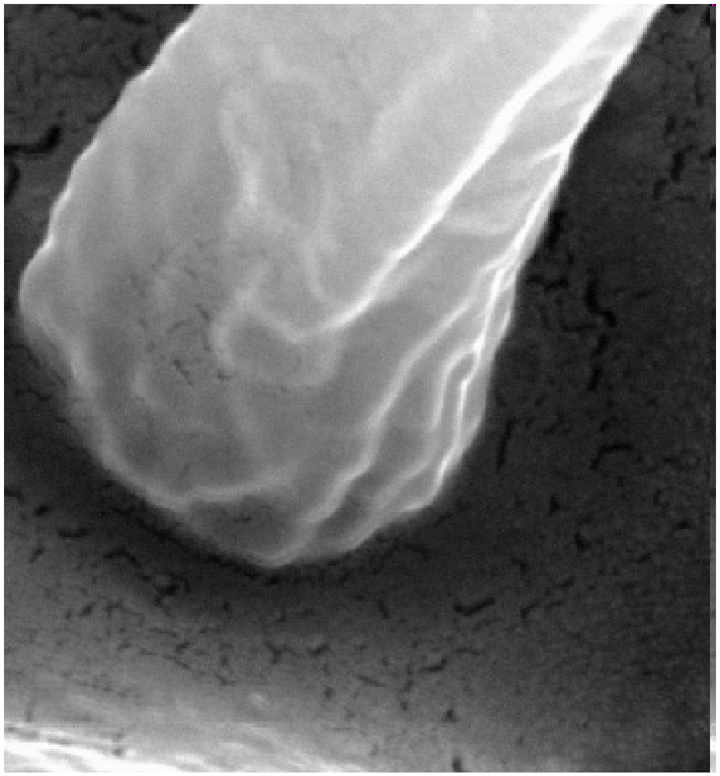
Size Matters



- 1 micrometer
  - In between the facets are bristles which give sensory input from the surface of the eye.

- source: CERN http://microcosm.web.cern.ch/microcosm

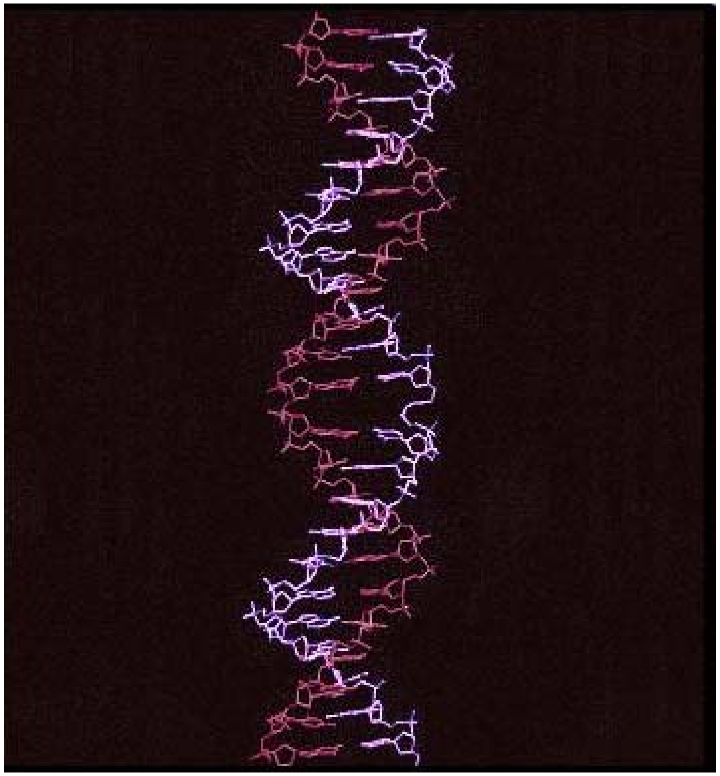
Size Matters



- 100 nanometers

source: CERN
http://microcosm.web.cern.ch/microcosm

Size Matters

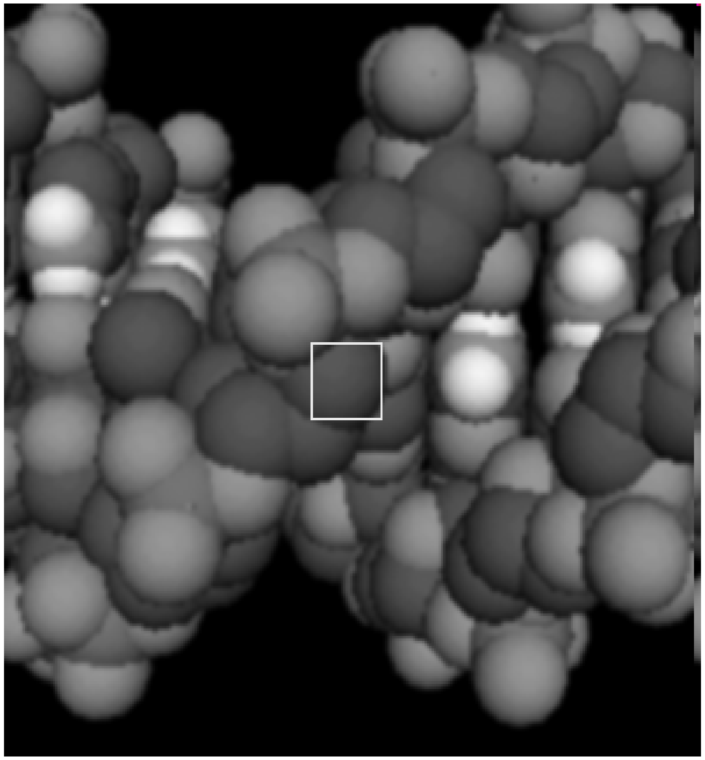


- 10 nanometers
  - At the center of the cell is the tightly coiled molecule DNA.
  - **It contains the genetic material needed to duplicate the fly.**

source: CERN http://microcosm.web.cern.ch/microcosm

source: CERN http://microcosm.web.cern.ch/microcosm

Size Matters



- 1 nanometer

source: CERN
http://microcosm.web.cern.ch/microcosm

Sizes of biological systems are at the nanoscale

Atom	0.1 nm
Water	0.2 nm
DNA (width)	2 nm
Protein	5 nm
Cell membrane	5 nm thick
Virus	75 – 100 nm
Materials internalized by cells < 100 nm	
Bacteria	1,000 – 10,000 nm
White Blood Cell	10,000 nm

Quantum mechanics is important at the nanoscale

Colloidal scale : electrostatics, van der Waals, Brownian

Nanometer scale: electrostatics, van der Waals, Brownian, quantum mechanics

Nanotechnology: the future

- Intel will be manufacturing devices by 2007 with feature sizes about 20 nanometers across.
- A red blood cell is on the order of ten thousand nanometers across.
- In 2-D we could stack about 250,000 components in the same area as a red blood cell.
- If the trends continue as far as 2017, which may be at the end-point of "Moore's Law" .
  We could manufacture a device the size of a red blood cell with 256,000,000 components.
  If we add the third dimension, that could translate into 65,536,000,000,000,000 components
  Inside the red blood cell.
- Future technical capability to produce a sophisticated robot to wander around
  the body doing whatever it has been programmed to do.

Drexler and Fishbine

Definition of Nanotechnology

- **A definition of what nanotechnology is, is not clear.**
- **Scientists and engineers have varied opinions what nanotechnology is.**
- **Further, people have been working at the nanoscale well before the word "nanotechnology" became popular.**

Definition of Nanotechnology

“It depends on whom you ask. Some folks apparently reserve the word to mean whatever it is they do as opposed to whatever it is anyone else does.” - S.M. Block, Stanford University

US National Nanotechnology Initiative (NNI): A possible definition

• Technology and research development at the atomic, molecular or macromolecular levels, in the length scale of approximately 1 to 100 nanometer range,

to provide a fundamental understanding of phenomena and materials at the nanoscale and to create and use structures, devices and systems that have novel properties and functions because of their small and/or intermediate size.

• Within these larger scale assemblies, the control and construction of their structures and components remains at the nanometer scale.

M.C. Roco

Nanotechnology: A short history

R.P. Feynman (1959) **"The principle of physics do not speak against the possibility of maneuvering things atom by atom."-APS meeting**

C.J. Pedersen, D.J. Cram, J.-M. Lehn (1970s) **Supramolecular chemistry**

H. Rohrer and G.K. Binnig (1981) **Scanning tunneling microscope**

Curl, Kroto and Smalley (1985) **Discovery of Buckeyballs**

Nanotechnology History

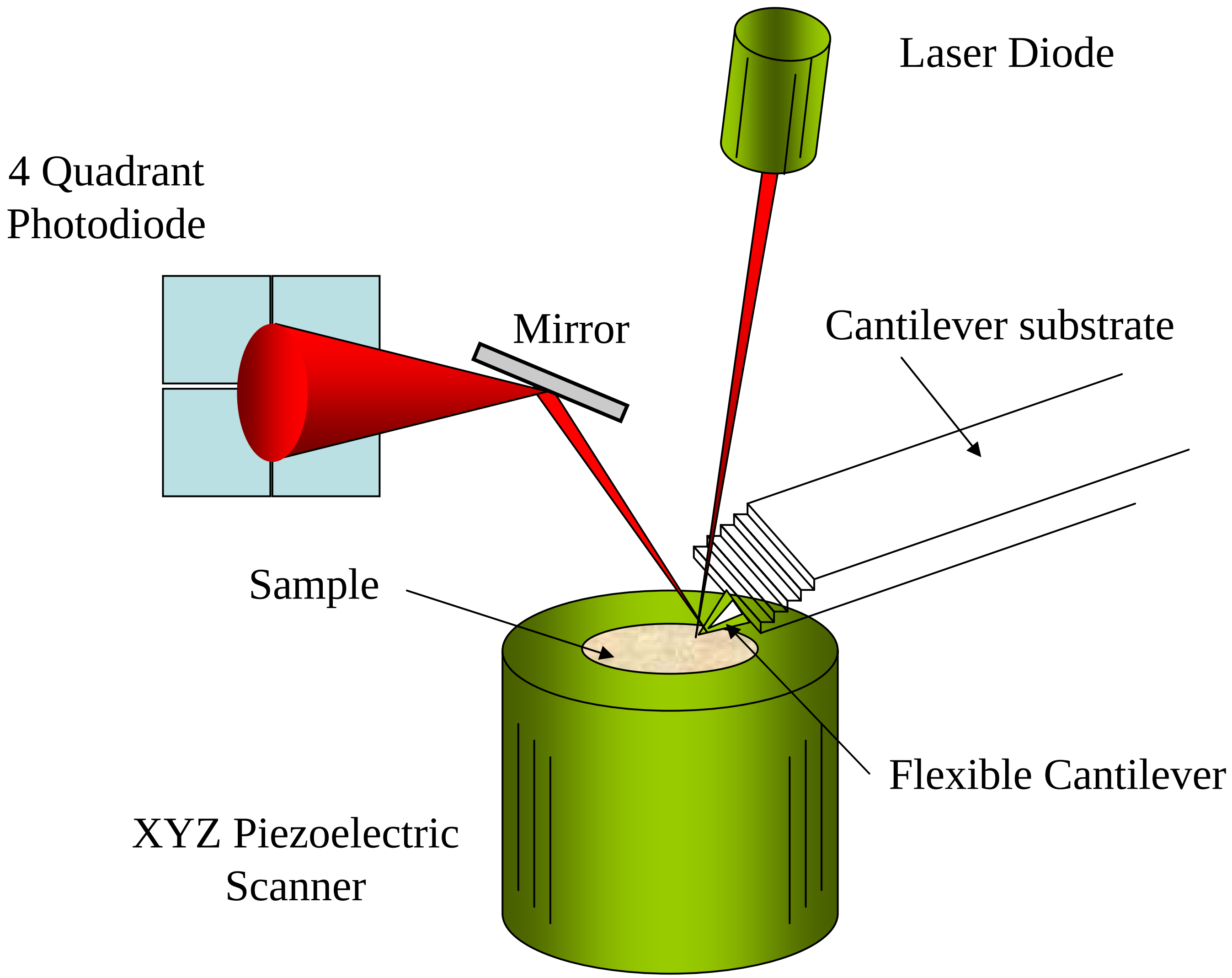
K.E. Drexler (1986) “Engines of Creation: The Coming Era of Nanotechnology”

D.M. Eigler (1989) Writes IBM’s name with individual xenon atoms

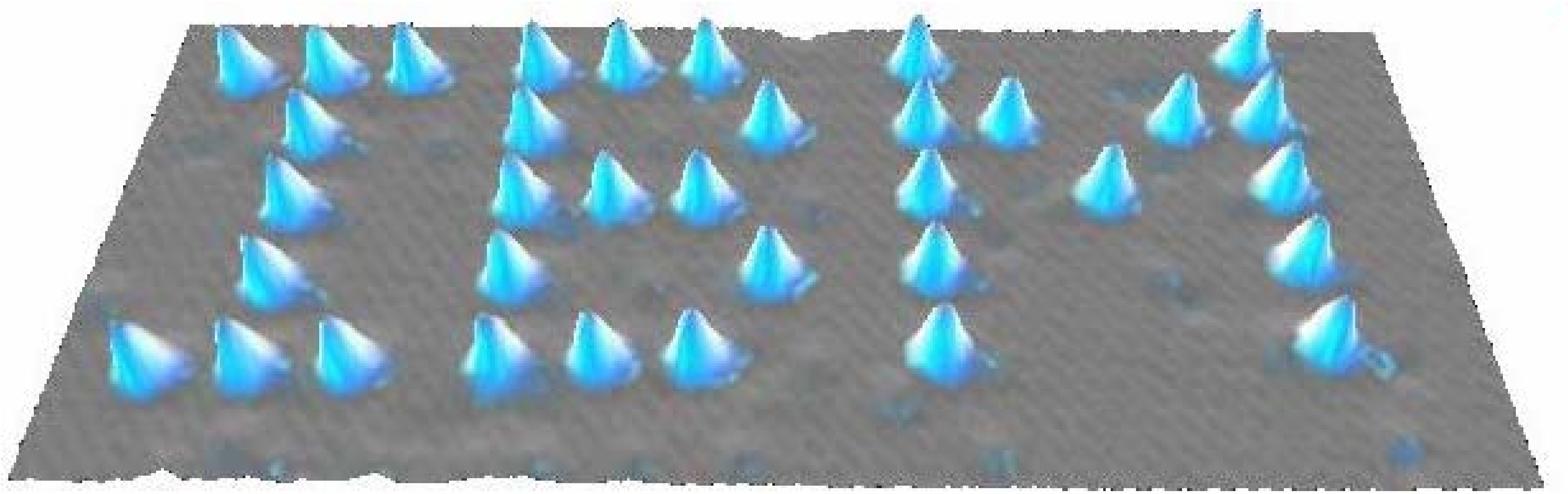
C. Dekker (1998) Creates transistor from carbon nanotube

J.M. Tour and M.A. Reed (1999) Single molecules can act as molecular switches

STM and AFM have created unique opportunities in research and fabrication



D.M. Eigler IBM - 1989



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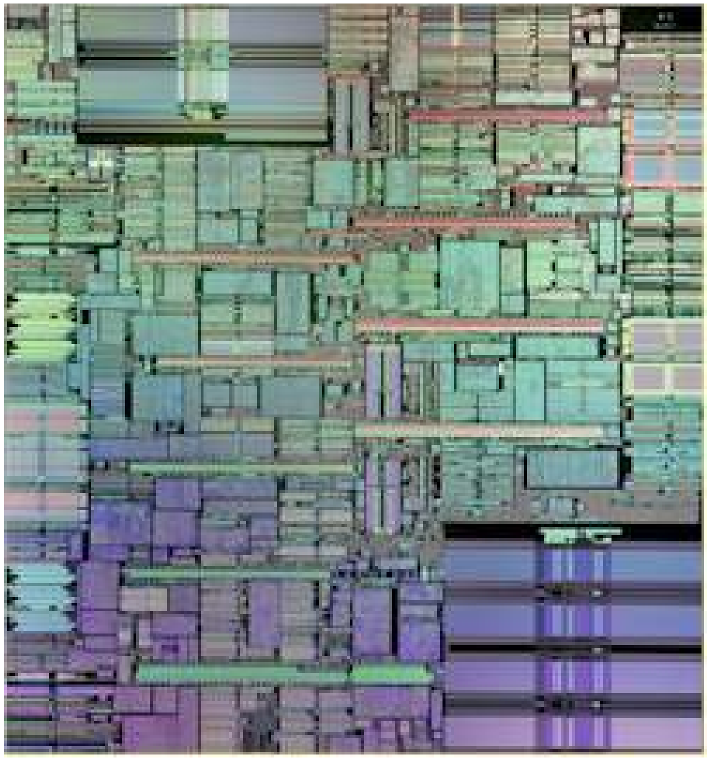
Integrated circuits (ICs) have driven the growth in nanotechnology



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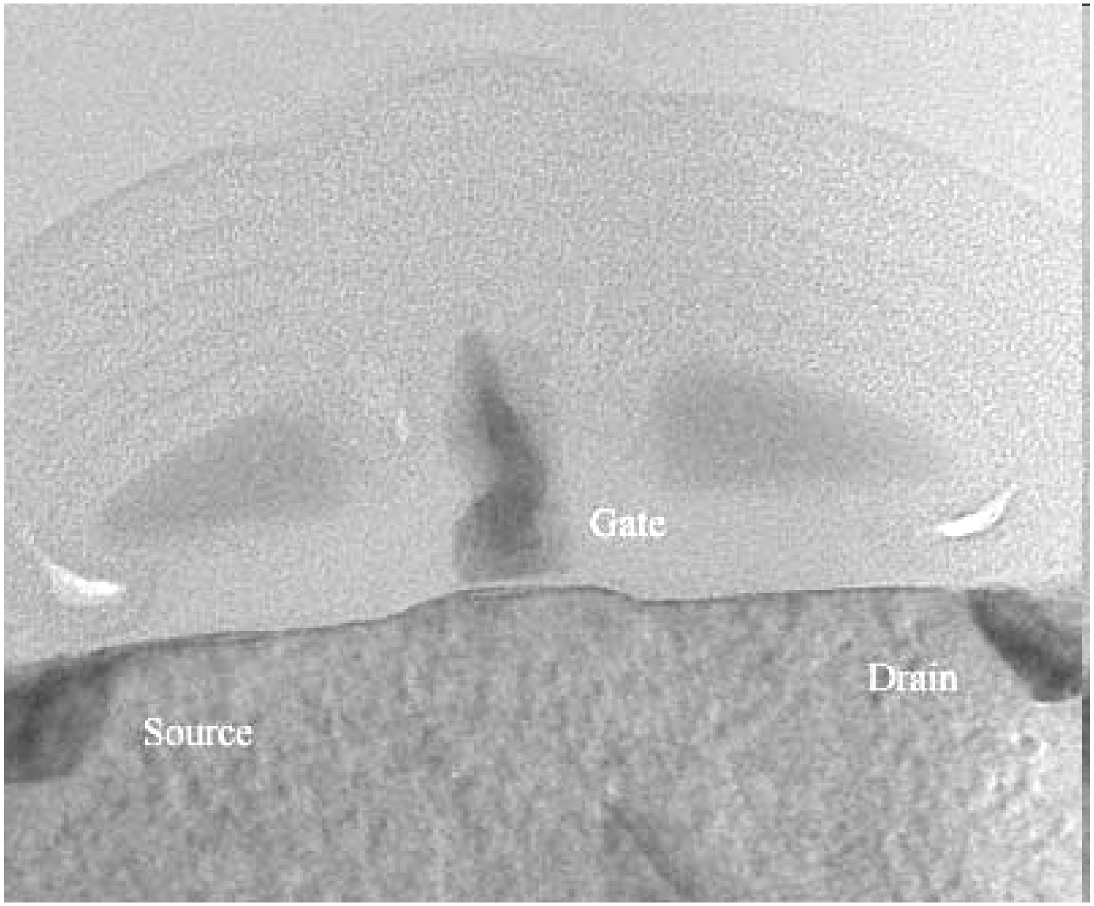
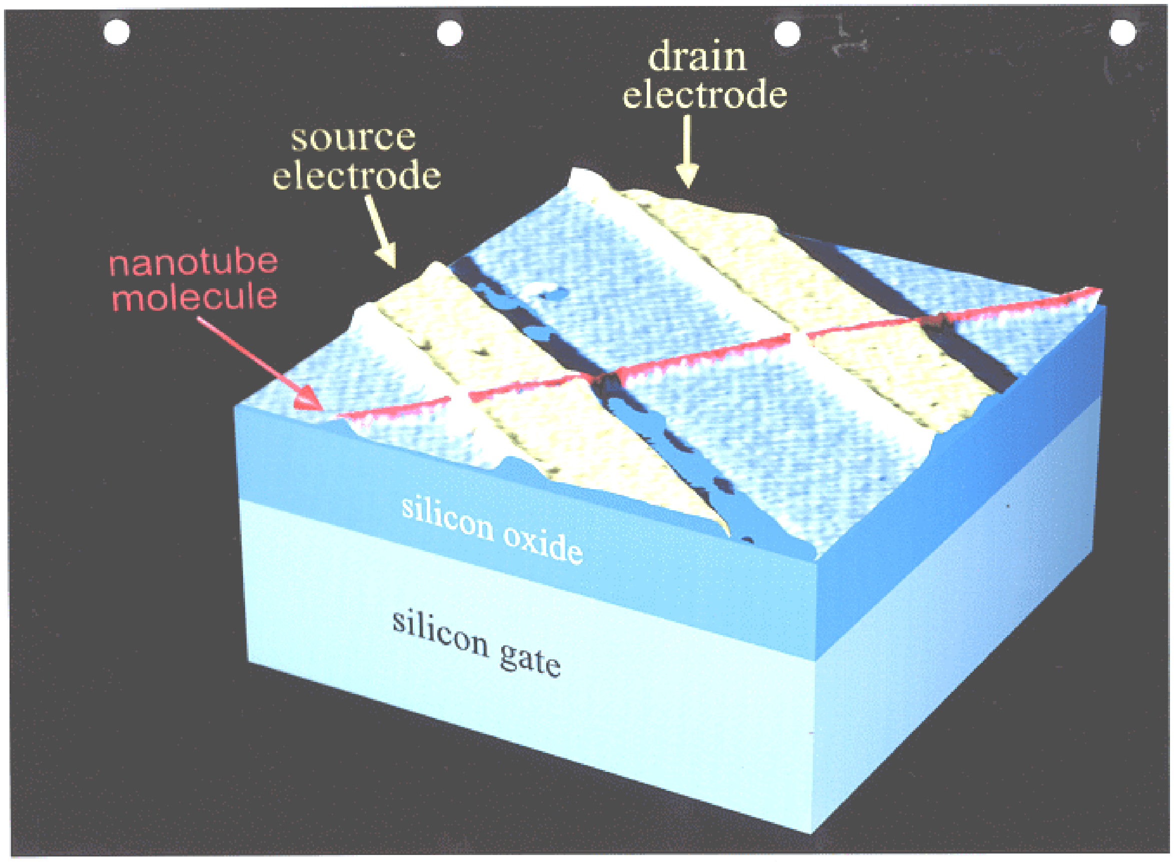
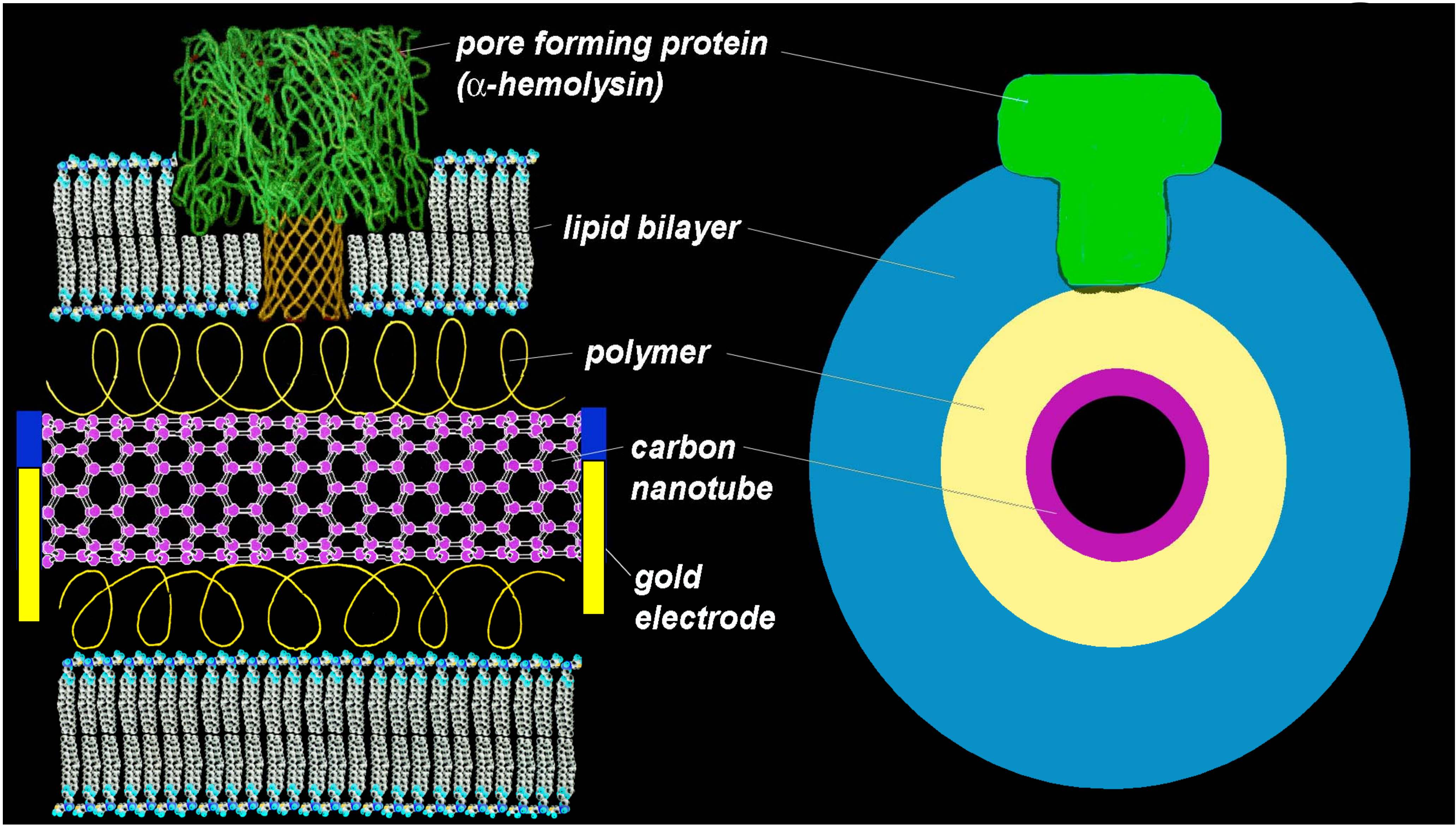
Prototype Intel 20 nm transistor



C. Dekker, TU Delft: <1 nm SWCNT transistor



Nanotubes can be used as sensors



Research in nanotechnology is rapidly growing

Estimated government sponsored R&D in $ millions/year

Fiscal Year	1997	2000	2001	2002	2003
W. Europe	200	270	400		
Japan	120	245	465	650	
USA	116	270	465	604	710
Others	70	110	380	520	

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Many Nano-Centers in the EC

- The Swiss National Center for Nano Scale Science at Universität Basel
- Nanoscience at Cambridge University
- London Center for Nanotechnology
- Center for Competence in Nano-Scale Analysis in Hamburg
- **U of Twente**
- Center of Competence in Nano-Scale Analysis in Hamburg
- Center for NanoScience based at Ludwig-Maximillians-Universität, München
- **Center for NanoMaterials at TU Eindhoven**
- Center for Ultrastructure Research, Austria
- Nano-Science Center at Københavns Universitet
- **Micro- and Nano-technology Research Center at TU Delft**

In the US the National Nanotechnology Initiative (NNI) supports research in:

- Theory, Modeling, and Simulation
- Experimental Methods and Probes
- Synthesis, Assembly, and Processing of Nanostructures
- Dispersions, Coatings, and Other Large Surface Area Structures
- Nanodevices, Nanoelectronics, and Nanosensors
- Consolidated Nanostructures
- Biological, Medical, and Health
- Energy and Chemicals
- Nanoscale Processes and the Environment

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US 2000 Patent Issues

Term	No. of Patents
Nanotechnology	99
Nanostructures	434
Nanofabrication	72
Nanodevices	10
Nanoprobes	14
Nanomechanical	23
Nanotubes	164
Carbon nanotubes	129
Molecular switches	56
Nanoclusters	44
Nanomagnetics	2

The MITRE Corporation 2002

Each year thousands of scientific publications on nanotechnology appear in the literature. Nano is in!

Nanofabrication

Development of nanotechnology depends on using nanofabrication to make structures smaller than 100 nm.

- **Photolithography (IC fabrication) could be modified to nm-scale structures, but it would be difficult and expensive.**
- **Nanofabrication methods can be divided into two categories:**

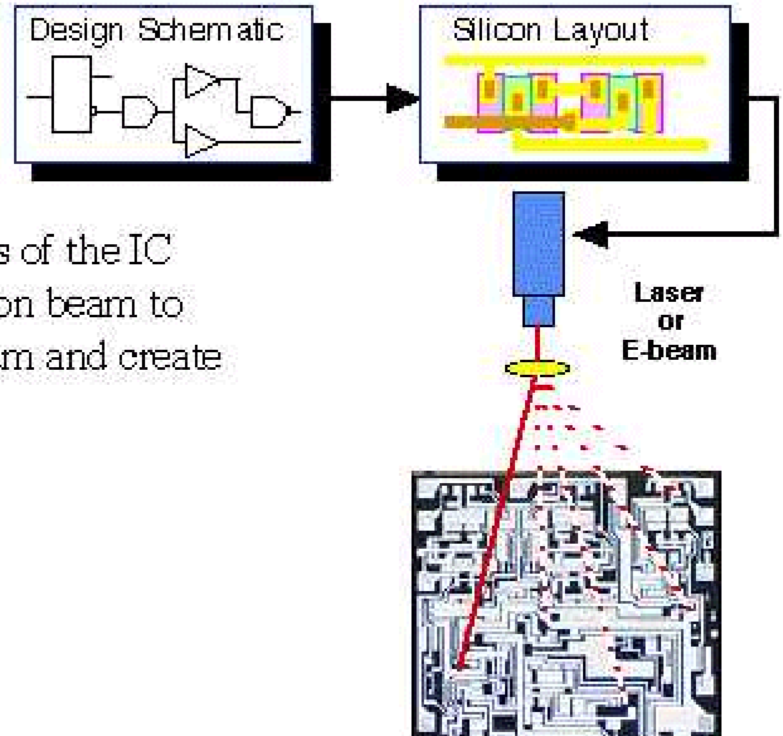
  top-down methods (carve and add molecules to a surface)

  bottom-up methods (assemble molecules on a surface)

G.M. Whitesides

The Mask-Making Process

- The Process
  - Start with ultra-pure glass plates with a surface deposition of chromium.
  - Computer generated layouts of the IC drive a laser beam or electron beam to selectively remove chromium and create the mask or reticle.
- Design Driven:
  - increased complexity
  - long write times
  - New Product Acceleration



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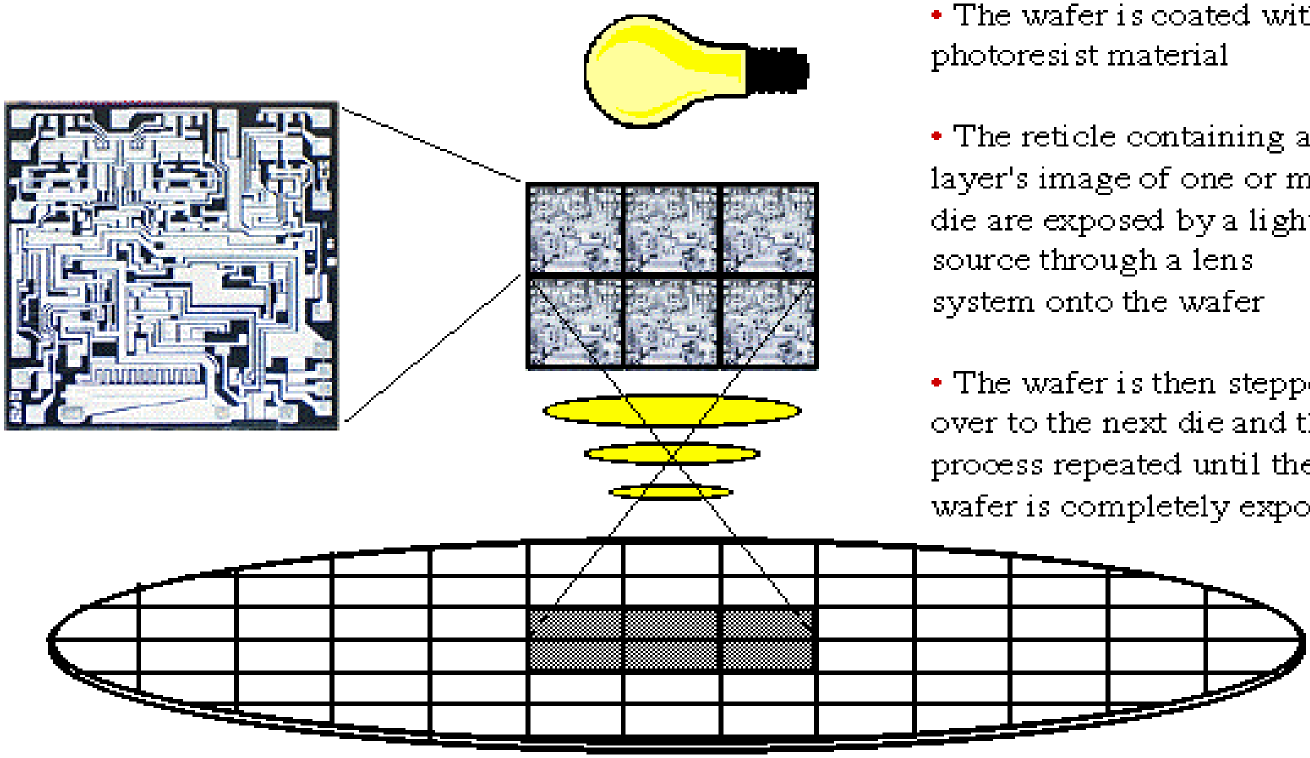
INFRASTRUCTURE

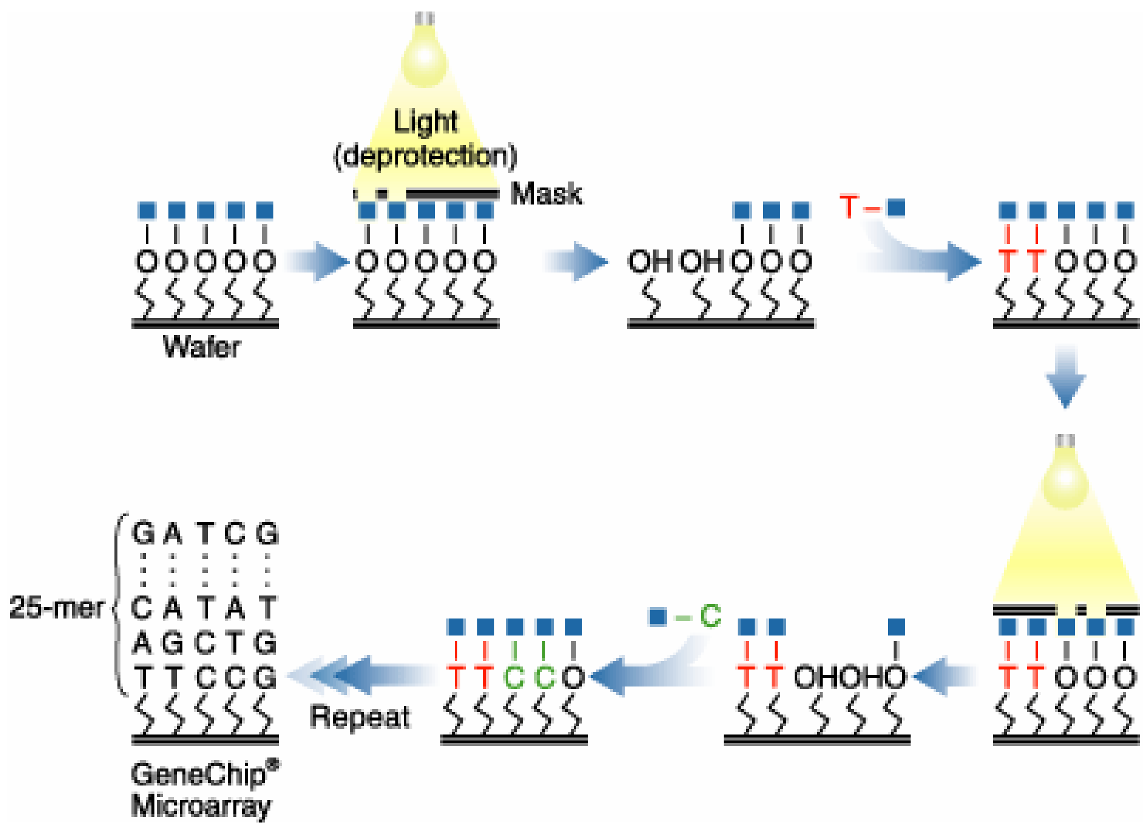
www.infras.com

Photolithography Process



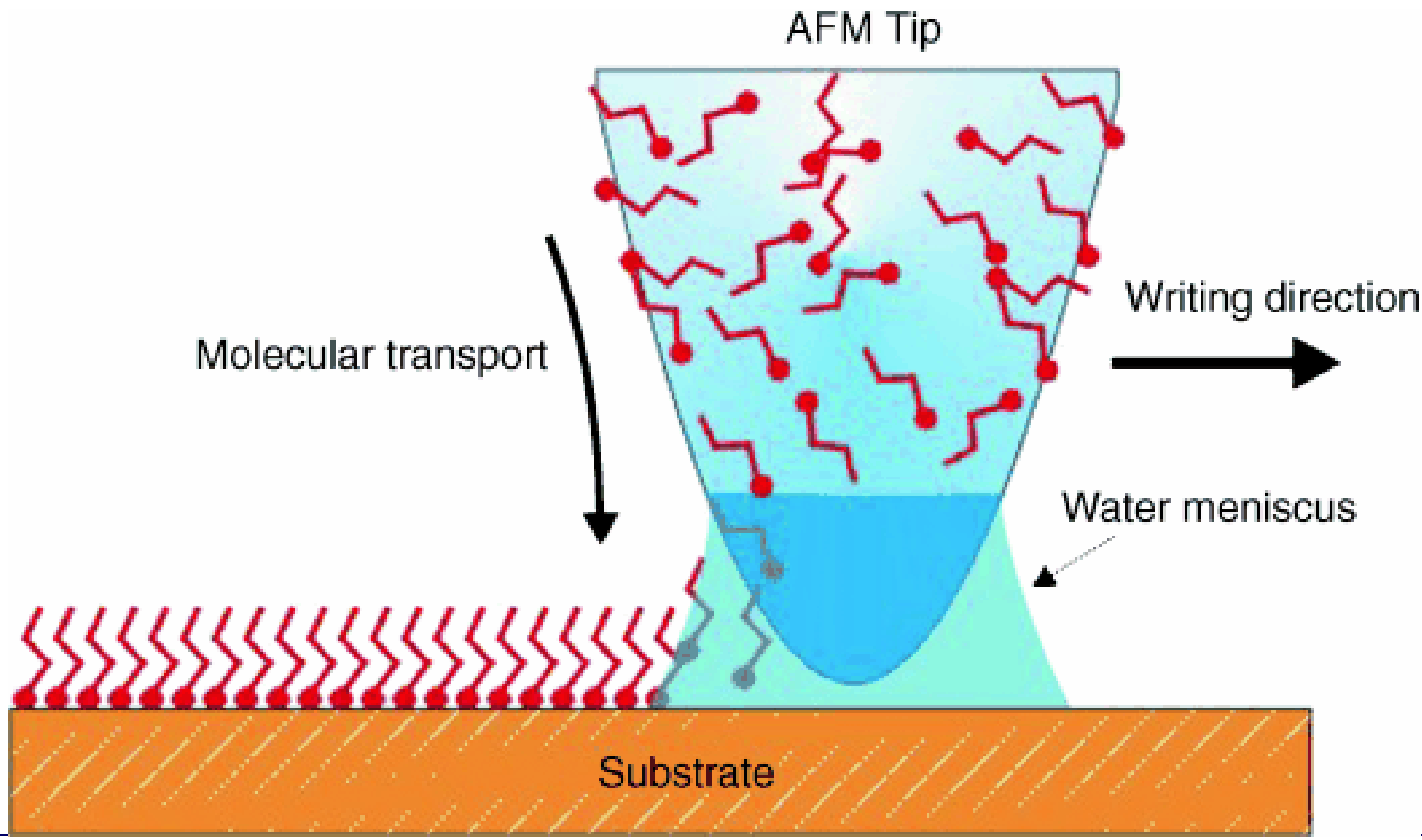
- The wafer is coated with photoresist material
- The reticle containing a layer's image of one or more die are exposed by a light source through a lens system onto the wafer
- The wafer is then stepped over to the next die and the process repeated until the wafer is completely exposed

Affymetrix uses a combination of photolithography and combinatorial chemistry to manufacture GeneChip® Arrays



Nanofabrication:Dip pen

From: Science



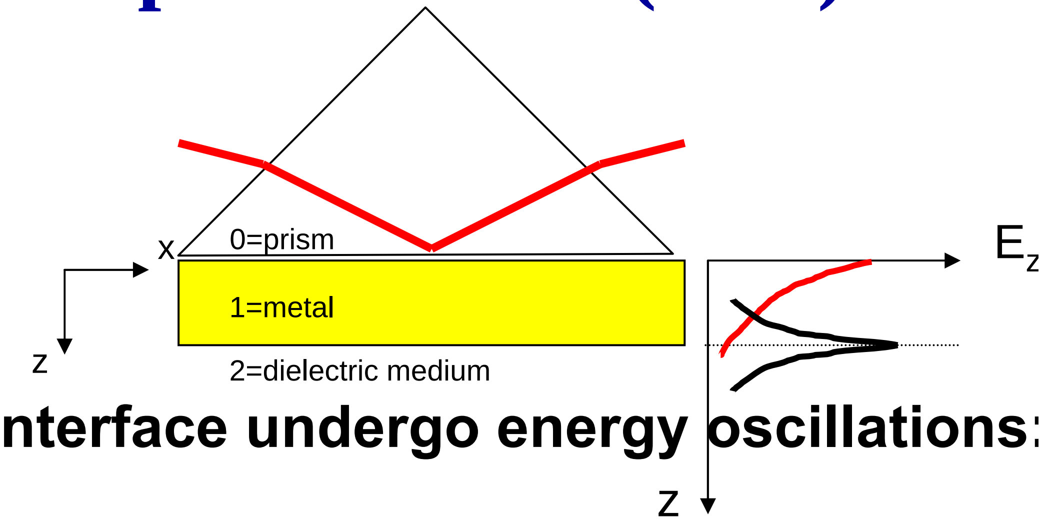
Applications in nanotechnology

- Catalysts
- Data Storage
- Drug Delivery
- Sensors
- Medical Devices
- Biomaterials
- Nanoparticles
- Microfluidics
- Separations
- Purification

Variety of methods (>50) are available for measuring nanosystems, for sensing and fabrication (surface techniques).

- **Atomic Force Microscopy - topography, fabrication, surface forces, sensing**
- **Surface Plasmon Resonance - Amount of material, sensing**
- **X-ray Diffraction - crystal structure**
- **Energy Dispersive X-ray Analysis - surface elemental analysis**
- **X-ray Photoelectron Spectroscopy - surface compound composition**
- **FTIR- composition, orientation of bonds**
- **SEM - amount, topography**
- **Fluorescence**
- **Etc., etc.**

Surface plasmon resonance phenomenon (SPR)

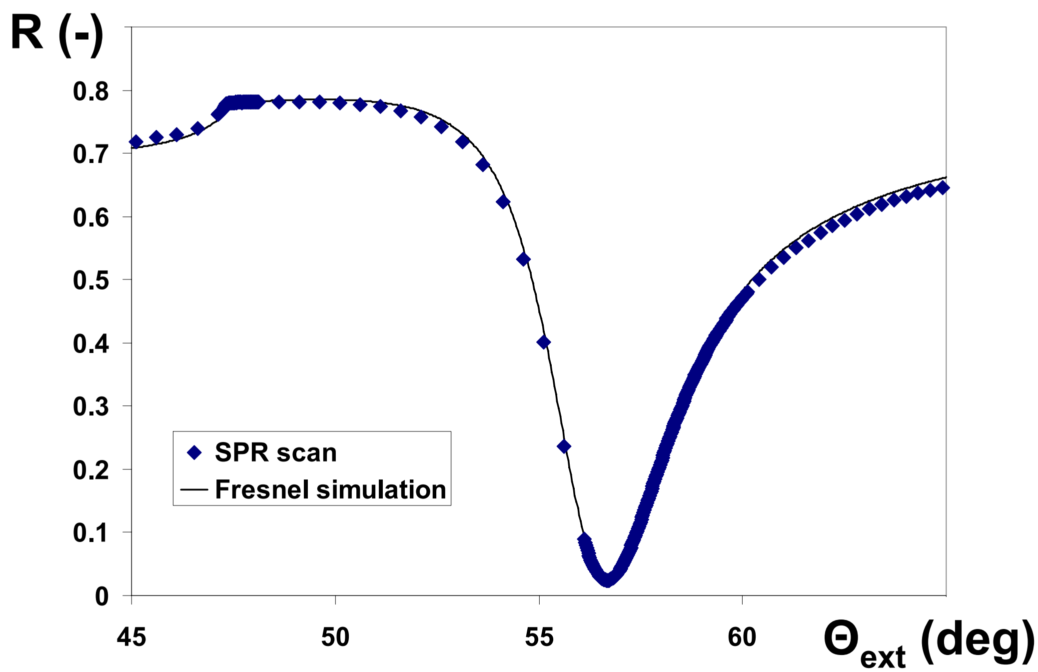


SPR results from the interplay of two interfacial phenomena:

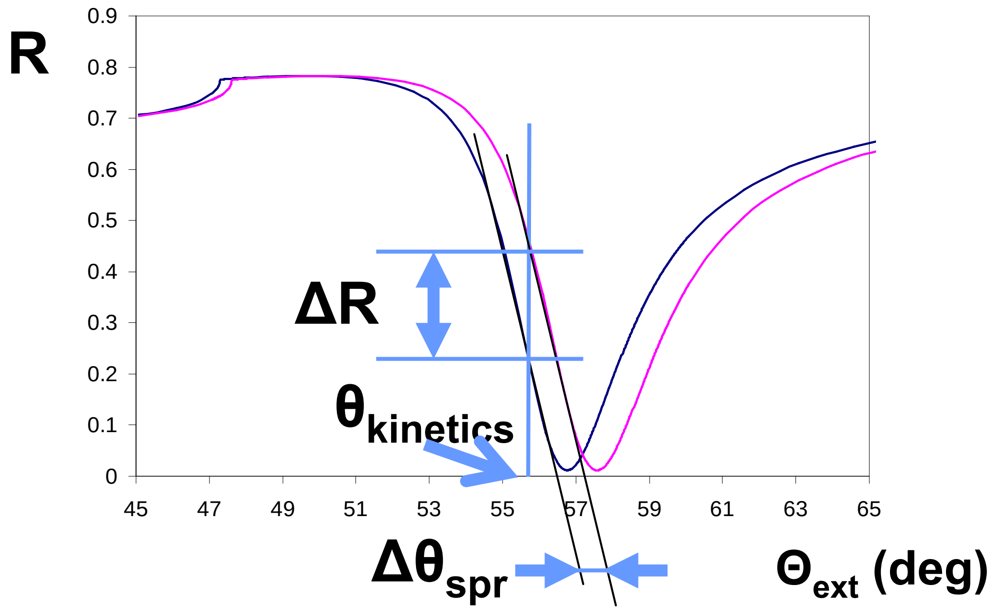
- Free electrons at a metal-dielectric interface undergo energy oscillations: **plasmon waves**

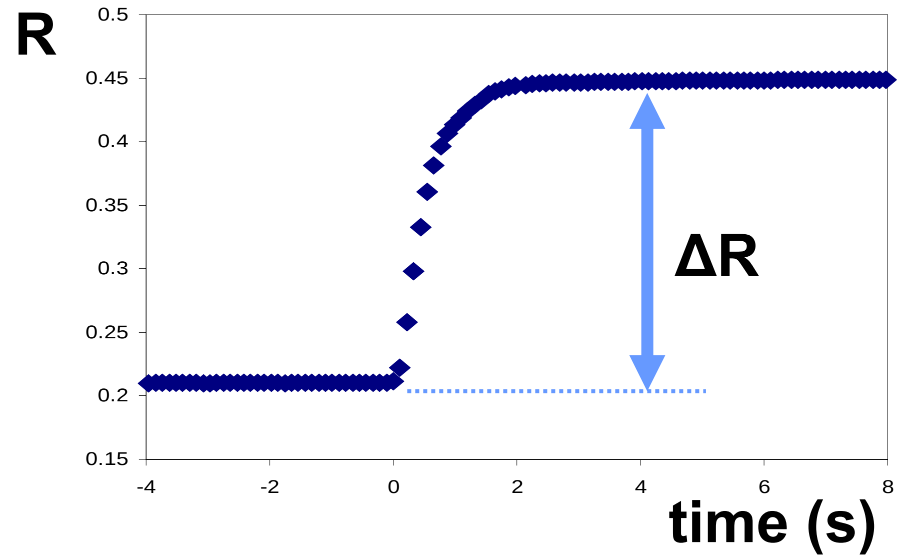
- In the regime of total internal reflection, an electromagnetic wave going
- through an interface gives rise to an electric field: **evanescent wave**

- Optical excitation of the surface plasmons results in the absorption of energy at the interface, hence we can detect a minimum in the intensity of reflected beam at a specific angle of incidence



The SPR experiment





• **<u>Equilibrium measurement</u>:** Changes in the dielectric constant within a nanometer of the interface result in a shift of the resonance angle ($\Delta\theta_{spr}$)

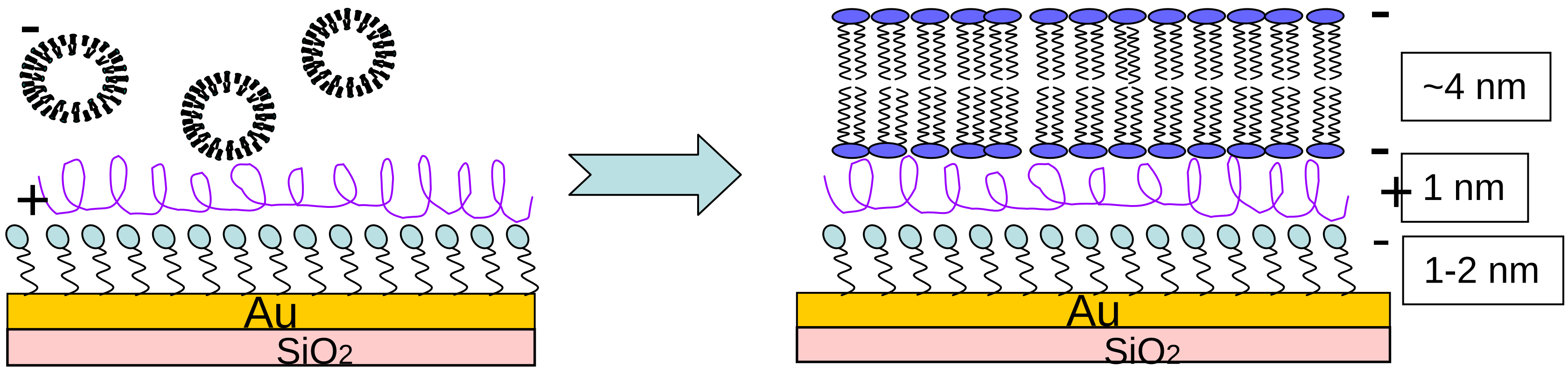
• **<u>Kinetics measurement</u>:** One can observe the evolution of the reflectance with time at a fixed angle

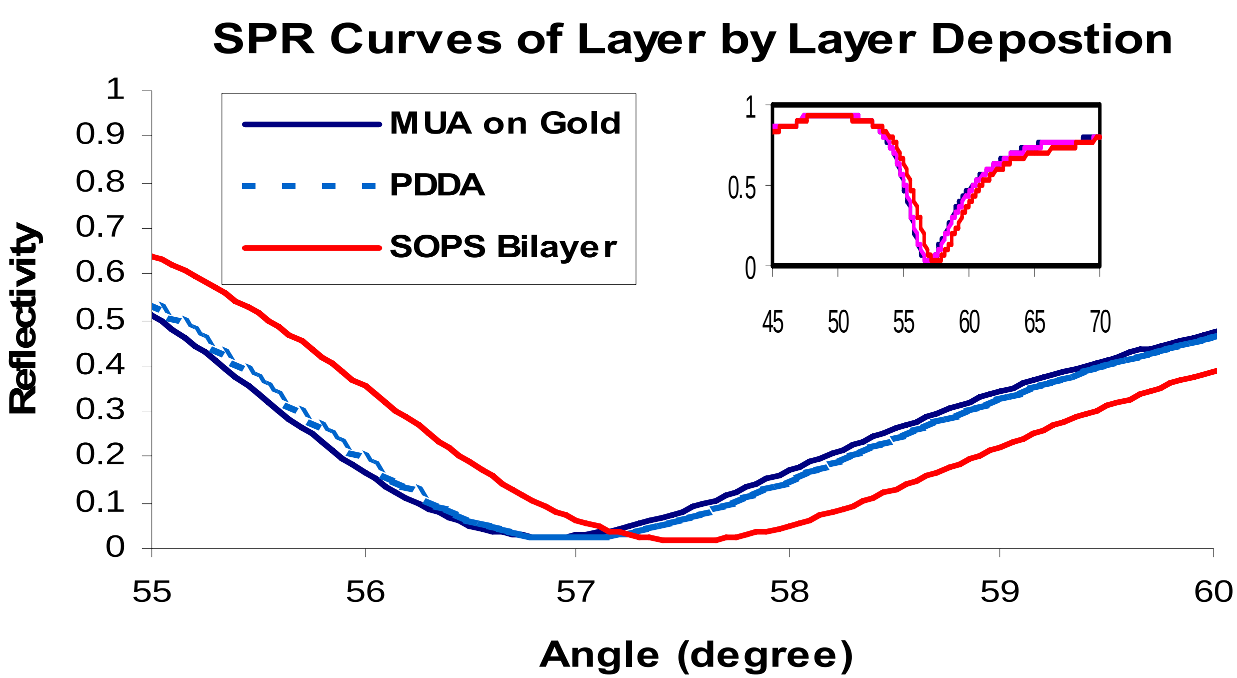
• Excess surface concentration Γ can be estimated from the experimental data

$$\Delta R \Rightarrow \Delta\theta_{spr} \Rightarrow d_{layer} \Rightarrow \Gamma$$

$$\Gamma = \frac{n_{layer} - n_{bulk}}{\frac{dn}{dc}} d_{layer}$$

Macromolecular Structures: Layer by Layer Deposition





Examples of Nanotechnology challenges in the life sciences

- Making materials and products bottom-up by building them up from atoms and molecules.
- Molecularly engineering of new molecules for bottom-up structures
- Understanding the forces that stabilize and maintain supermacromolecular structures.
- Developing nanocomposite materials that are stronger than steel, but a fraction of the weight (e.g. for implantable materials)
- Using gene and drug delivery to detect and treat cancerous cells or diseases
- Developing nanosensors for pollutants, viruses, toxins, bacteria, cellular activity, monitoring bioprocesses, etc.
- Removing toxins to promote a cleaner environment.
- Developing molecular machines for biological functions.

Closing comments

Nanotechnology is an exciting interdisciplinary field which has tremendous potential to develop new science and novel materials, devices, sensors and processes. The development of this dynamic field depends on close collaboration between chemists, physicists, biologists, material scientists, and engineers to bring together their expertise to solve unique problems.