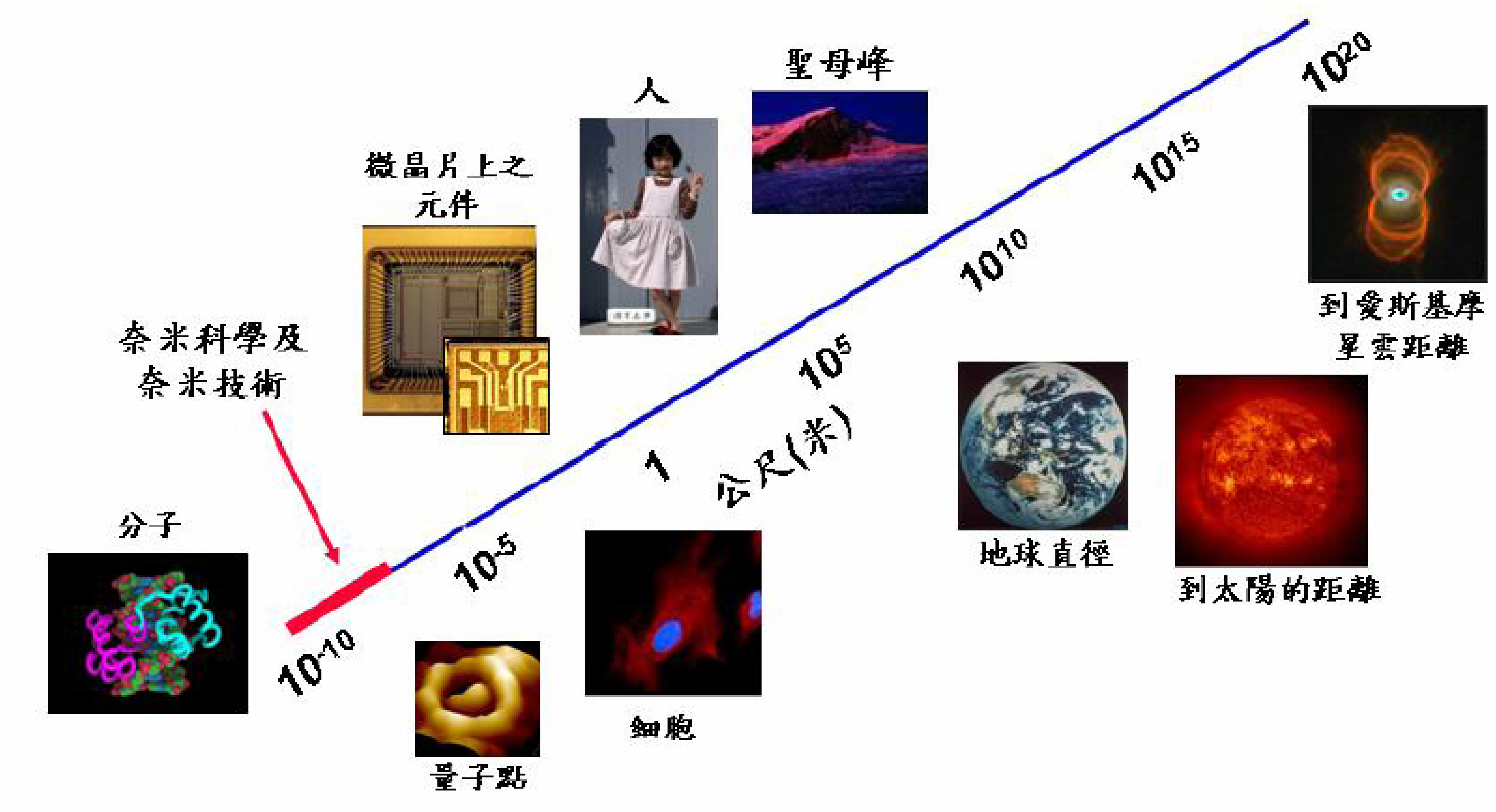
張恆雄老師

從奈米科技到奈米生物技術

奈 米 生 醫 工 程 研 究 室

有多大？有多小？



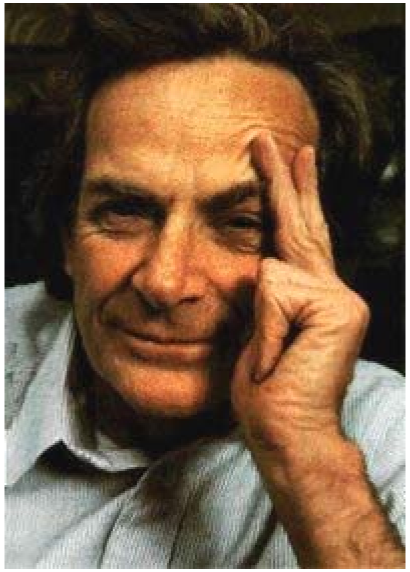
聖母峰
人
微晶片上之
元件
奈米科學及
奈米技術
分子
10^{-10}
10^{-5}
1
10^{5}
10^{10}
10^{15}
10^{20}
公尺(米)
量子點
細胞
地球直徑
到太陽的距離
到愛斯基摩
星雲距離

奈米科學的里程碑(I)

- 4000 BC Democritus 提出"原子論"
- 1905 Einstein 提出"Brown 運動理論"
  Sugar Molecule ~1nm
- 1931 發明電子顯微鏡
- **1959 Feymann lectures "There's Plenty of room at the bottom"**

Richard Feynman…

"There's Plenty of Room at the Bottom“



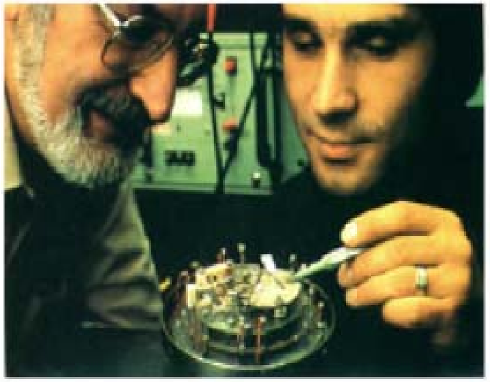
1959年12月29日，諾貝爾獎得主李察費曼（Richard P. Feynman）教授在美國物理學會的聚會裡發表演說，暢談沒有任何物理定律限制科學家在原子的微觀條件下改造、操控或組成物質，並大膽與精確地預言，科學家將從這些微小物質之中，發現許多新鮮及豐富的性質。

理查・費曼（Richard P. Feynman）著；吳程遠等譯，「費曼的主張」
費曼演講－窺究到底，空間還多的很
費曼演講－微小機械

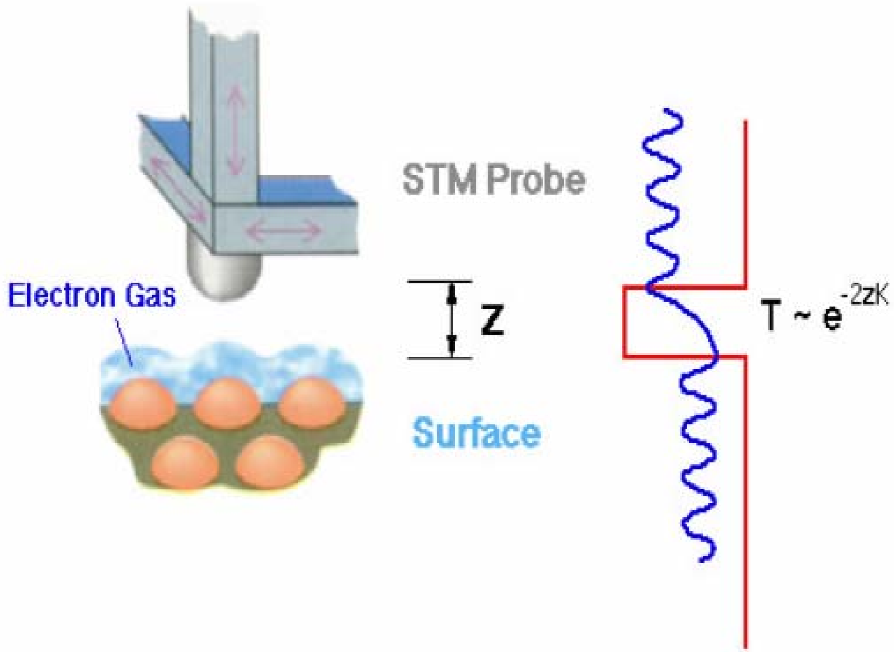
奈米科學的里程碑(Ⅱ)

- 1962 Ryogo Kubo（九保亮五）提出quantum confinement theory
- 1968 發明Molecular Beam Epitaxy，MBE
- 1974 Norio Taniguchi（谷口紀男）引進“奈米技術” 一詞
- **1982 Binnig & Rohrer 發明掃描穿隧式顯微鏡STM**

掃描穿隧顯微鏡（STM）

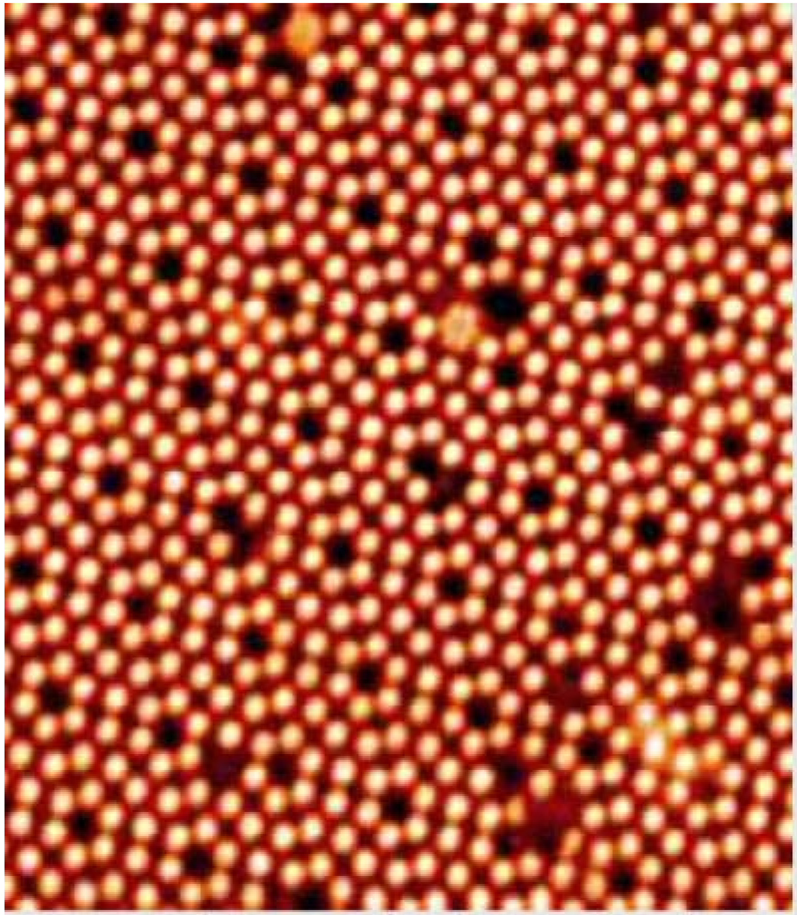


• G. Binnig, H. Rohrer, Ch. Gerber, and E. Weibel, *Appl. Phys. Lett.* **40**, 15 (1982)

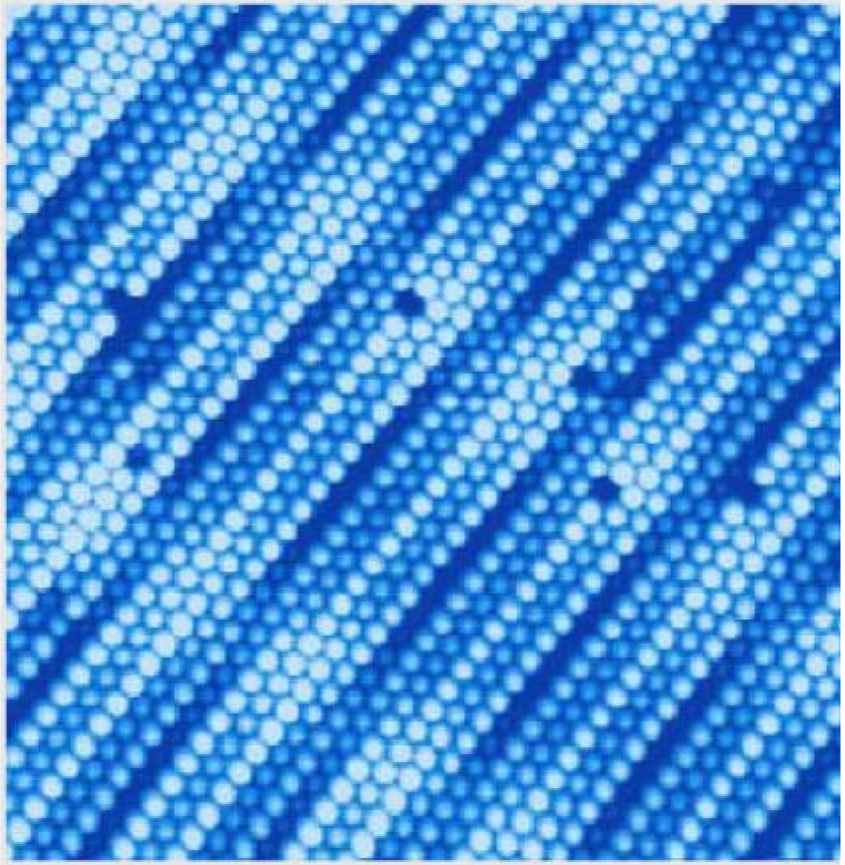


• 掃描穿隧顯微鏡是利用一極細的金屬尖針接近具導電性樣品的表面進行掃描，再根據量子穿隧效應來獲得樣品表面上的原子結構圖像。

原子影像



Atomic Resolution on Si(111)
Si(111)7x7; U_{gap} = 1.99 V, It = 2.0 nA, 20 nm x 20 nm



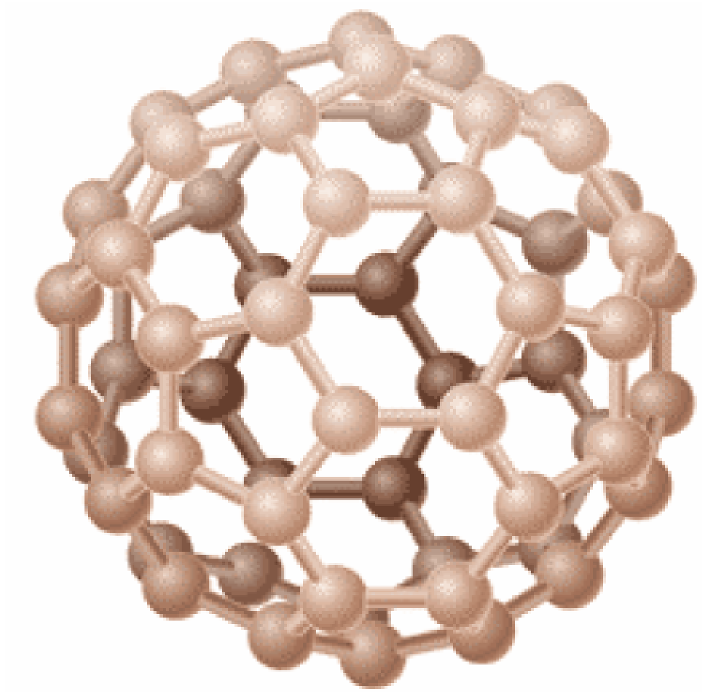
Atomic Resolution on Pt(100)
E. Bergene, Trondheim, Norway; *Published in Surf. Sci. 306 1/2 (1994) 10-22*

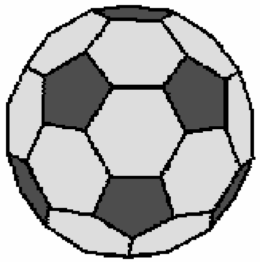
奈米科學的里程碑(Ⅲ)

- 1984 Gleiter採用氣體冷凝方法，成功製備出鐵奈米微粉
- **1985 Curl J r., Kroto & Smalley 等人發現 C60 分子**

The famous "buckyball" C60

H. W. Kroto, J, R. Heath, S. C. O'Brien, R. F. Curl, and R. E. Smalley, *Nature* (London) **318** 162 (1985).





Superconducting

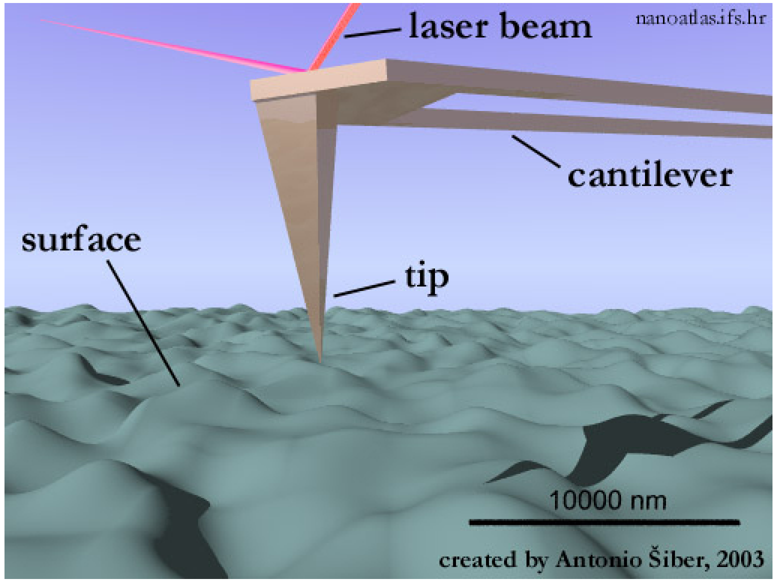
Photonic applications

Biological applications

12個正五角形和20個正六角形所構成。共有32個面。

奈米科學的里程碑(Ⅳ)

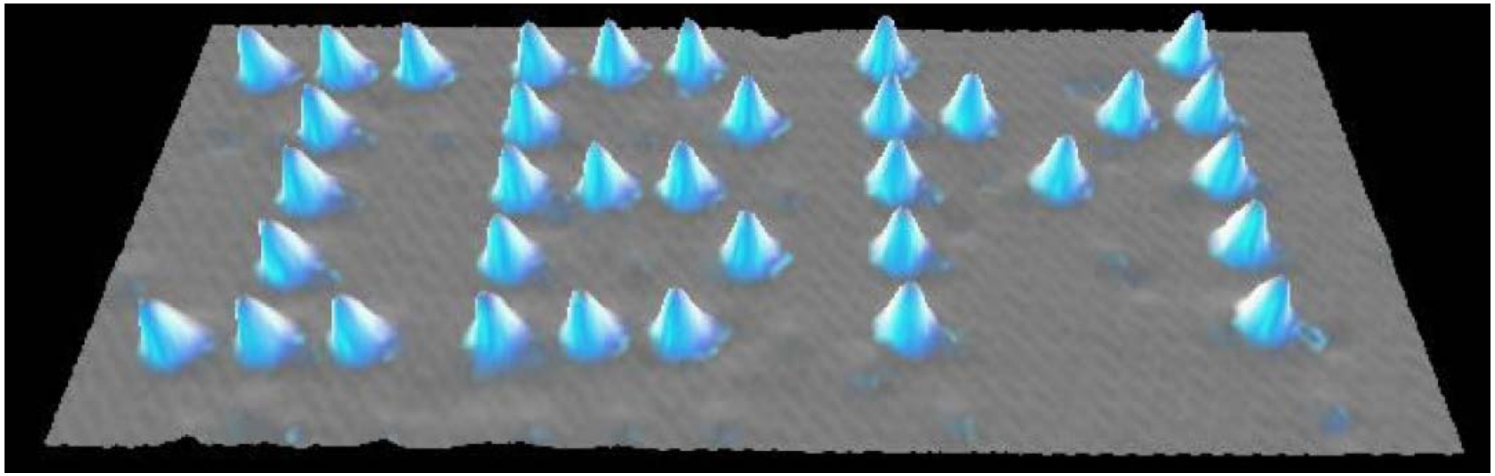
- 1986 Drexler 出版“Engines of Creation” 一書
- **1986 Binnig, Quate & Gerber 發明AFM**



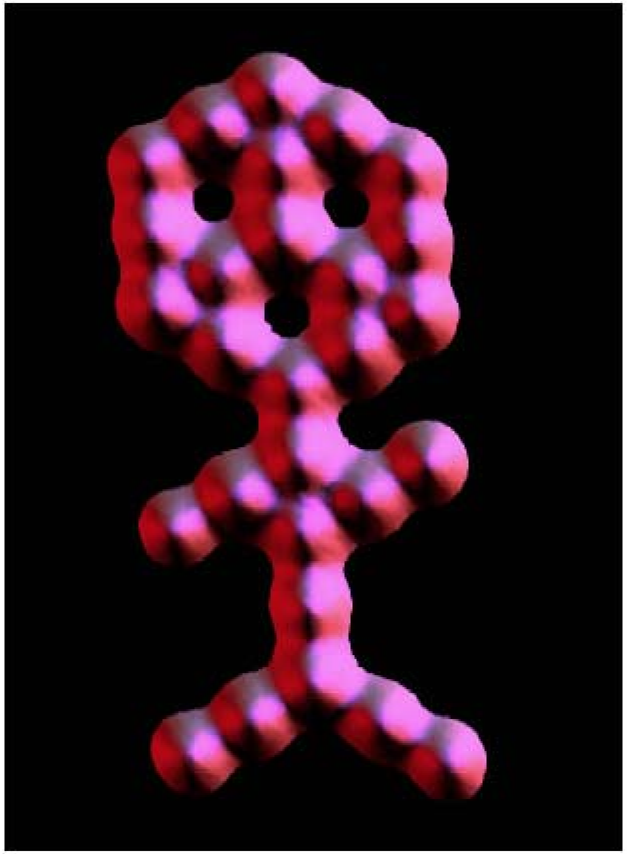
當以尖針掃描樣品表面時，尖針與樣品表面原子間的作用力所造成的微小偏轉可被偵測出來，而獲得其表面原子排列的圖像。

奈米科學的里程碑(Ｖ)

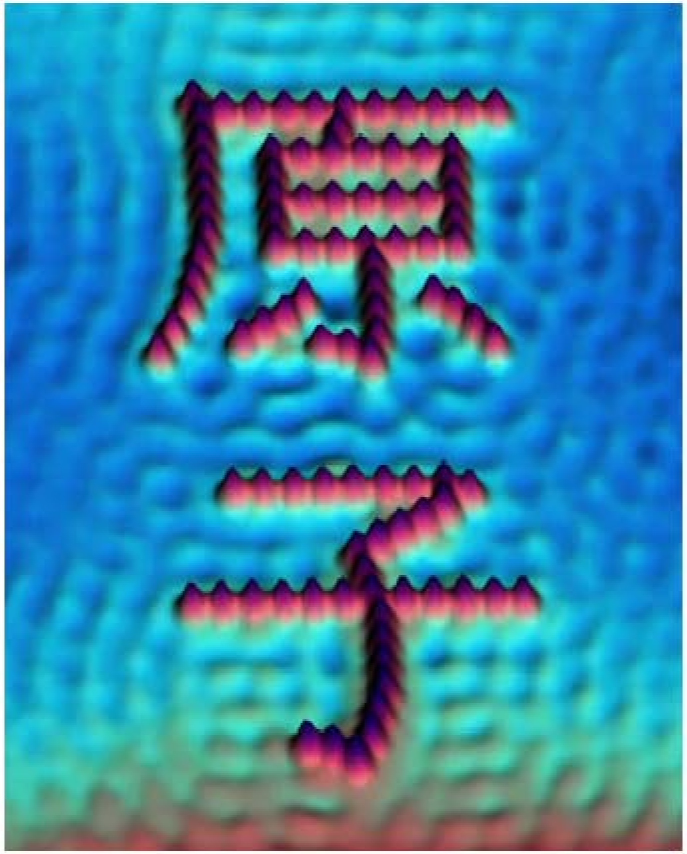
- 1987 Siegel 成功製備出奈米陶瓷TiO_2多晶體
- 1988 法國A. Fert等人在Fe / Cr 多層膜中發現巨磁阻（giant magnetoresistance, GMR）效應
- **1990 Eigler 利用掃描穿隧式顯微鏡探針，將Xe 原子排列成IBM三個英文字母，這是人類首次操縱原子**



STM Image Gallery by IBM



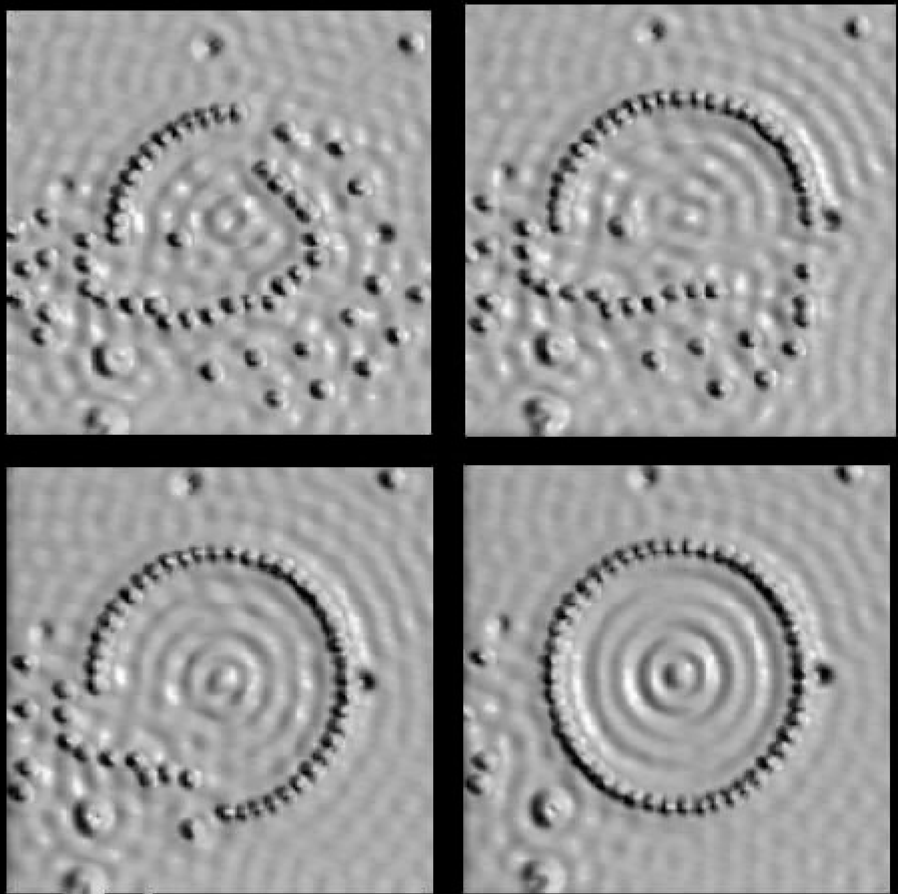
Co分子在Pt表面上所排列出的「分子人」，其身高只有5 nm。



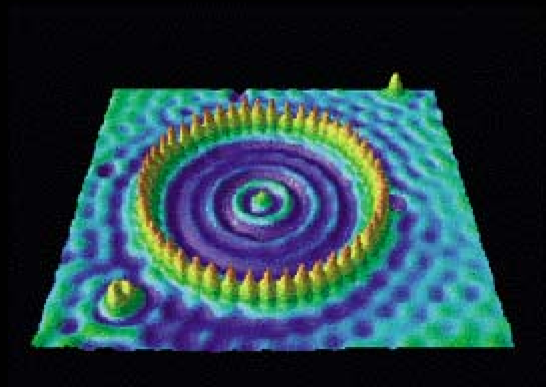
在Cu(111)表面上用101個Fe原子寫下「原子」二個迄今為止最小的漢字。

量子圍欄
Fe/Cu(111)

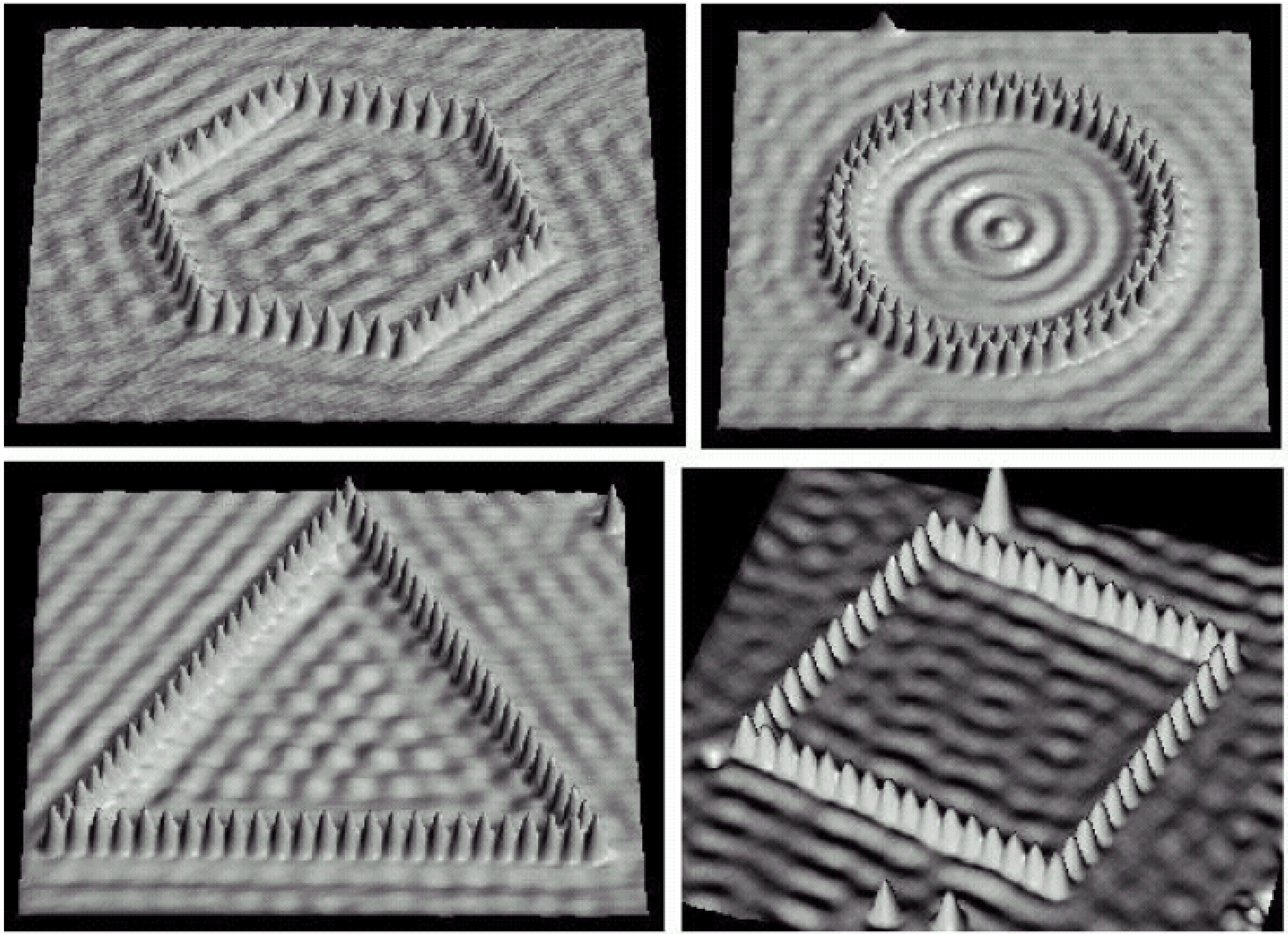
M.F. Crommie, C.P. Lutz, D.M. Eigler, Science 262, 218 (1993)



圖中顯示用掃描隧道顯微鏡的針尖在銅表面上搬運和操縱48個鐵原子，使它們排成圓形。銅的價電子的電子雲密度分布在鐵原子圍成的區域內形成駐波。



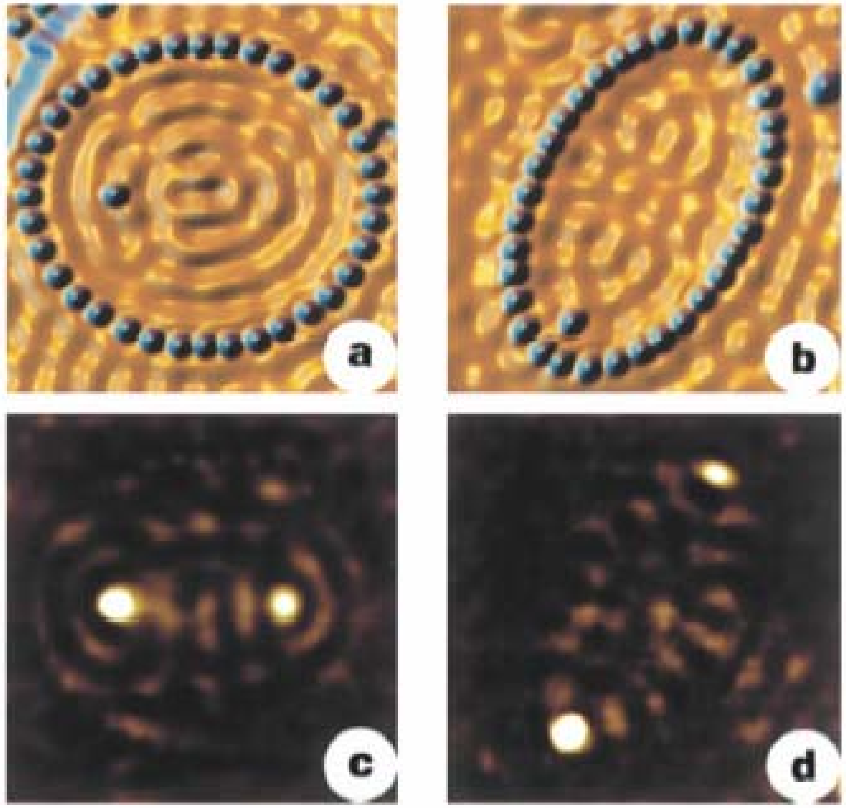
各種量子圍欄



D.M. Eigler, IBM, Almaden

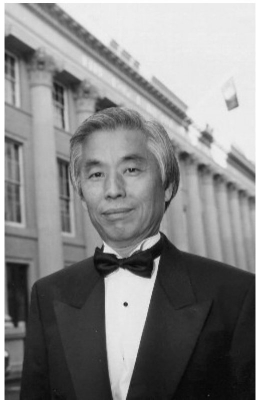
量子幻象、海市蜃樓
Co/Cu(111)

H.C. Monoharan, C.P. Lutz, D.M. Eigler, Nature 403, 512 (2000)



將磁性鈷原子放到橢圓形圍欄的一個焦點上時，在另一個焦點區檢測到了跟那個遠處鈷原子周圍的表面電子相同的電子態，儘管那裡實際上並沒有磁性原子！

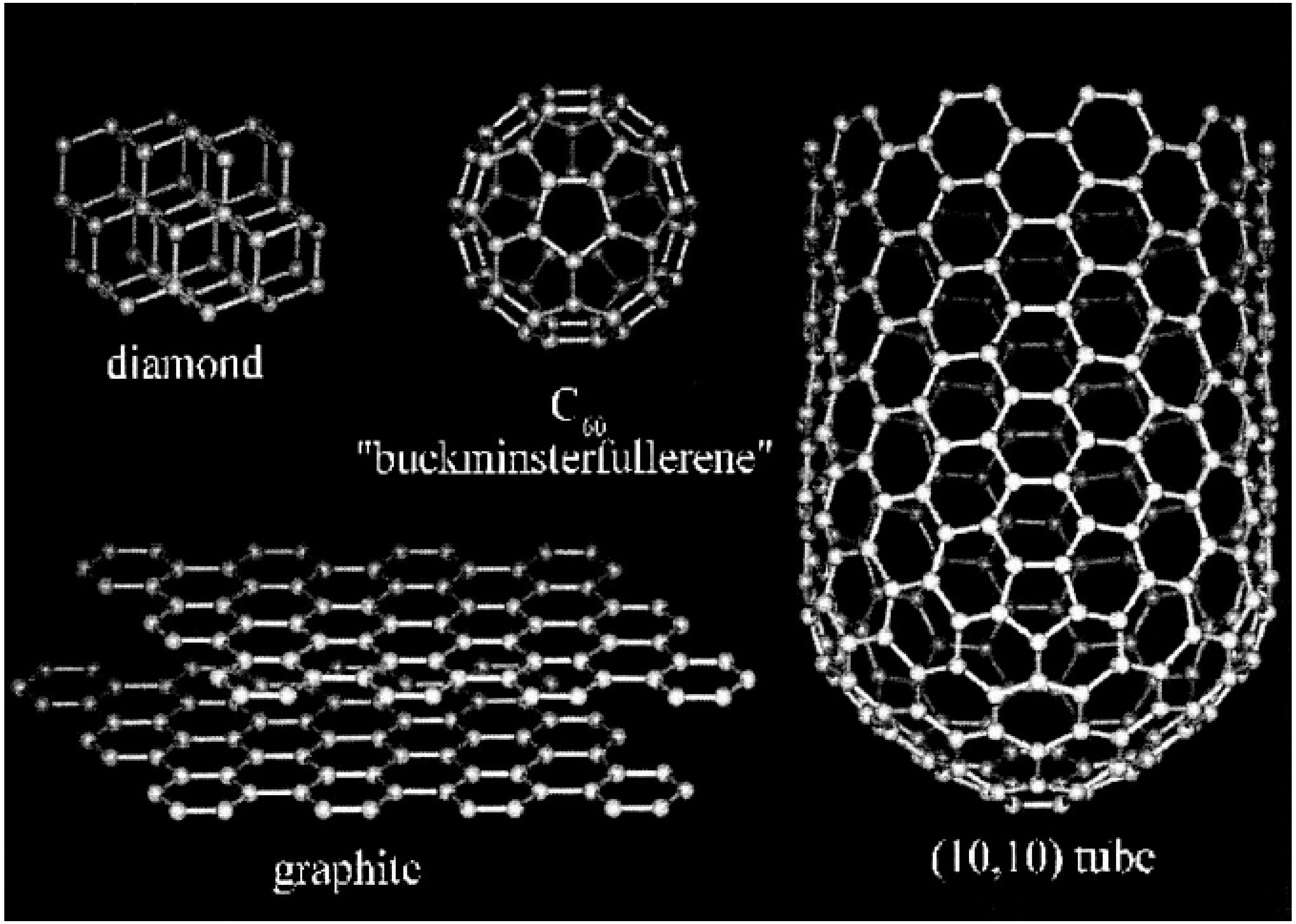
奈米科學的里程碑(VI)



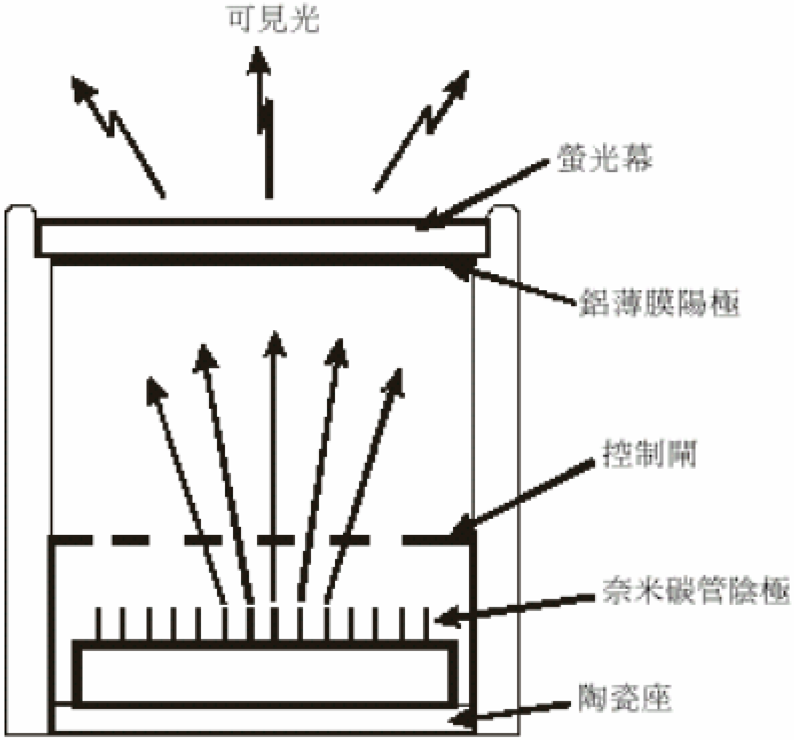
- **1991 Sumio Iijima（飯島澄男）發現CNT**

奈米碳管(carbon nanotube, CNT)於1991年被製備，由於質輕、高韌性，並具有類似鑽石的楊氏係數，以及特殊的電子傳輸特性，被認為是最佳的奈米元件材料之一。此外，由於其尖端直徑可達到1 nm，因此也是最佳的奈米探針材料。

碳的同素異型結構



利用碳奈米管所做的三原色影像平面顯示器



韓國的三星(Samsung)公司研究人員以碳奈米管為元件，已經成功的研究出4.5英吋全彩影像平面顯示器，而且準備推出解析度為576 X 242像素的9英吋全彩平面顯示器。

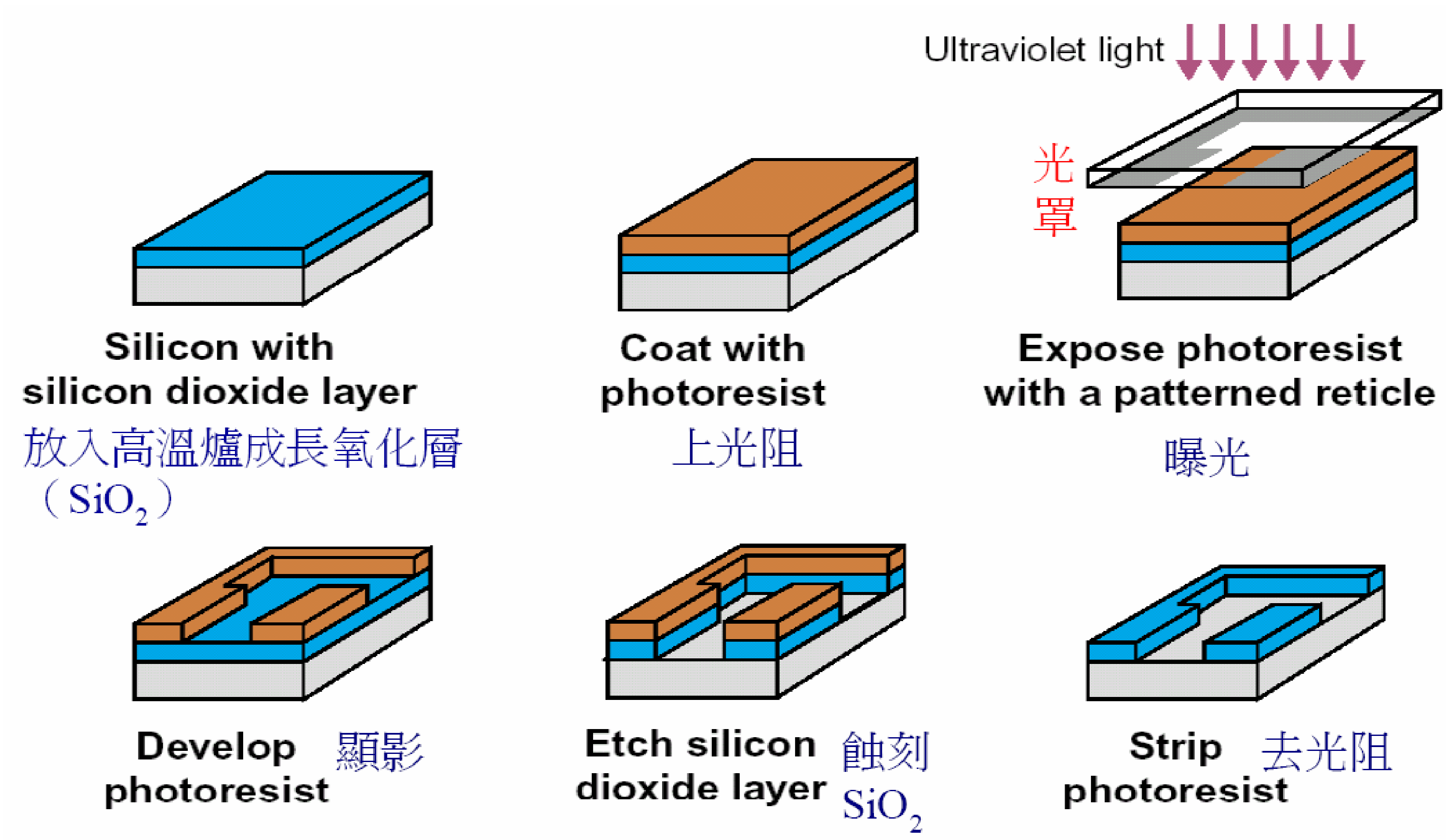
奈米科學的里程碑(VI)

- 1994 Adleman “DNA Computing”
- 1994 IBM “Magnetoresistive head”
- 1998 Dekker created Transistor from CNT
- 1999 Tour/Reed “molecular switch”
- **2000 前美國總統柯林頓在2000年宣佈一項美國國家2001年科研計劃“國家奈米技術創新”（英文為NationalNanotechnology Initiative，縮寫為NNI）投資四億九千七百美元於奈米技術**
- 2001 First nerve cell-silicon microchip built

奈米材料的製備方法

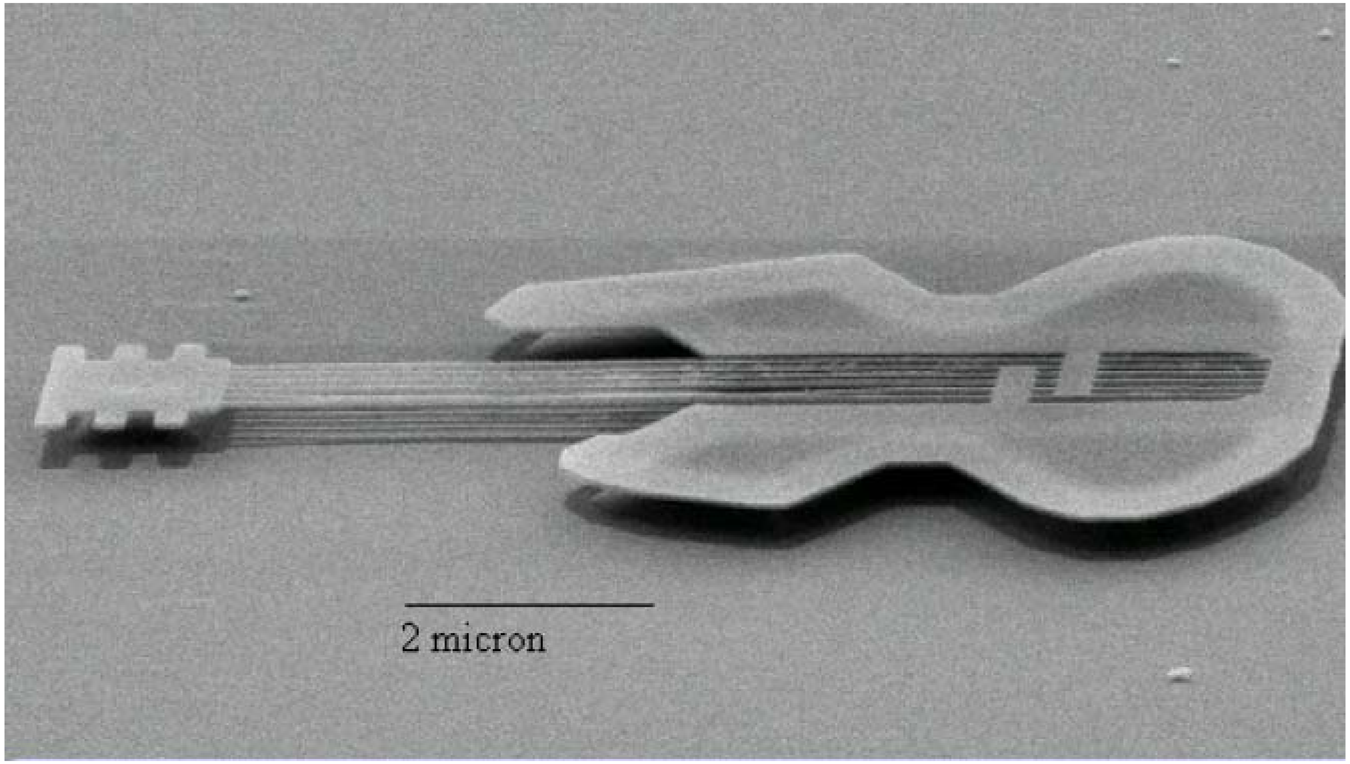
- Top-down：物理方式通常利用微影蝕刻（lithography）、乾濕式蝕刻（etching）等蝕刻方法，即所謂的由上而下（top down）的方法來製備奈米粒子。
- Bottom-up：化學方式通常所用的方法是利用由下而上（bottomup）的方法，也就是以原子或分子為基本單位，利用溶液微胞侷限、電解、生物模板、溶膠- 凝膠、化學氣相沉積（chemicalvapor deposition）等方法，漸漸往上成長成奈米粒子。

半導體製造過程

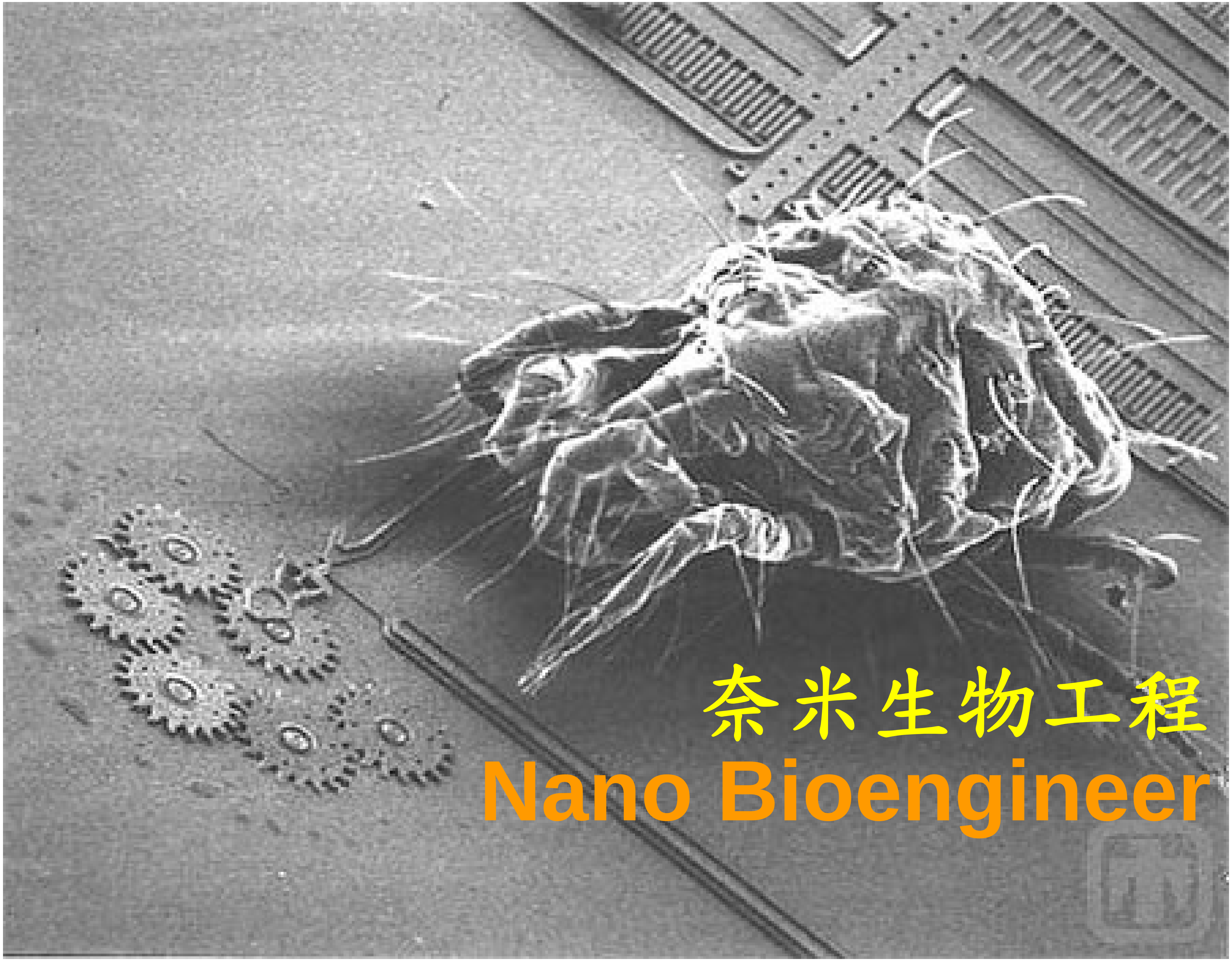


Ultraviolet light
光罩
Silicon with silicon dioxide layer
放入高溫爐成長氧化層（SiO2）
Coat with photoresist
上光阻
Expose photoresist with a patterned reticle
曝光
Develop photoresist
顯影
Etch silicon dioxide layer
蝕刻 SiO2
Strip photoresist
去光阻

以電子束蝕刻作成的奈米吉他



世界上最小的吉他，全長10mm。含六根絃，每根50nm寬。

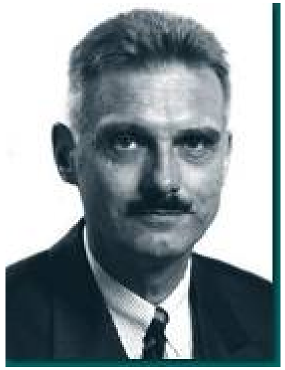

奈米生物工程
Nano Bioengineer

張恆雄老師淺談

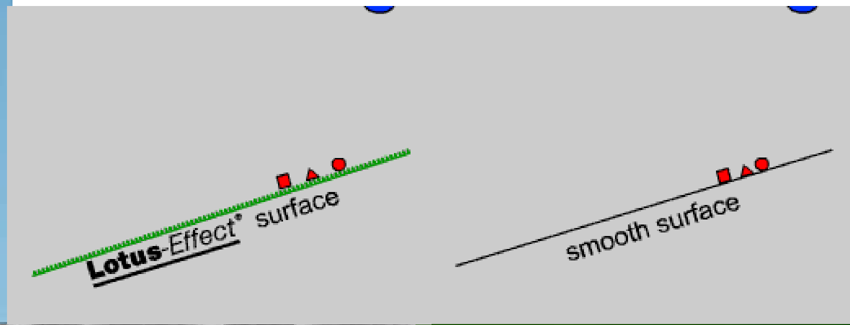
奈米生物工程

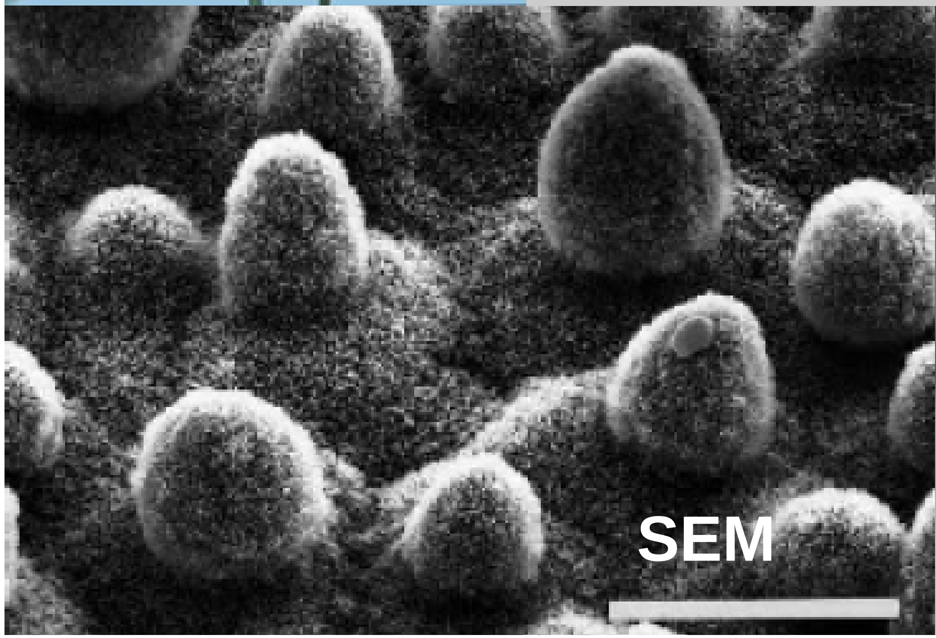
Nano Bioengineer

蓮花效應
Lotus Effect

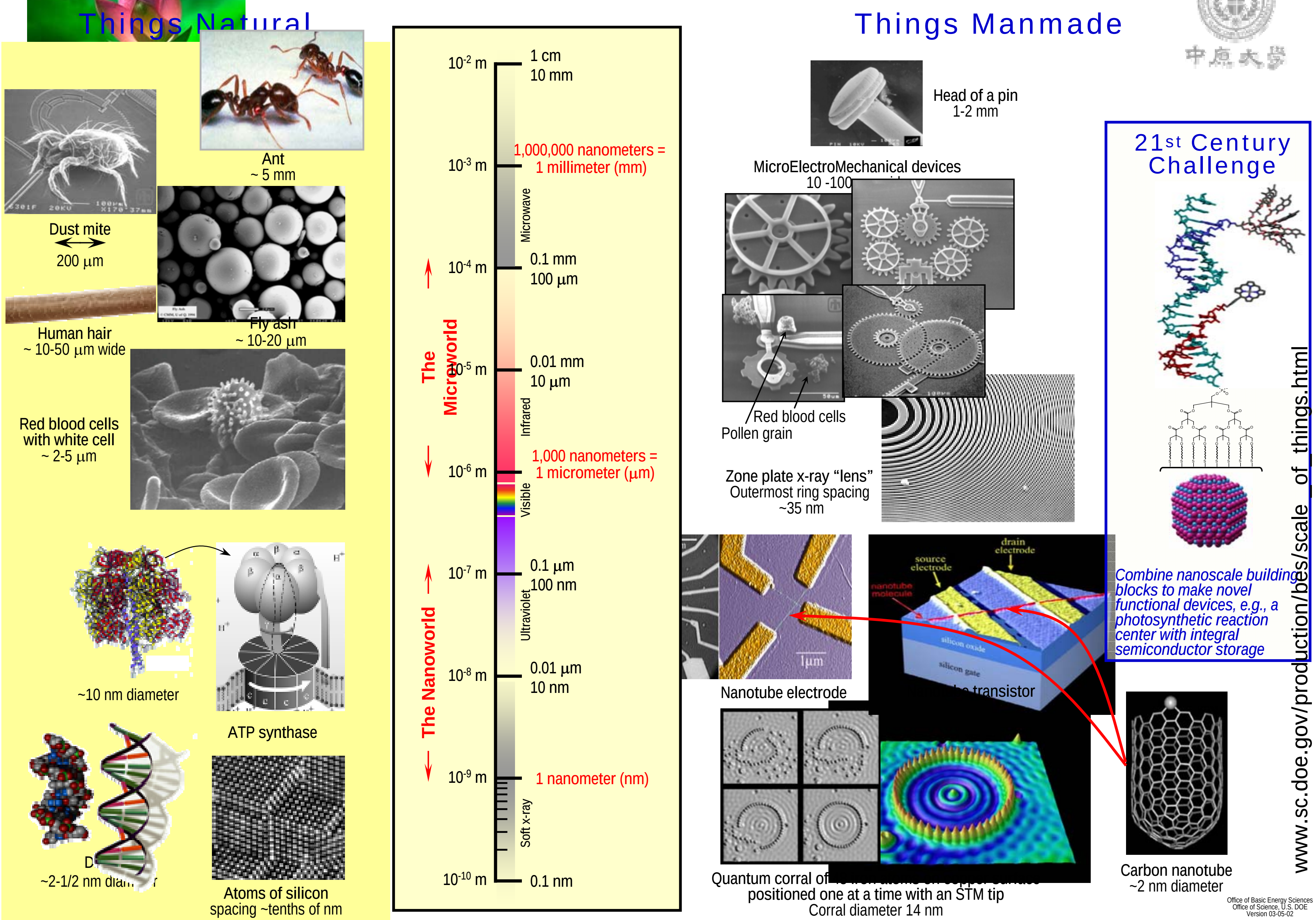


Professor Wilhelm Barthlott
University of Bonn
lotus@uni-bonn.de



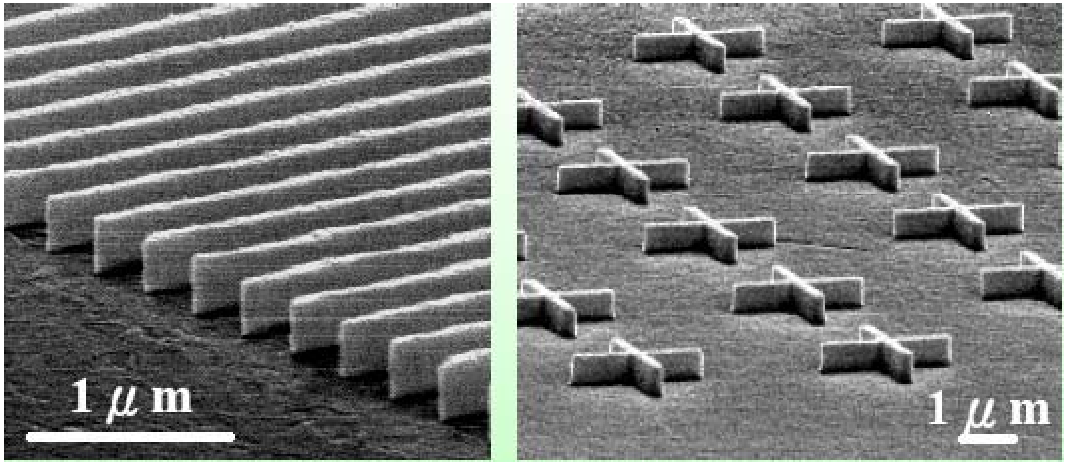


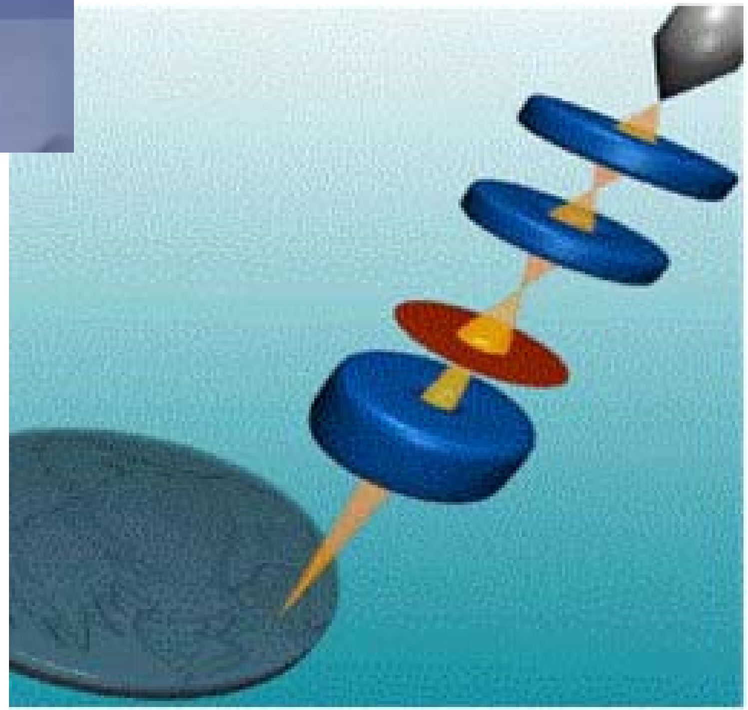
The Scale of Things -- Nanometers and More

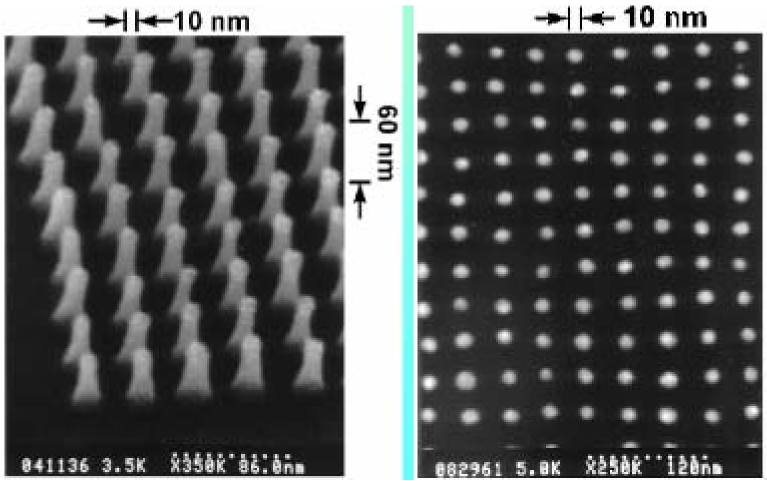


探索奈米世界的利器—

電子束微影術 (Electron-Beam Lithography)







電子束微影可輕易達成數百至數奈米尺寸的線寬，除了可以用來製作光微影所需的光罩(mask)外，它還有一獨特的優點：直寫(direct write)，即不需要光罩就能定義圖形，可輕易畫出不同的設計，方便研究上用，目前許多新穎的量子元件如量子點、量子線等，大部分都是利用電子束微影製作而成。

http://nano.nchc.org.tw/dictionary/ebl.html

Biological Self Assembly is *Heirarchical*

Monomer molecules - amino acids, lipids

↓

Polymers - DNA, RNA, polysaccharides, proteins

↓

Assemblies - membranes, organelles

↓

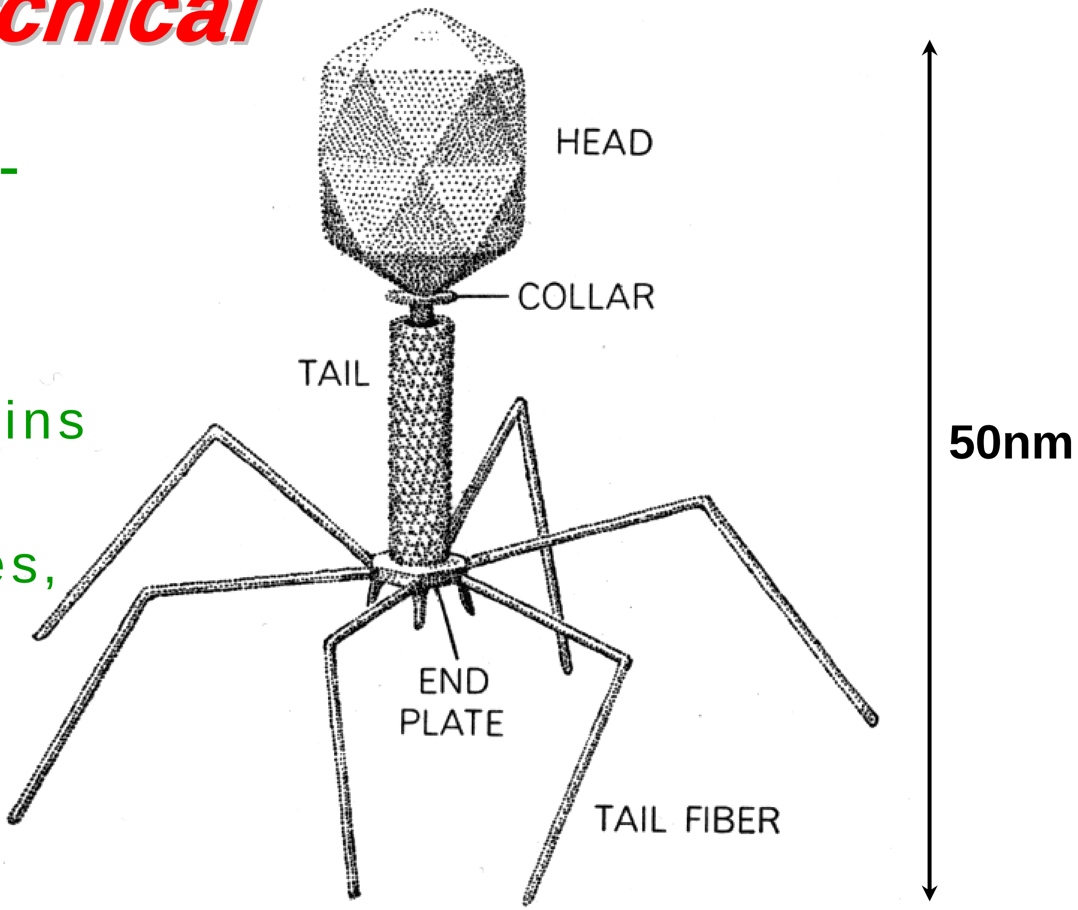
Cells

↓

Organs

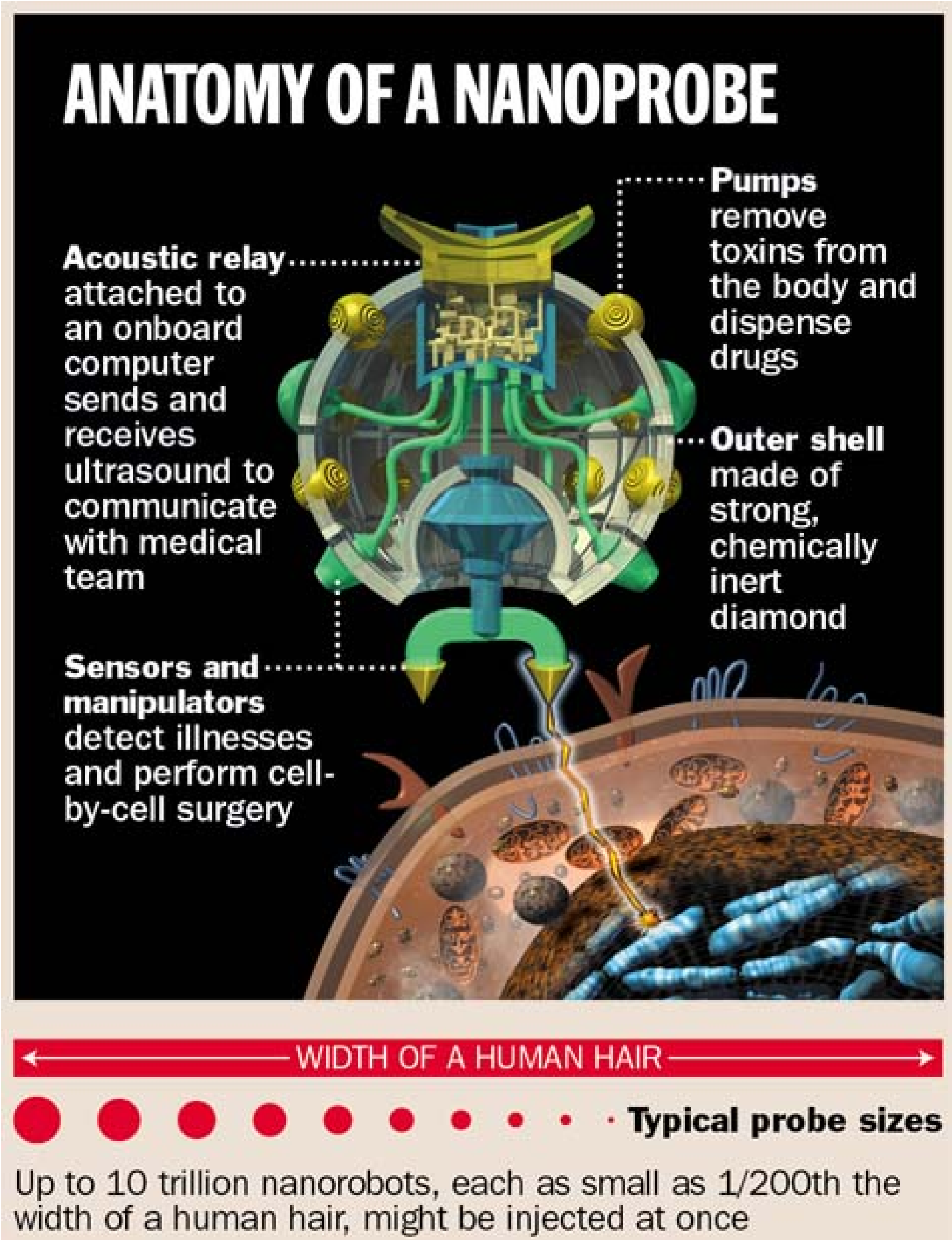
↓

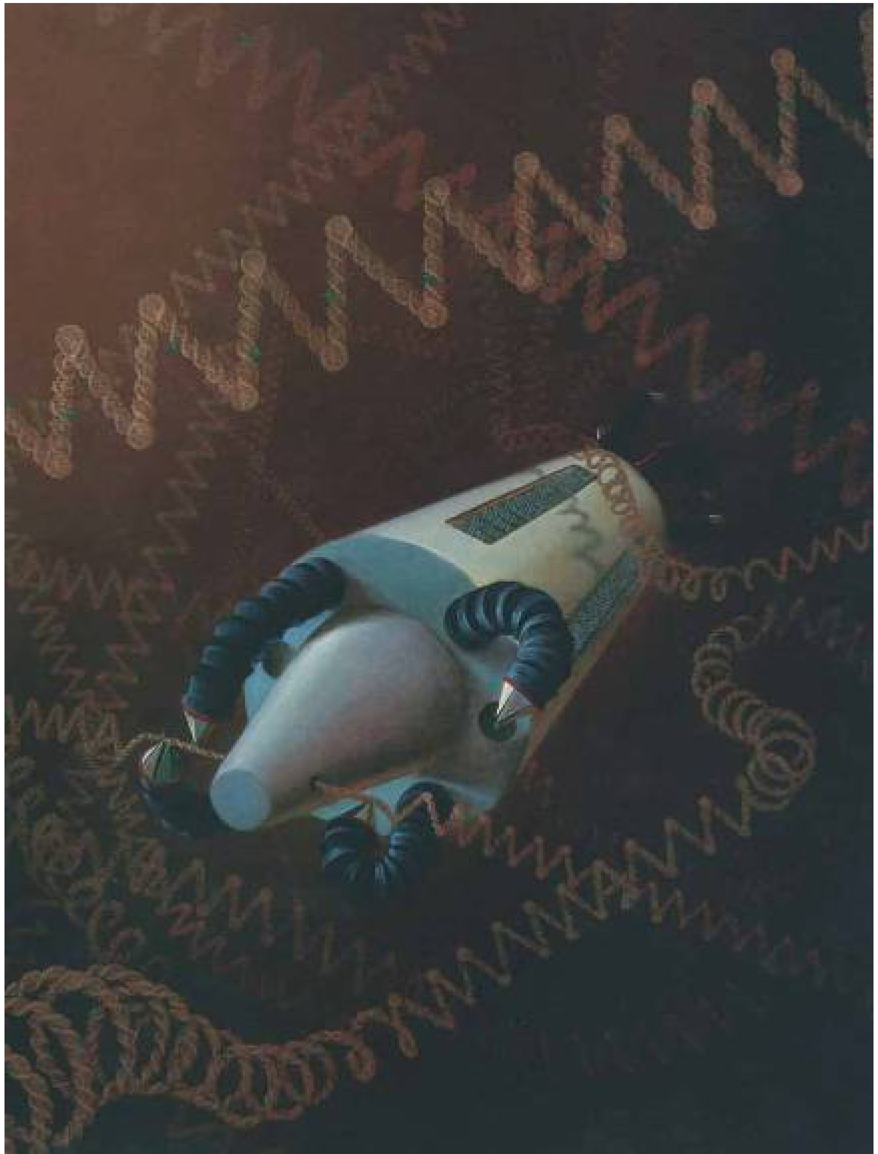
Organisms

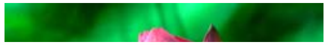


T4 Bacteriophage

Scientific American, February 1965


ANATOMY OF A NANOPROBE
Acoustic relay attached to an onboard computer sends and receives ultrasound to communicate with medical team
Pumps remove toxins from the body and dispense drugs
Outer shell made of strong, chemically inert diamond
Sensors and manipulators detect illnesses and perform cell-by-cell surgery
WIDTH OF A HUMAN HAIR
Typical probe sizes
Up to 10 trillion nanorobots, each as small as 1/200th the width of a human hair, might be injected at once





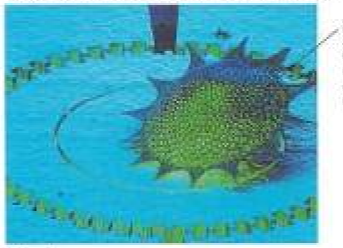
Nanorobots

Technology is shrinking fast. Computing technology that would have filled a warehouse 30 years ago can now be squeezed onto a chip a fraction of the size of your thumbnail. The very smallest scale of engineering is called nanotechnology. A nanometer is a billionth of a meter, about the width of ten atoms. Nanotechnology may, one day, be capable of producing fully working robots to that scale, called nanorobots or nanobots. Working at an almost atomic level, nanobots could build complex items cheaply and repair clothes, equipment, and even people without being noticed. They could also be used to rid the atmosphere of pollution and to repair holes in the ozone layer.

A mere wisp A row of 20,000 of these stick figures is more narrow than a human hair.

Bottom up

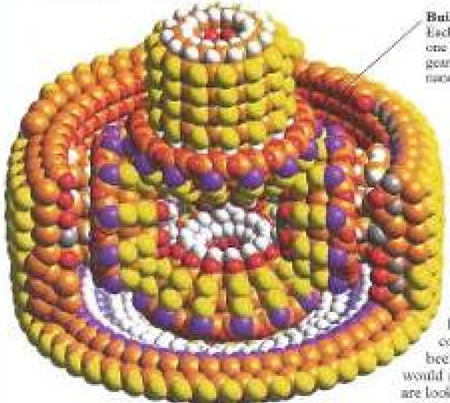
Researchers are looking at different ways to construct nanobots. The "bottom up" approach uses individual atoms and molecules as building blocks. This stick figure was created from just 28 carbon monoxide molecules.



Putting it in context A plankton skeleton, just 0.008 in (0.2 mm) across, sits on one of the engine's cogs, measuring 0.02 in (0.5 mm).

Top down

Known as "top down," one potential way of building nanomachines is to miniaturize existing machines. There have been some incredible feats, including this fully working electric motor, just 0.07 in (1.8 mm) in size.



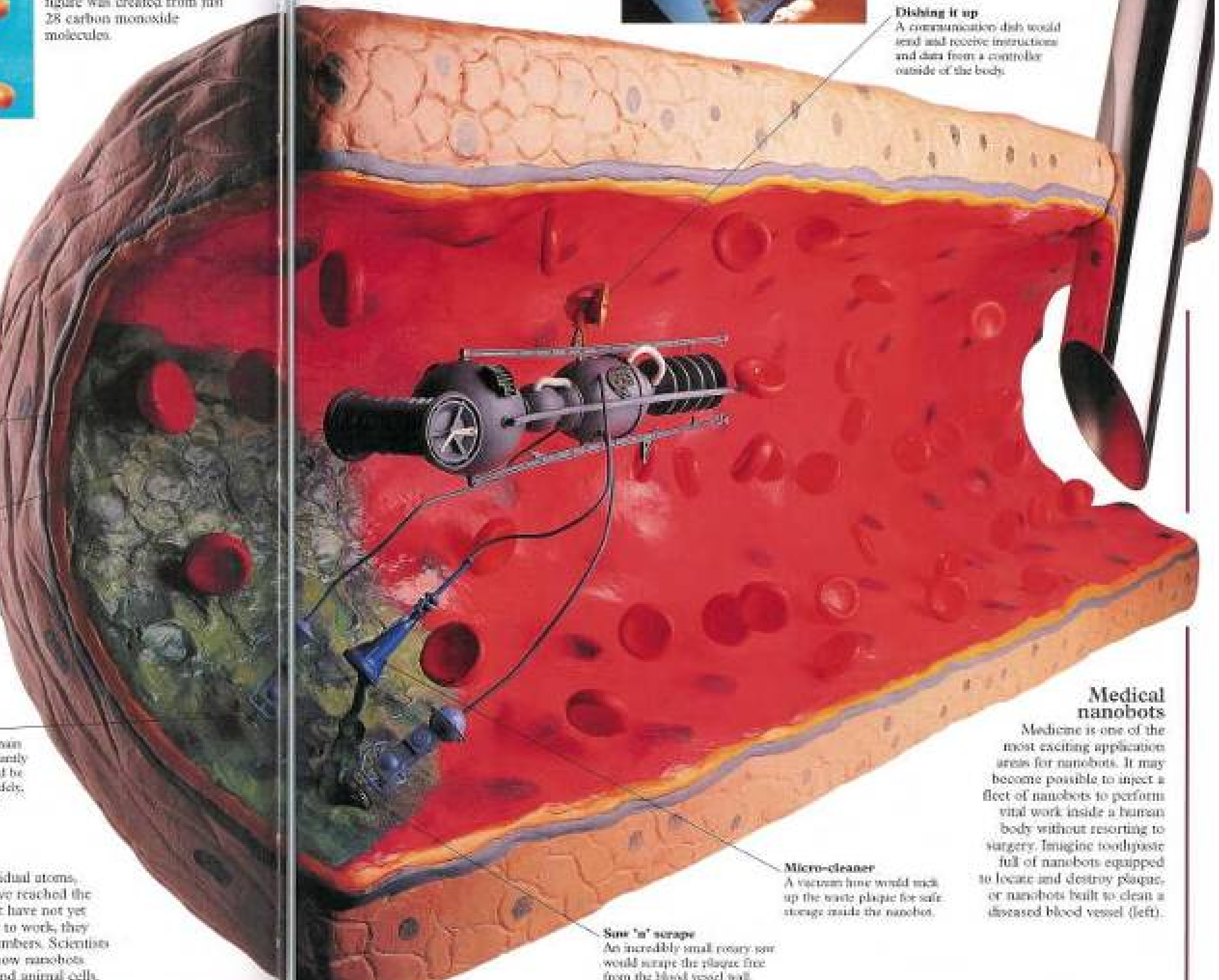
Building atoms Each ball represents one atom. The whole gear measures just a few nanometers in diameter.

A nanogear

Machines made from individual atoms, like this differential gear, have reached the computer modeling stage, but have not yet been built. For nanotechnology to work, they would need to be made in huge numbers. Scientists are looking to nature for ideas on how nanobots may be self-replicating, like plant and animal cells.

May the force be with you

This nanomanipulator is a big step toward an assembler that can build nanobots from atoms. It uses an atomic force microscope, together with sophisticated handling tools, to manipulate minute particles.



Blood vessel wall

Red blood cell

Plaque attack The diseased section of the blood vessel is covered with a type of plaque containing cholesterol.

Waste away The nanobot would either remain inside the blood system, constantly performing its task, or it would be programmed to biodegrade safely, carrying the waste plaque out of the human body.

Getting the needle A hypodermic syringe, less than 0.02 in (0.5 mm) in diameter, would inject nanobots into the blood vessel.

Dishing it up A communication dish would send and receive instructions and data from a controller outside of the body.

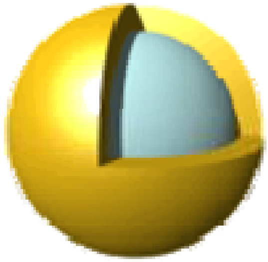
Micro-cleaner A vacuum hose would suck up the waste plaque for safe storage inside the nanobot.

Saw 'n' scrape An incredibly small rotary saw would scrape the plaque free from the blood vessel wall.

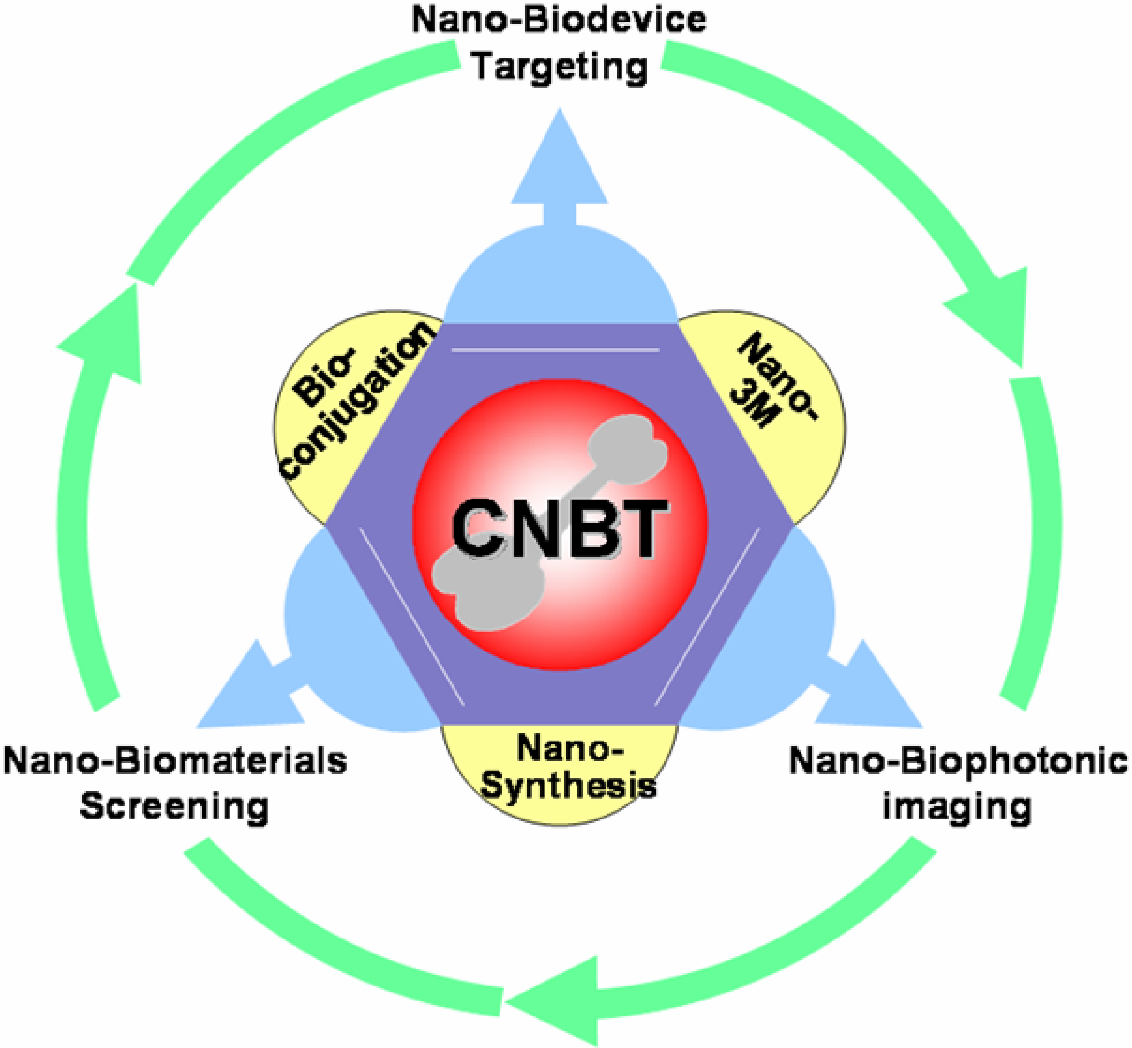
Medical nanobots

Medicine is one of the most exciting application areas for nanobots. It may become possible to inject a fleet of nanobots to perform vital work inside a human body without resorting to surgery. Imagine toothpaste full of nanobots equipped to locate and destroy plaque, or nanobots built to clean a diseased blood vessel (left).

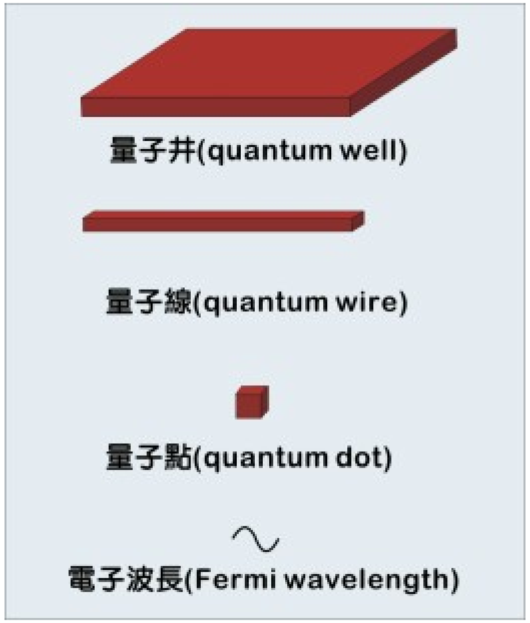
奈米生物工程師特質



CNBT Future Development



量子點
Quantum Dots



若要嚴格定義量子點，則必須由量子力學(quantum mechanics)出發。我們知道電子具有粒子性與波動性，電子的物質波特性取決於其費米波長(Fermi wavelength)

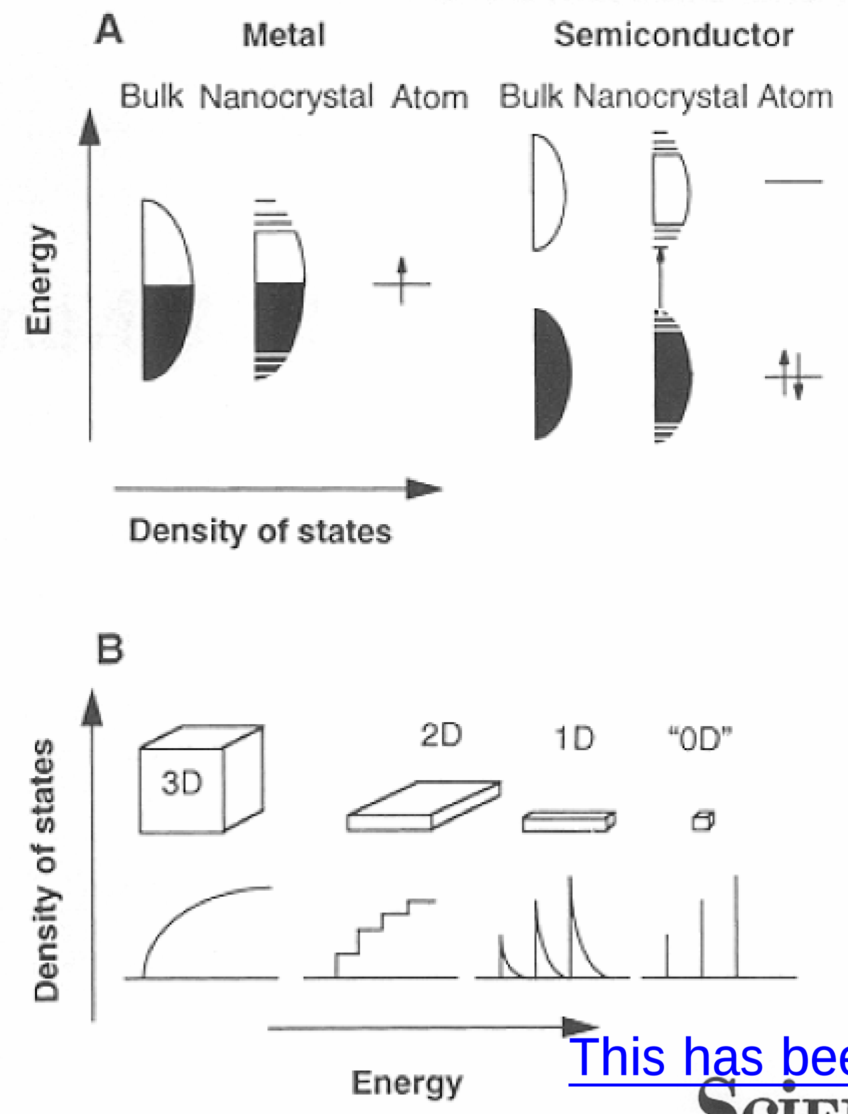
$$\lambda F = 2\pi / kF$$

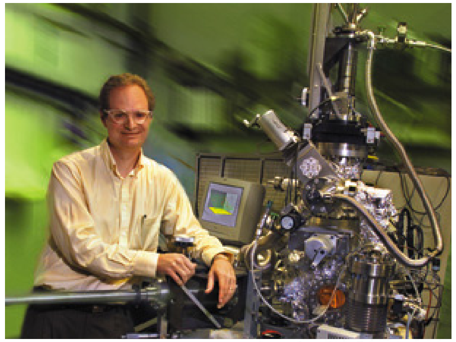
在一般塊材中，電子的波長遠小於塊材尺寸，因此量子侷限效應不顯著。如果將某一個維度的尺寸縮到小於一個波長（如圖所示），此時電子只能在另外兩個維度所構成的二維空間中自由運動，這樣的系統我們稱為量子井(quantum well)；如果我們再將另一個維度的尺寸縮到小於一個波長，則電子只能在一維方向上運動，我們稱為量子線(quantum wire)；當三個維度的尺寸都縮小到一個波長以下時，就成為量子點了。

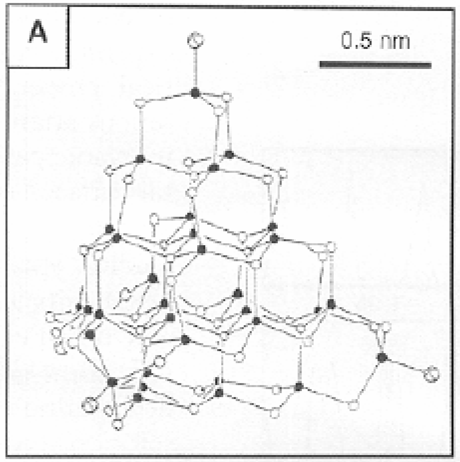
Science 1996

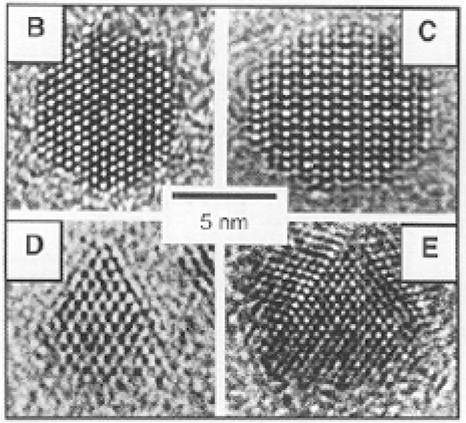
Semiconductor Clusters, Nanocrystals, and Quantum Dots

A. P. Alivisatos







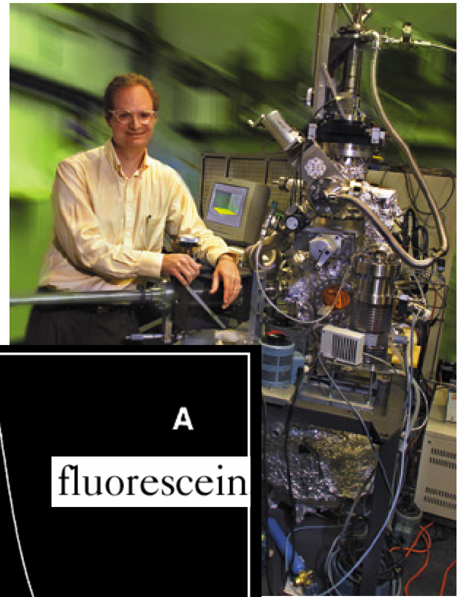


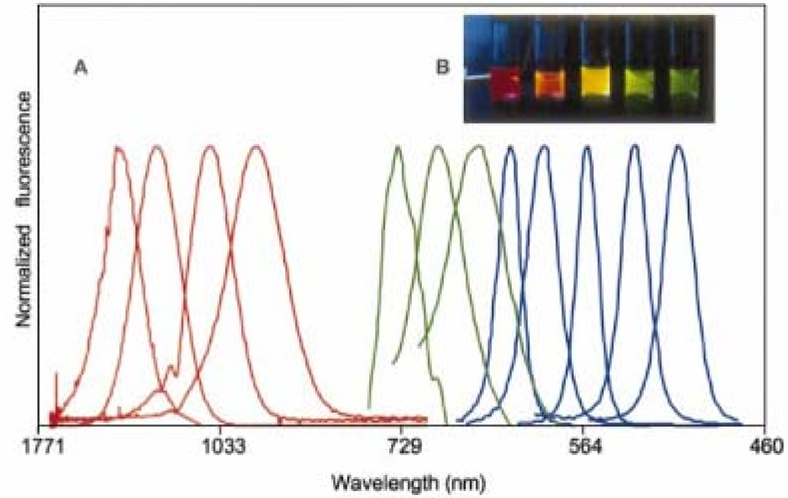
SCIENCE 16 February 1996, Volume 271, pp. 933–937

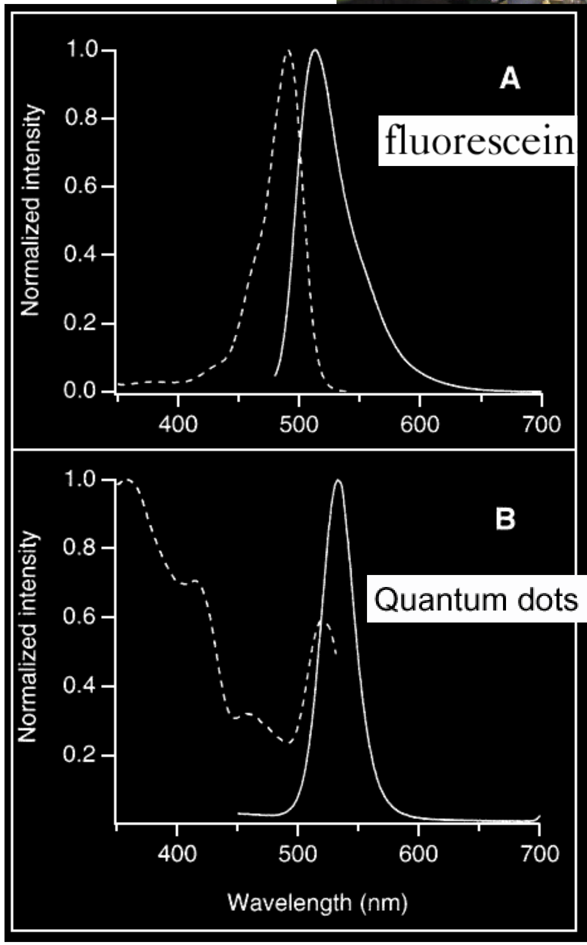
Science 1998

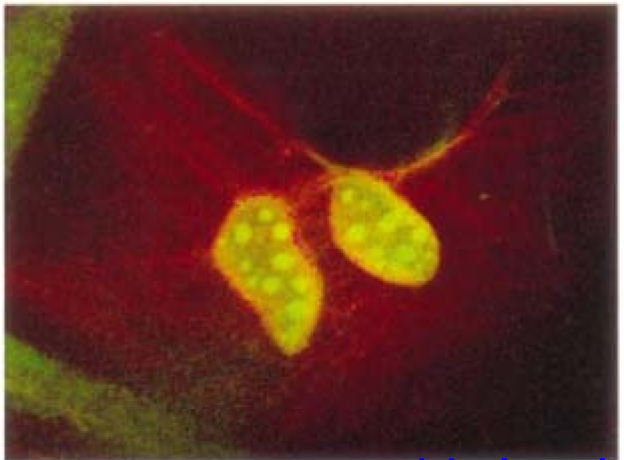
Semiconductor Nanocrystals as Fluorescent Biological Labels

Marcel Bruchez Jr., Mario Moronne, Peter Gin, Shimon Weiss,* A. Paul Alivisatos*







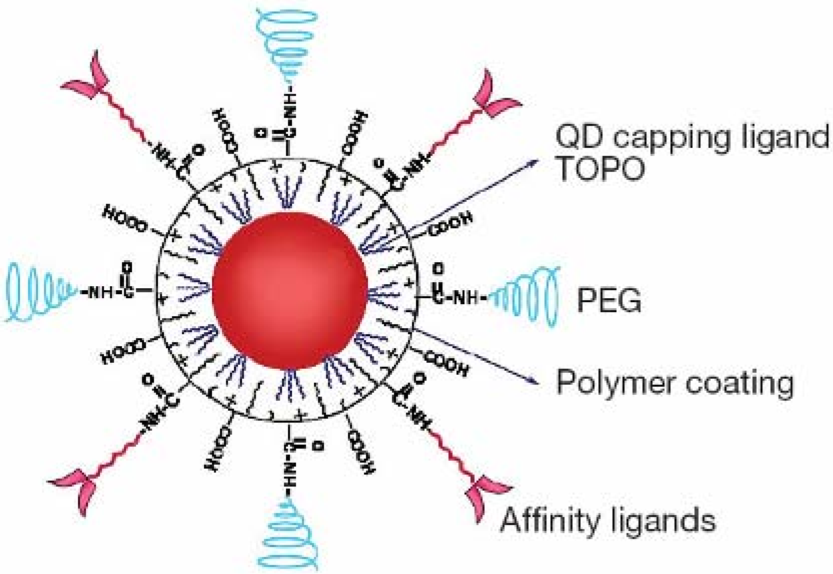


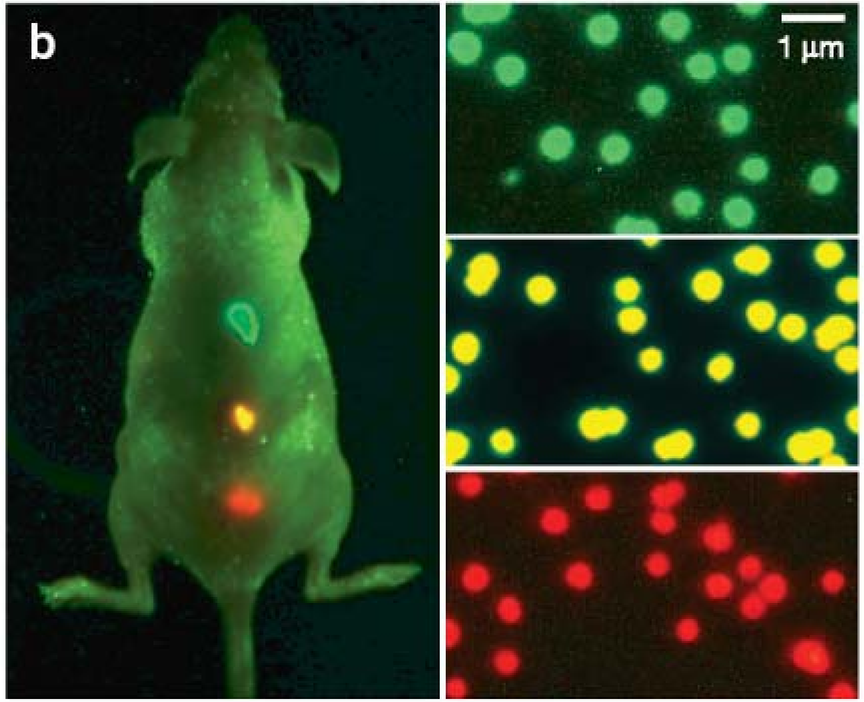
This has been cited more than **846** times.

SCIENCE VOL 281 25 SEPTEMBER 1998

In vivo cancer targeting and imaging with semiconductor quantum dots

Xiaohu Gao,[1] Yuanyuan Cui,[2] Richard M Levenson,[3] Leland W K Chung[2] & Shuming Nie[1]



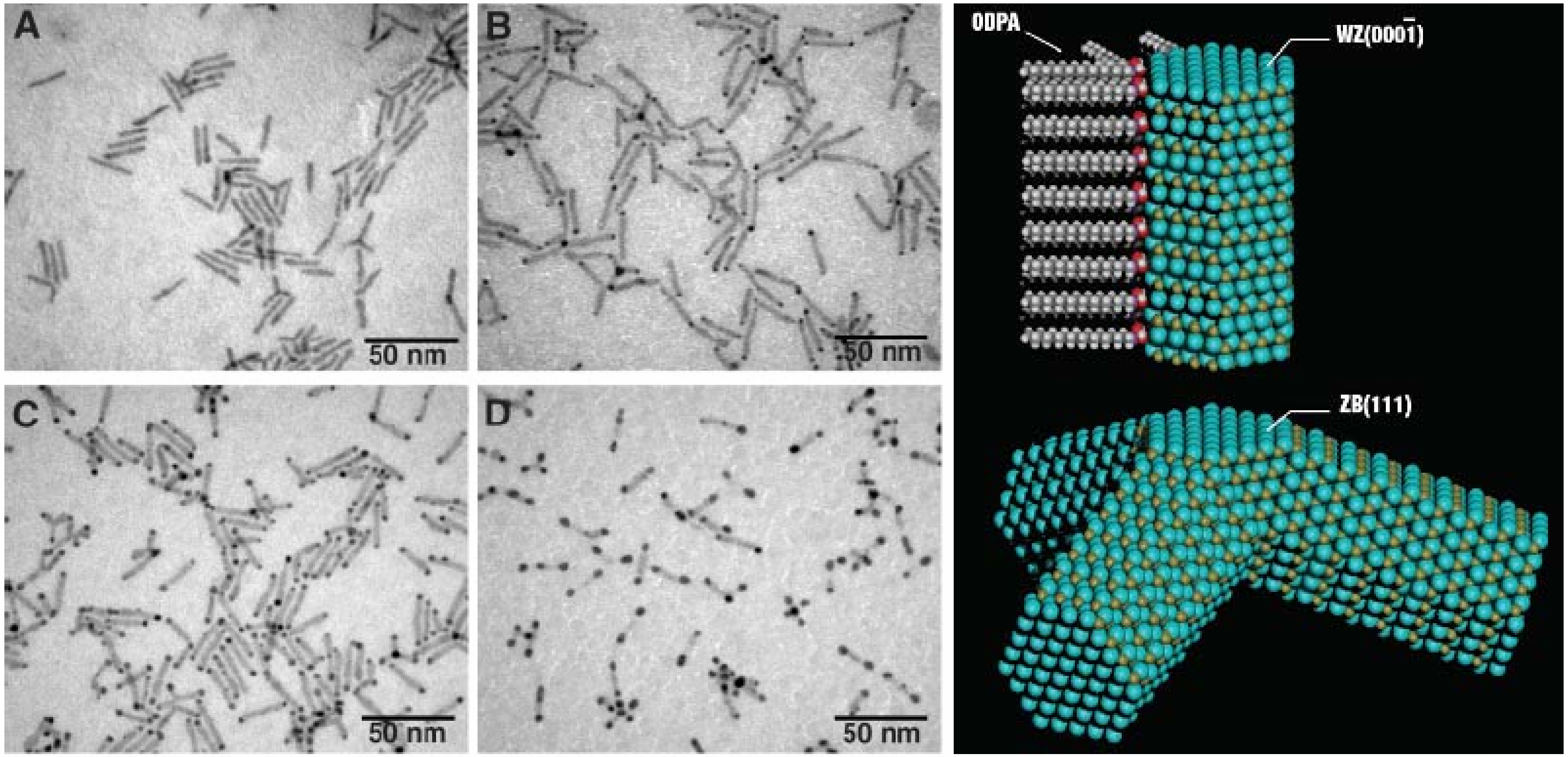


nature biotechnology@nature.com 2004
VOLUME 22 NUMBER 8 AUGUST 2004

Science 2003

Selective Growth of Metal Tips onto Semiconductor Quantum Rods and Tetrapods

Taleb Mokari,[1,2] Eli Rothenberg,[1,2] Inna Popov,[2] Ronny Costi,[1,2] Uri Banin[1,2*]



This has been cited more than **37** times.

SCIENCE VOL 304 18 JUNE 2004 1787

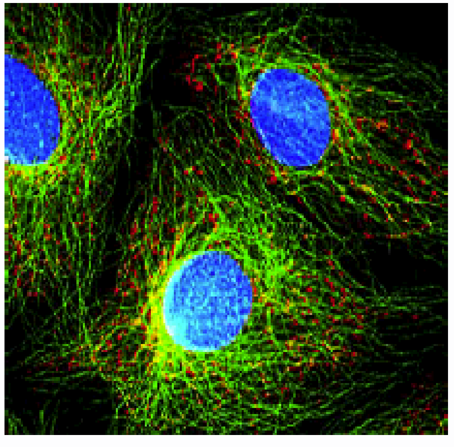
Biological Applications

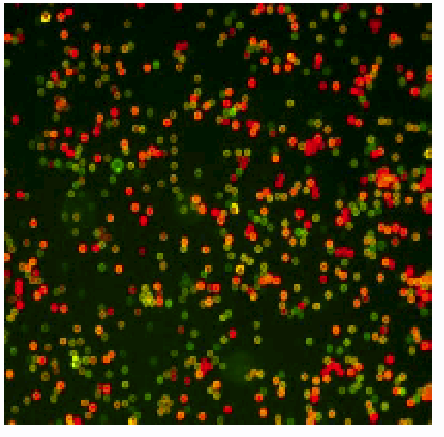
Quantum dots

Bio-labeling

QBead^{TM} encoded beads

Future applications





- Detection reagents for microscopy
- DNA chips
- flow cytometry
- immunoassays, …

Platform for Multiplexed assays:

- proteomics
- genotyping
- gene expression)

- Live cell imaging
- *in vivo* imaging,…