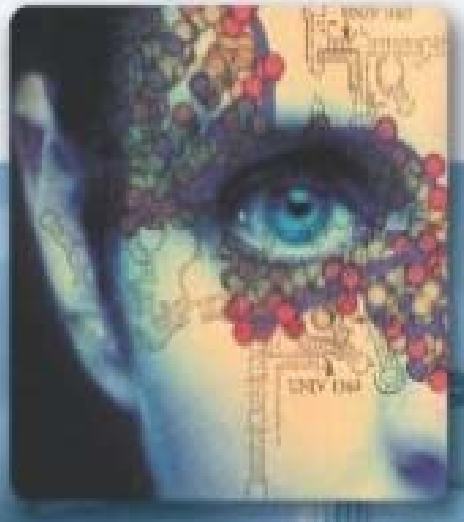


奈米粒子，毒藥或是良藥?

nanotechnology

交大奈米科技研究所

黃國華所長

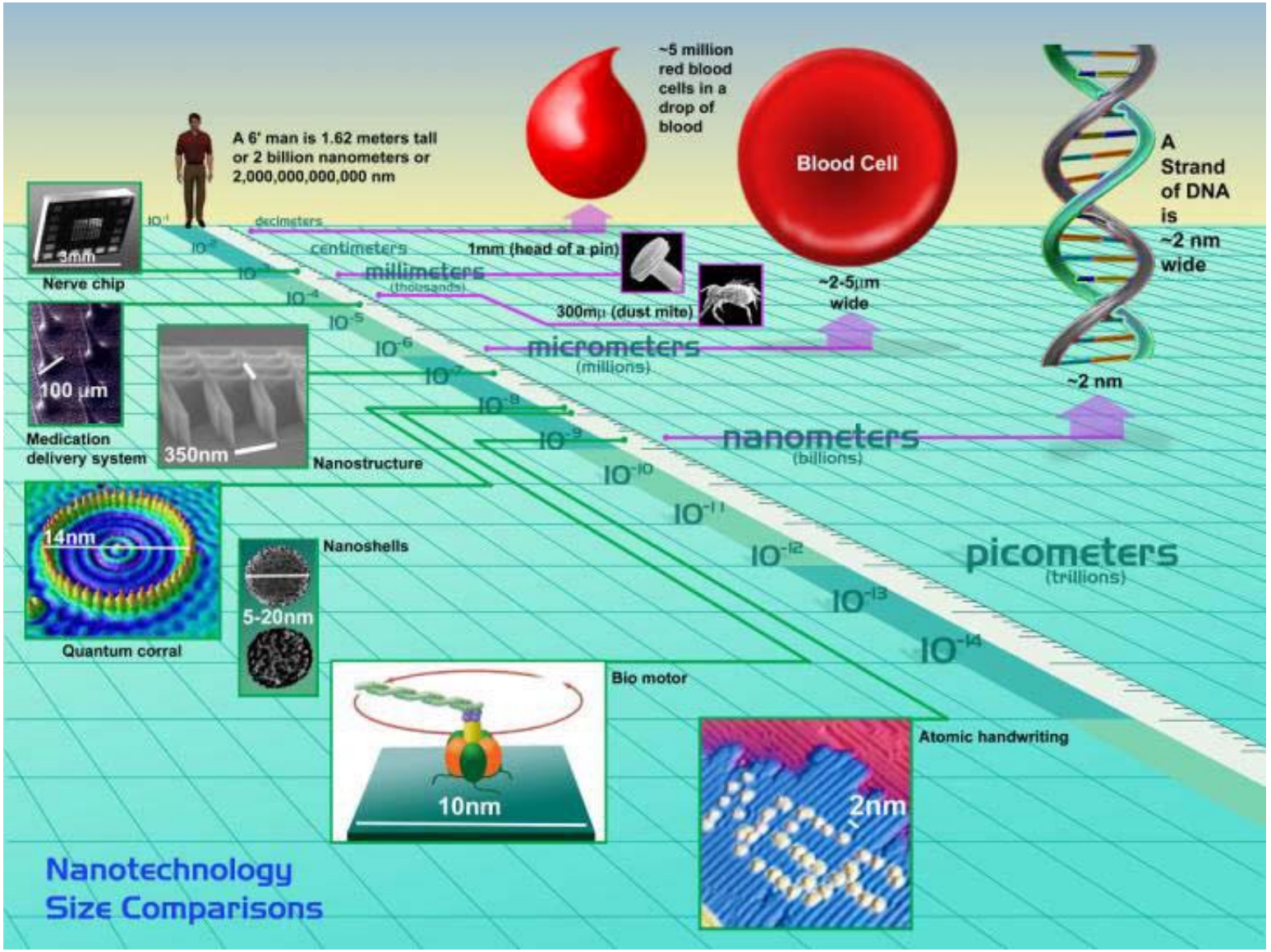
奈米世界在哪裡?

1奈米多大?

什麼是奈米效應?

例舉大自然的奈米現象

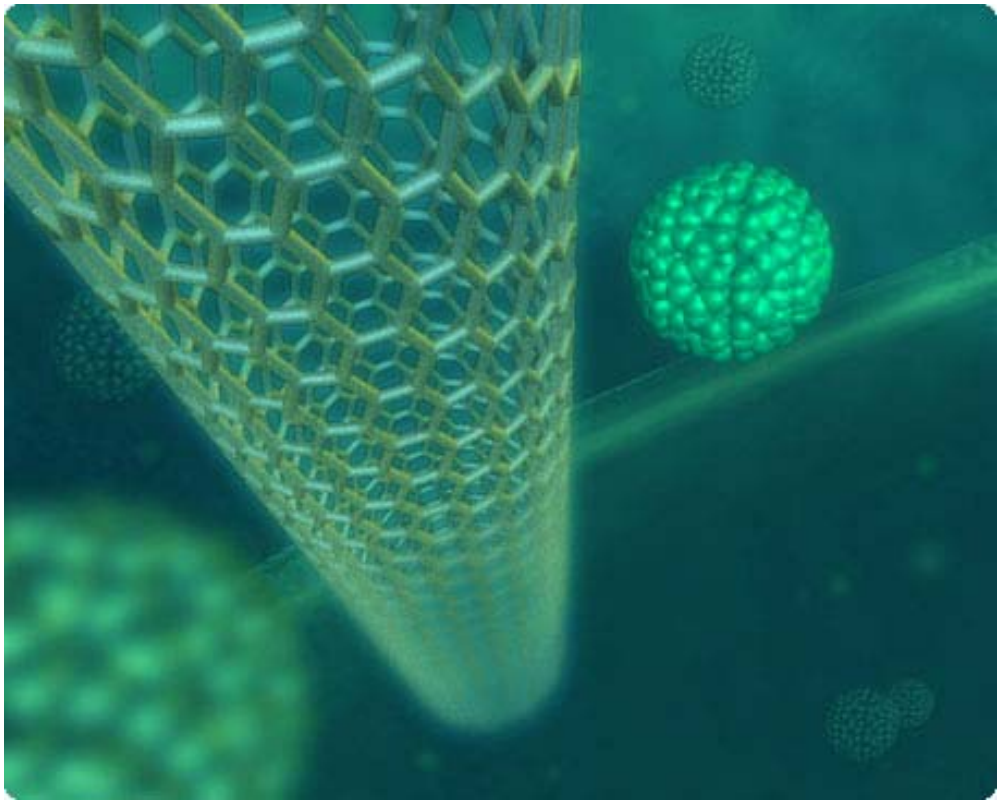
奈米世界在哪裡


~5 million red blood cells in a drop of blood
Blood Cell
A Strand of DNA is ~2 nm wide
A 6' man is 1.62 meters tall or 2 billion nanometers or 2,000,000,000,000 nm
decimeters
centimeters
millimeters
(thousands)
micrometers
(millions)
nanometers
(billions)
picometers
(trillions)
1mm (head of a pin)
300mμ (dust mite)
~2-5μm wide
~2 nm
3mm
Nerve chip
100 μm
Medication delivery system
350nm
Nanostructure
14nm
Quantum corral
Nanoshells
5-20nm
Bio motor
10nm
Atomic handwriting
2nm
Nanotechnology
Size Comparisons

Nanotechnology

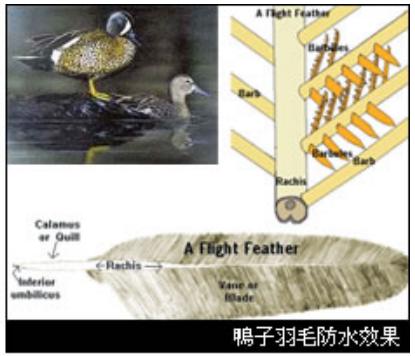
Nanometer多大?

0.1 nm → 1m

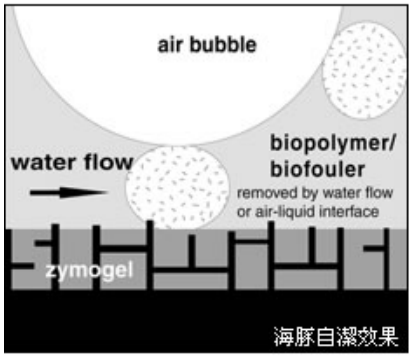


自然中的奈米現象


海豚出水



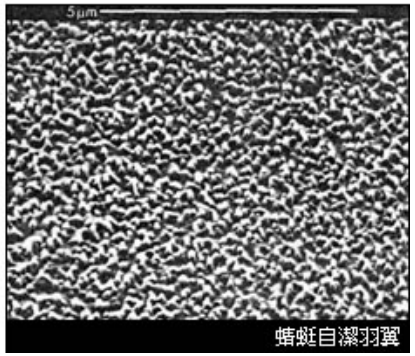
鴨子羽毛防水效果



海豚自潔效果


蜻蜓


蓮花自潔效應

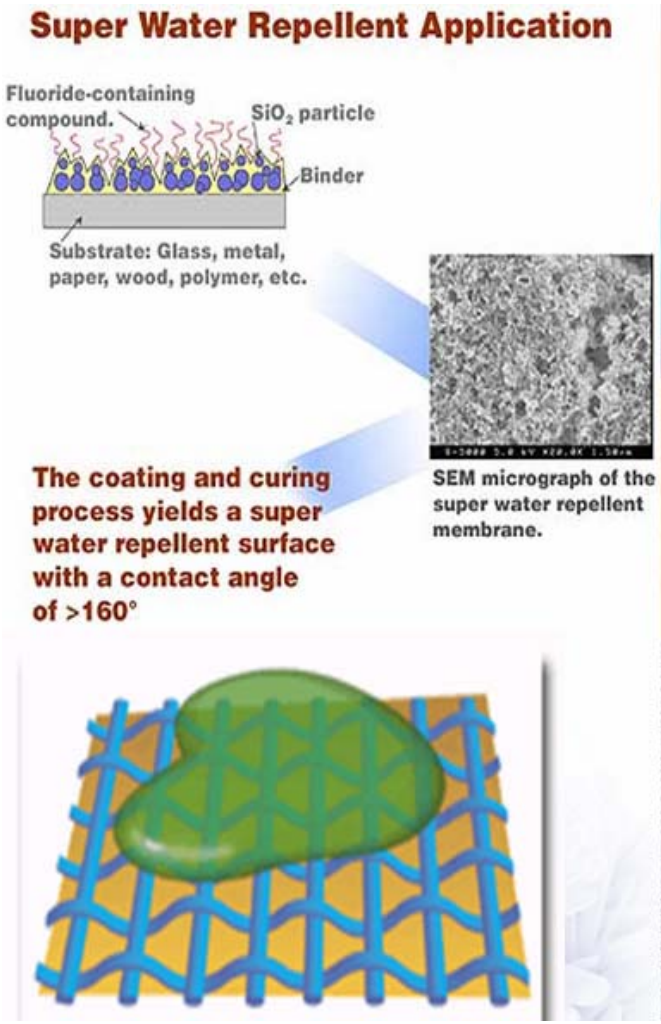


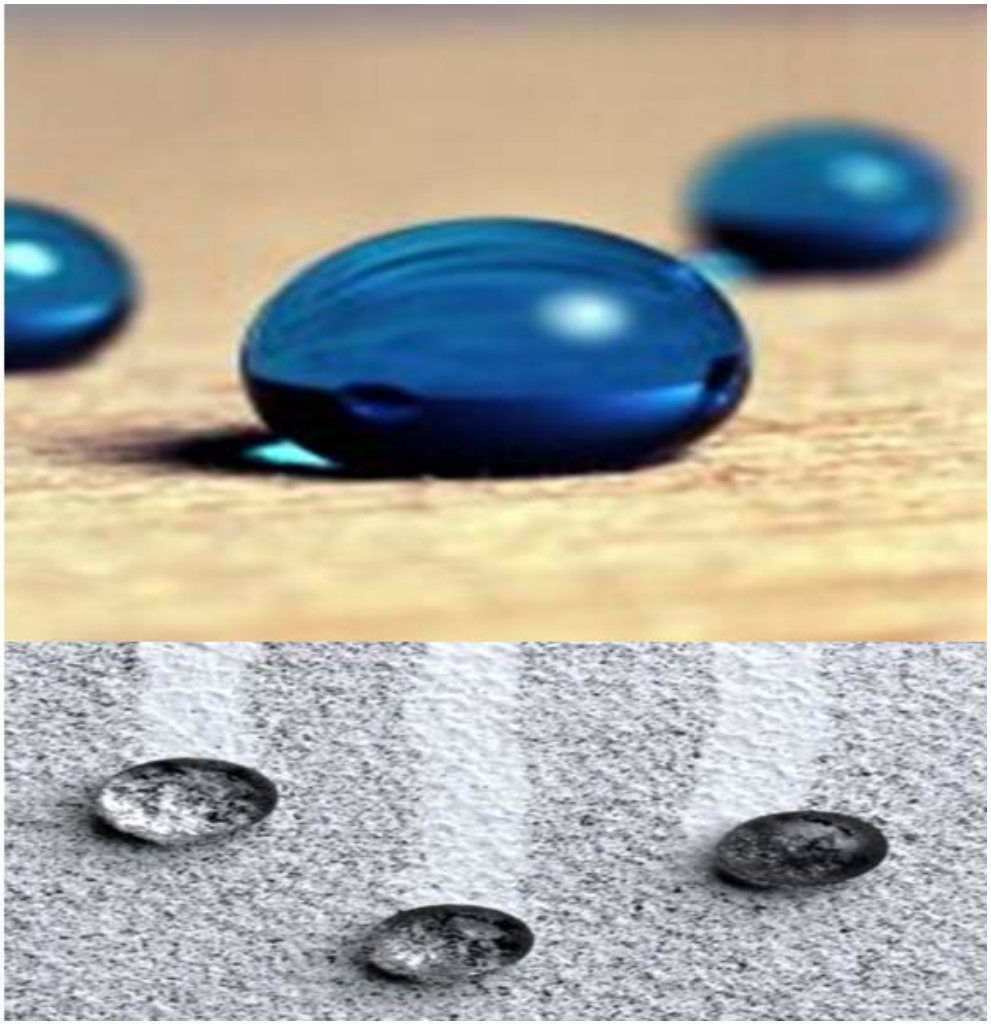
蜻蜓自潔羽翼

大自然就是導師-蓮葉效應(lotus effect)的啟示

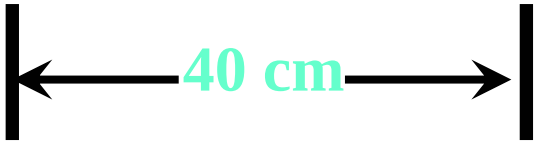
- 愛蓮說是我國北宋理學創始人周敦頤(1017-1073)的著作。其中『出淤泥而不染』，比喻形容一個人的人品非常高潔，雖然在一個混濁惡劣的環境中，潔身自好，不被環境所影響

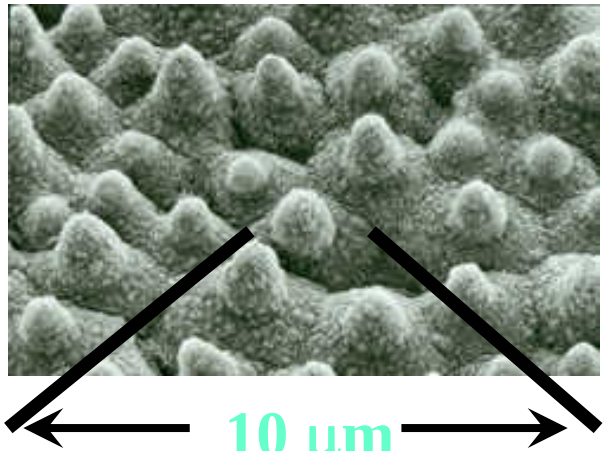
蓮葉效應(lotus effect)的應用

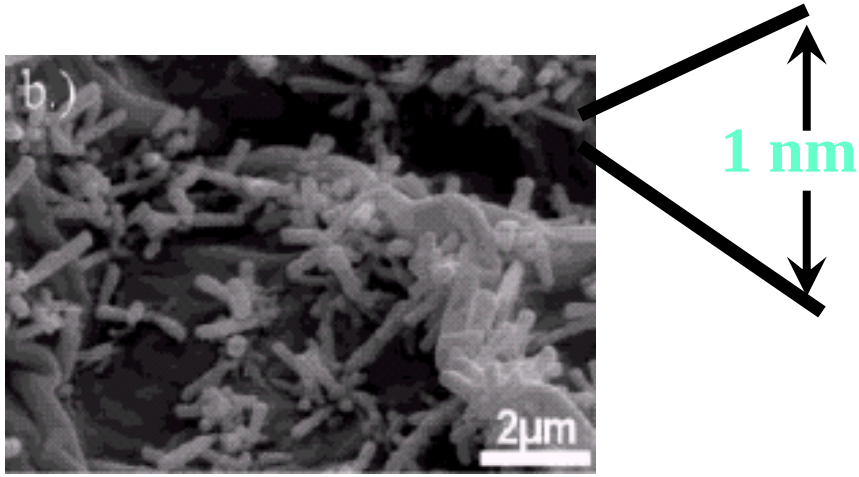




Super Hydrophobic Surface





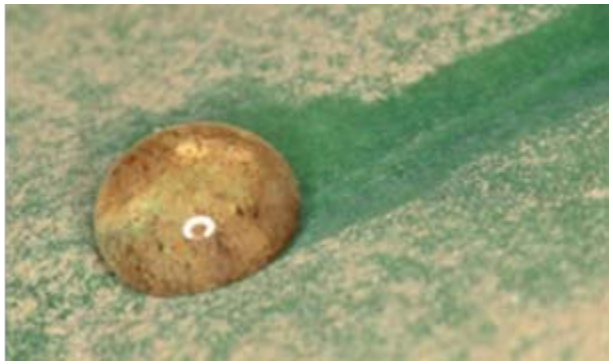


Langmuir, v20, p2405 (2004)

Micro- and Nanostructured Lotus Surface

在電子顯微鏡下，蓮葉的表面具有大小約5~15μm細微突起的表皮細胞(epidermal cell)，表皮細胞上又覆蓋著一層直徑約1nm纖毛狀盤交錯結的蠟質結晶(wax crystal)

Contact angle = 170^{o}



With lotus effect !

Without lotus effect !

Nature Materials, v2, p301 (2003)

Lotus Effect

蠟質結晶本身的化學結構具有疏水性，為一疏水性非常高的碳氫化合物化學物質，即低表面能材料，所以當水與這類表面接觸時，會因表面張力而形成水珠，再加上葉表的細微結構之助，使水與葉面的接觸面積更小而接觸角變大，因此加強了疏水性，同時也降低污染顆粒對葉面的附著力。能夠將空氣保留在突起物間的底部，使外在的污物或液體無法完全沾附於蓮葉上；被侷限在這奈米粗糙層中的空氣，其情形猶如在蓮葉表面形成一層氣墊(Air Cushion)，污物或液體是由空氣所支撐著；使灰塵和蓮葉的接觸面積減少，因此減少了灰塵和蓮葉間的吸附力量。而當水滴由葉面上滾過時，由於灰塵和水滴間的接觸面積大，灰塵粒子和水滴間有較強的吸附力，所以很容易就被水滴帶走。這就是蓮花為何能出污泥而不染了。

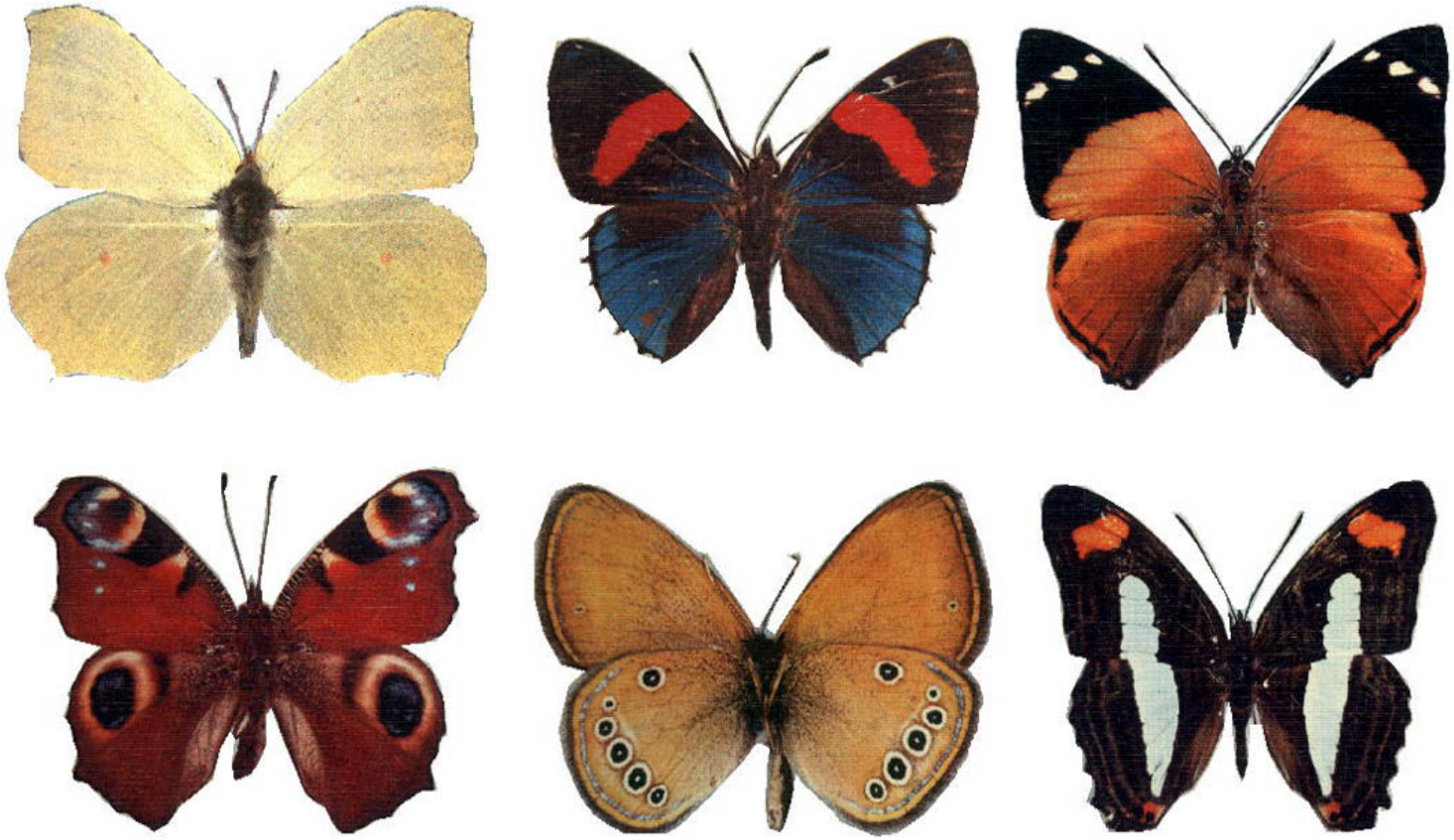
Lotus effect naming by W. Barthlott, and C. Neinhuis, Planta, v202, p1 (1997)

Water Walking of Water Strider

水黽

身體細長，非常輕盈；前腳短，可以用來捕捉獵物；中腳和後腳很細長，長著具有油質的細毛，具有防水作用。前進方式是以中腳插入水中，然後動作。

http://www-math.mit.edu/~dhu/Striderweb/striderweb.html

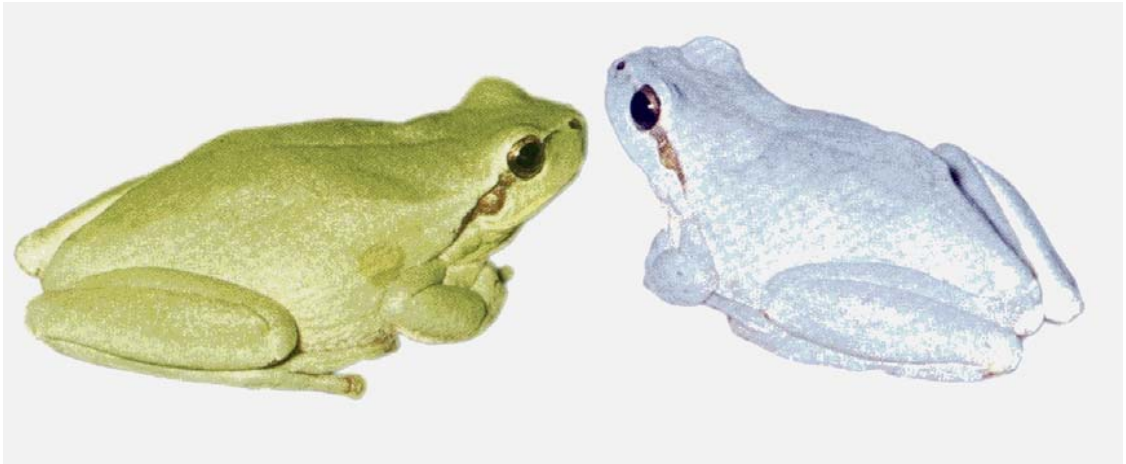


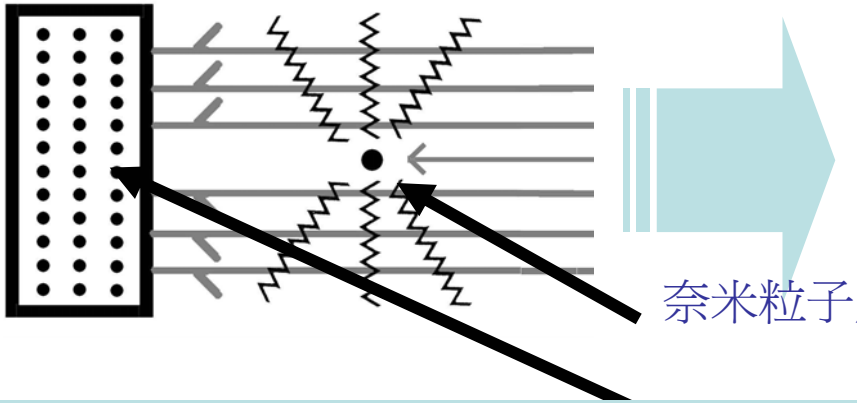
Nature is full of wonderful colors!

動物沒有綠色或是藍色的顏料

羽毛或皮膚呈現亮藍色或是亮綠色 是因爲動物體內有 **Melanin (黑色素)**.

Looks are deceiving!





Tyndall Blue

(Why is the sky blue?)

奈米粒子反射波長較短的光

Nature is the master of nanotechnology.

Yellow screen of β-carotene

β-carotene

Aggregated melaninic background

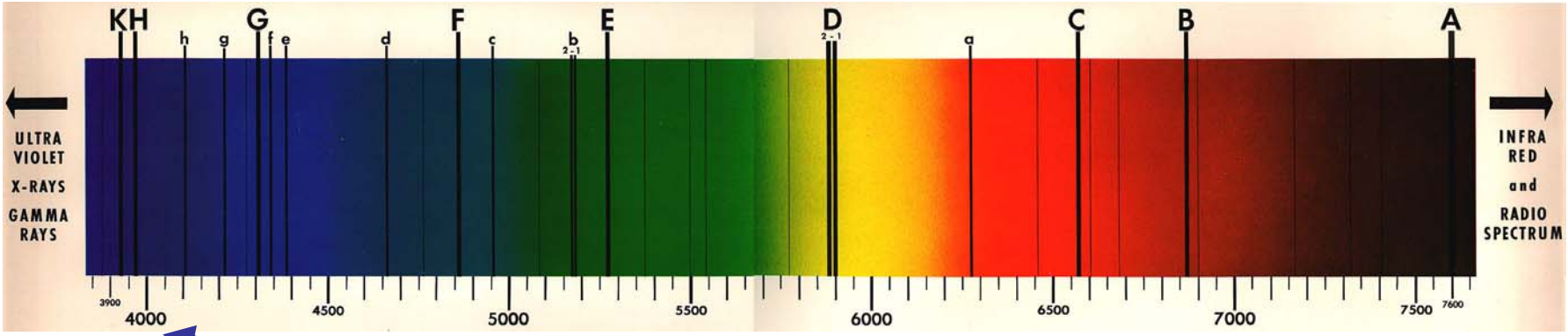
奈米工具

- 1.掃瞄隧道顯微鏡(STM)
- 2. 原子力顯微鏡(AFM)
- 3.電子顯微鏡：
  穿透式（TEM）
  掃瞄穿透式（STEM）
  掃瞄式（SEM）

Nanotechnology is sound. But how do we start…..

To SEE things, we need light which is an electro-magnetic wave. The characteristic property of wave is wave length…

Complete spectrum of sun light

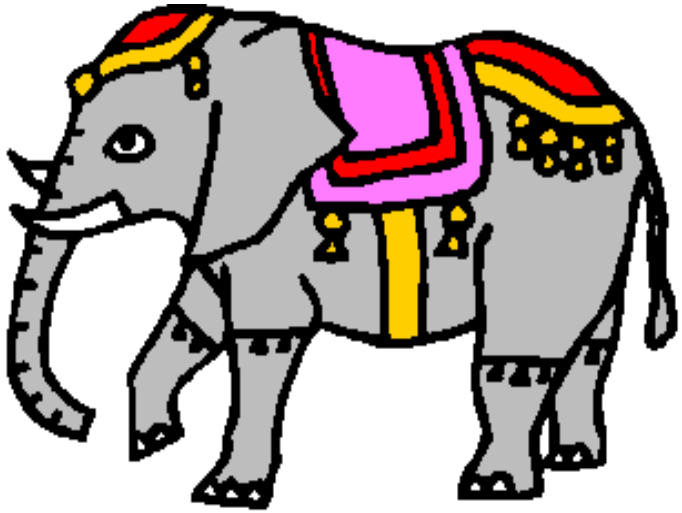


400 nm

Objects smaller than 400 nm is “invisible”!

In nano-world everybody is blind. We can only FEEL…

Ray Charles



the elephant was like a branch of a tree.

elephant was like a snake or a rope.

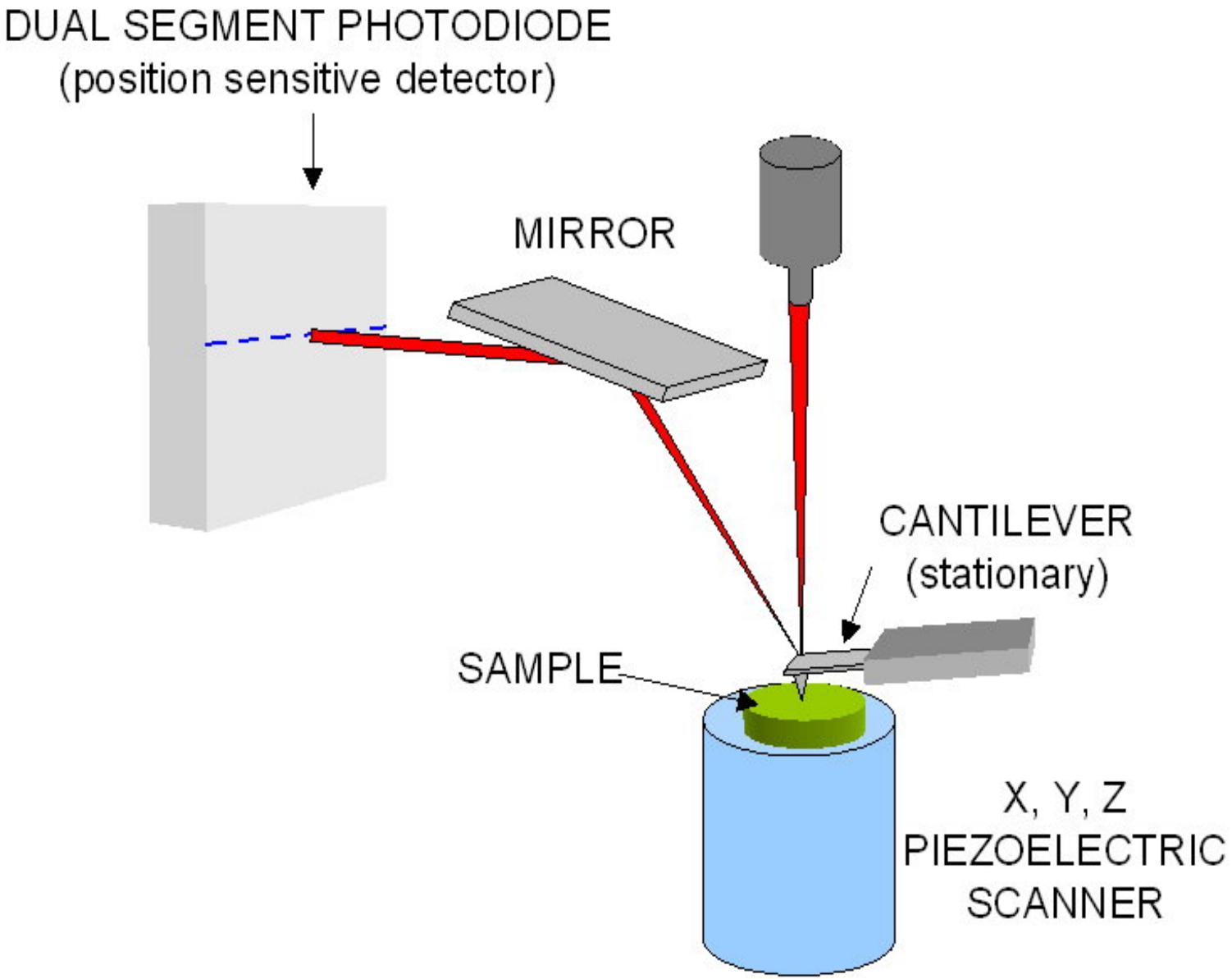
the elephant was like a pillar.

the elephant was a huge fan.

the elephant was like a wall.

AFM (Atomic Force Microscope)
A “Feeling Instrument”…

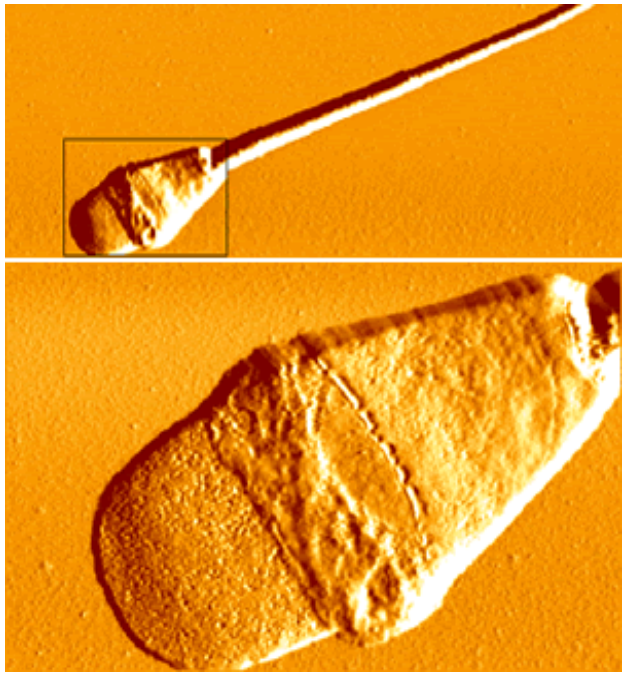
The first of the SPM techniques was the Scanning Tunneling Microscope (STM), developed by Binnig & Rohrer, which got them the Nobel prize for Physics in 1986.

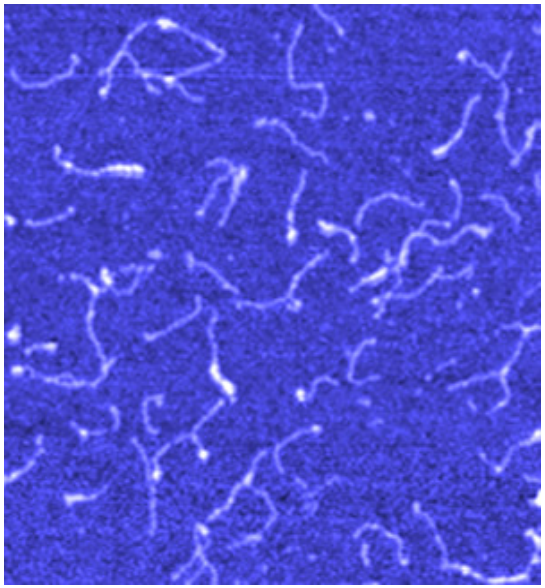

DUAL SEGMENT PHOTODIODE
(position sensitive detector)
MIRROR
CANTILEVER
(stationary)
SAMPLE
X, Y, Z
PIEZOELECTRIC
SCANNER

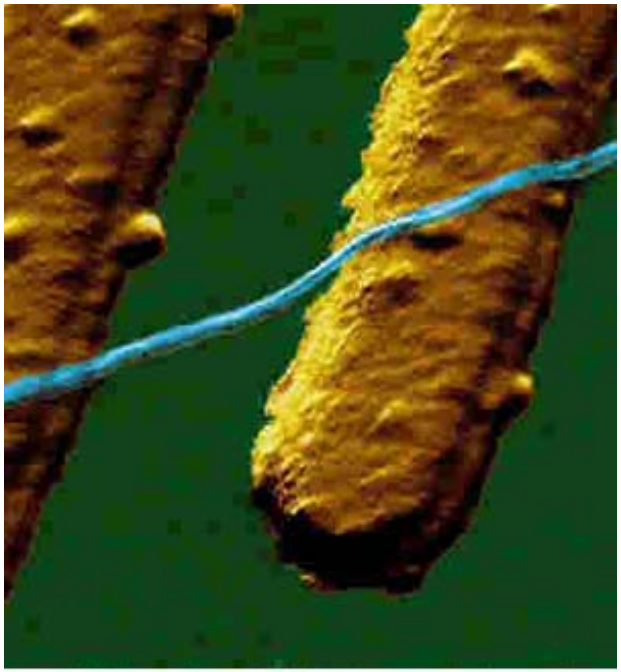
MORE 1

MORE 2

Images from Atomic Force Microscope







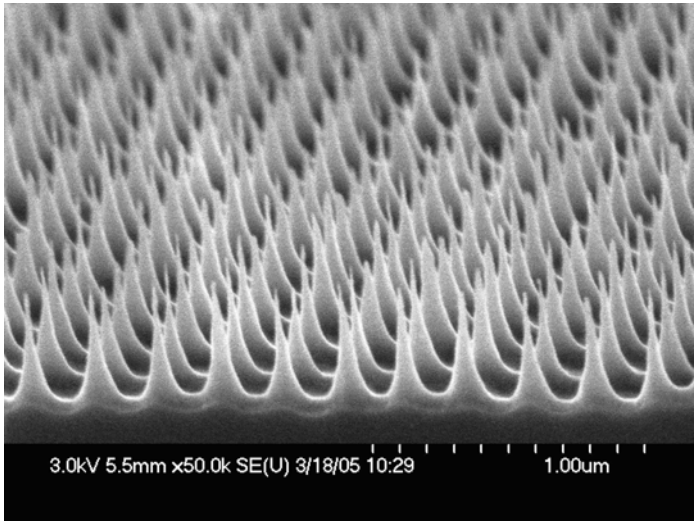
AFM image of an individual carbon nanotube between Pt electrodes spaced by 50 nm. Tans et al., *Nature* **386** (1997) 474.

電子顯微鏡：穿透式（**TEM**）
掃瞄穿透式（**STEM**）掃瞄式（**SEM**）

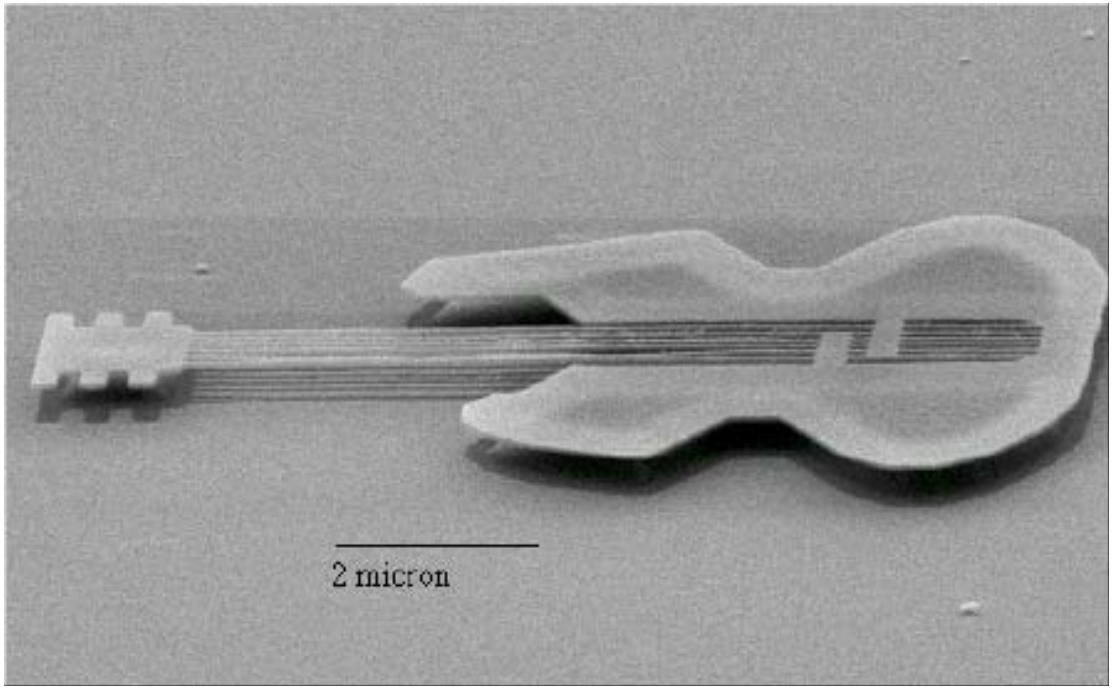
TEM

STEM

SEM

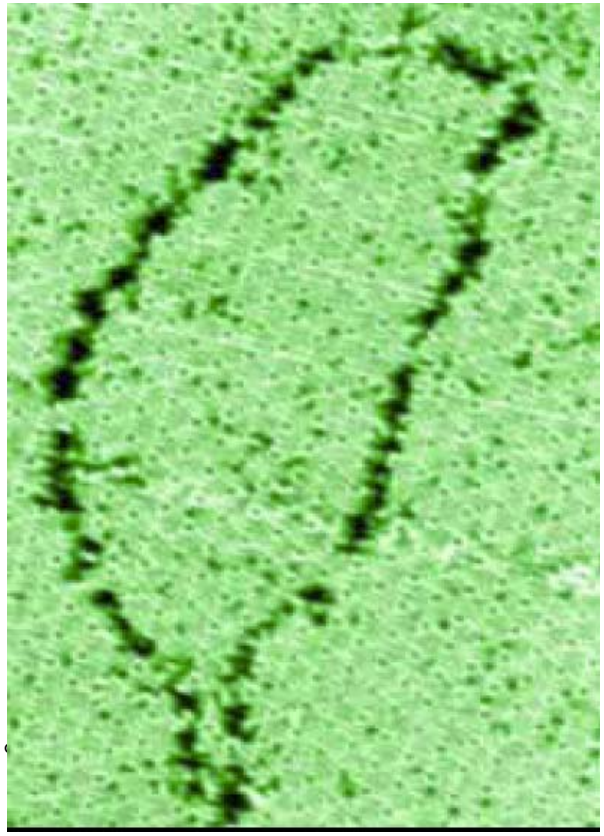


奈米吉他



世界上最小的吉他，全長10μm。含六根絃，每根50nm寬。

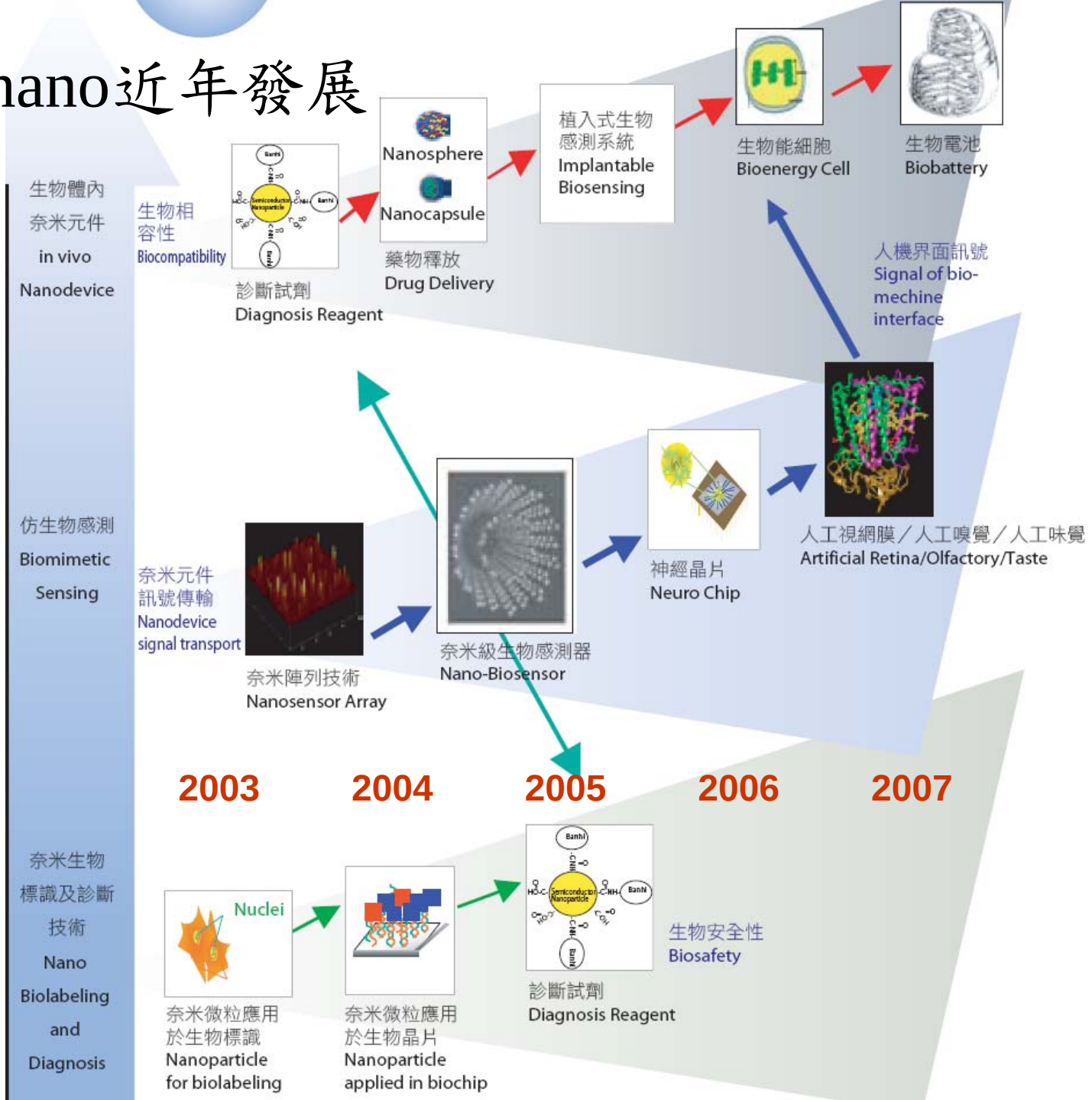
奈米臺灣



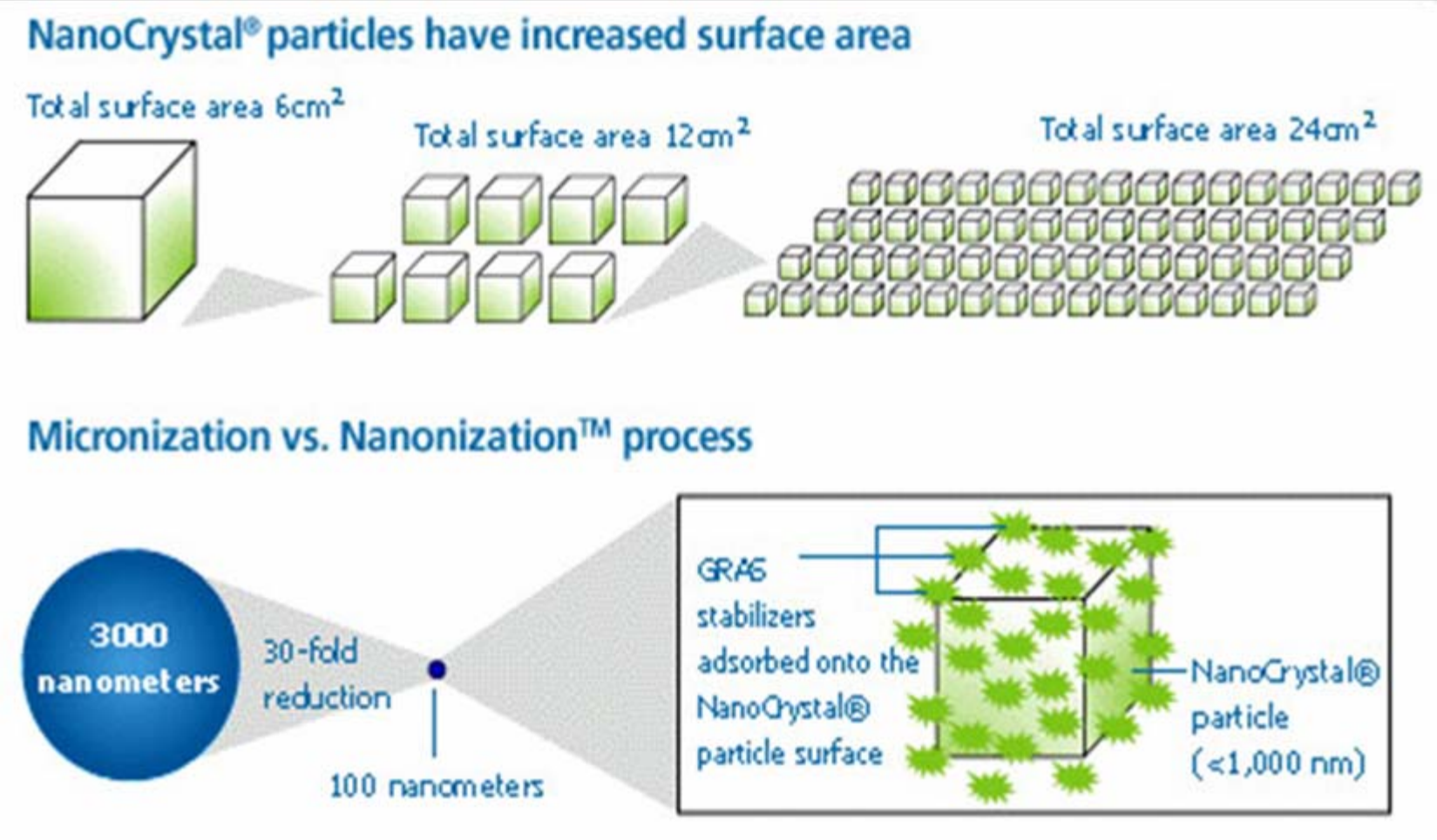
70x 100nm

奈米醫學

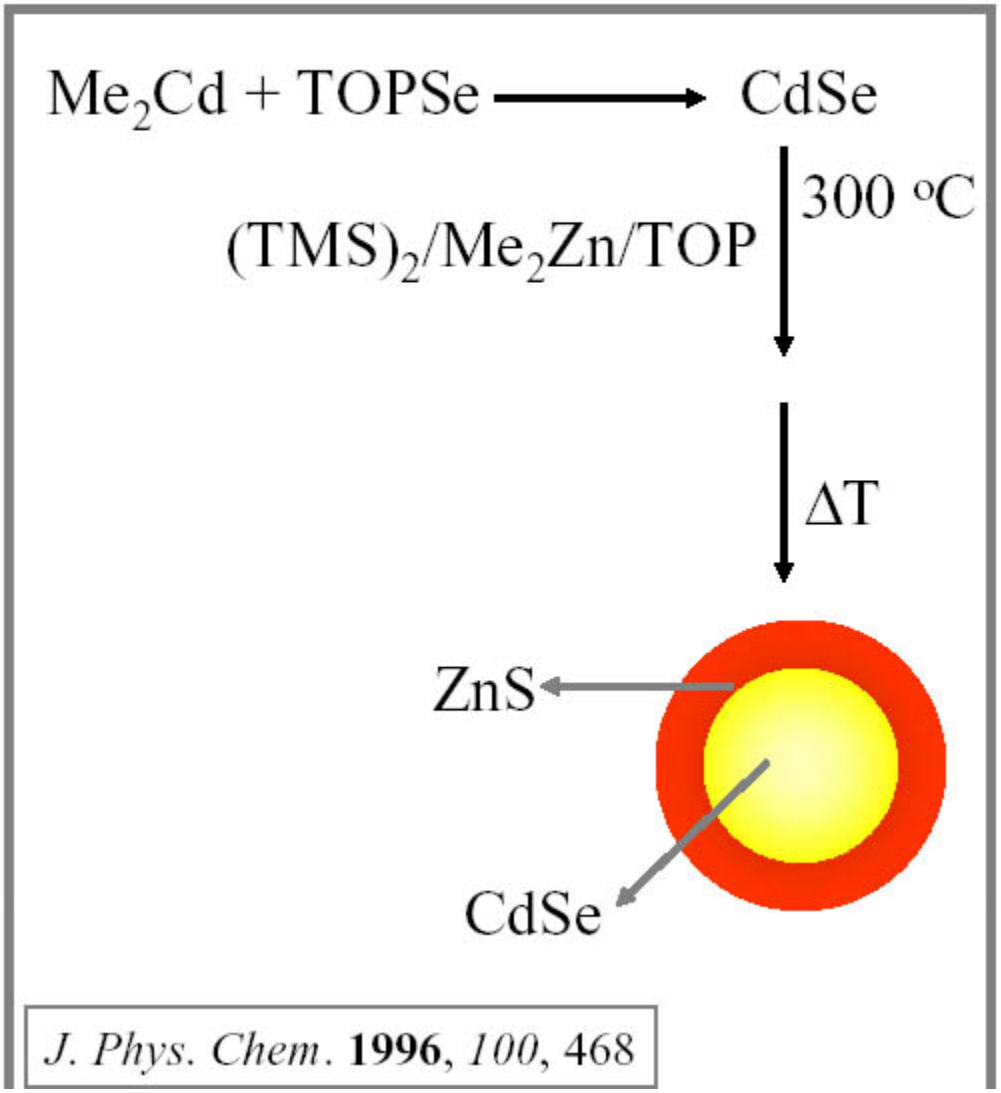
Bio nano近年發展



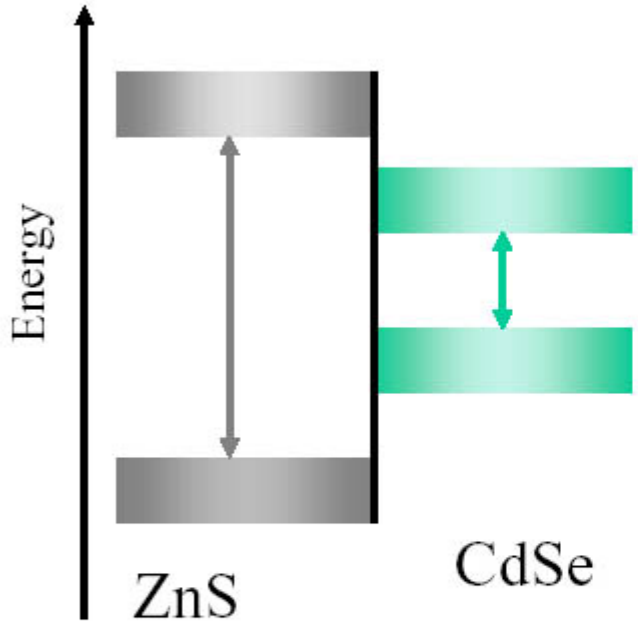
奈米化→表面效應
量子效應

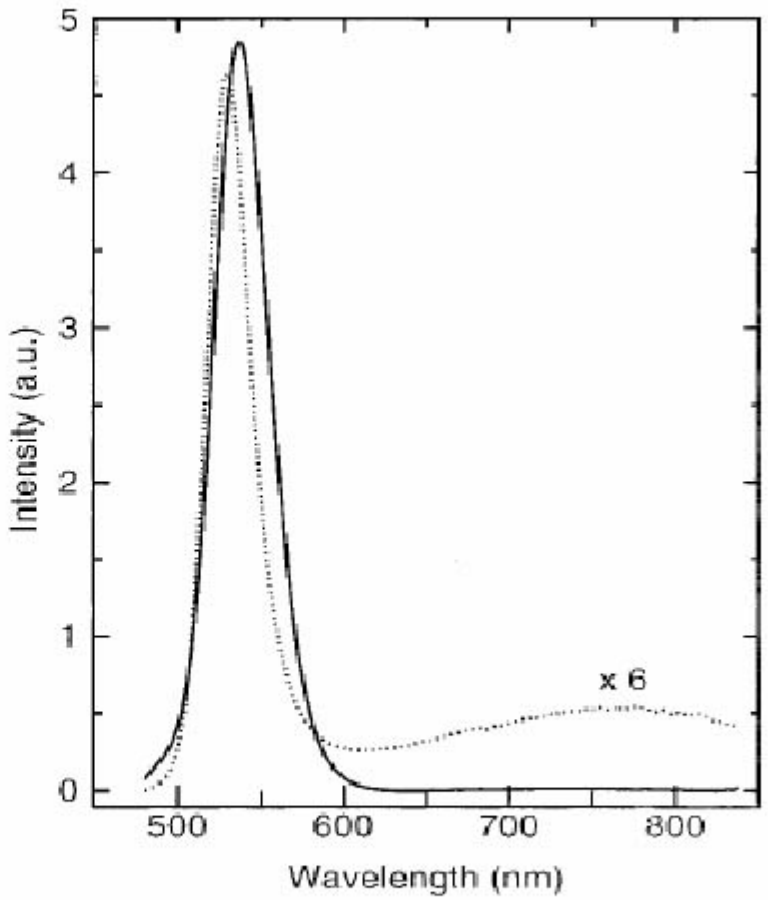


Synthesis of ZnS-Capped CdSe QDs



ZnS-Capped CdSe QDs



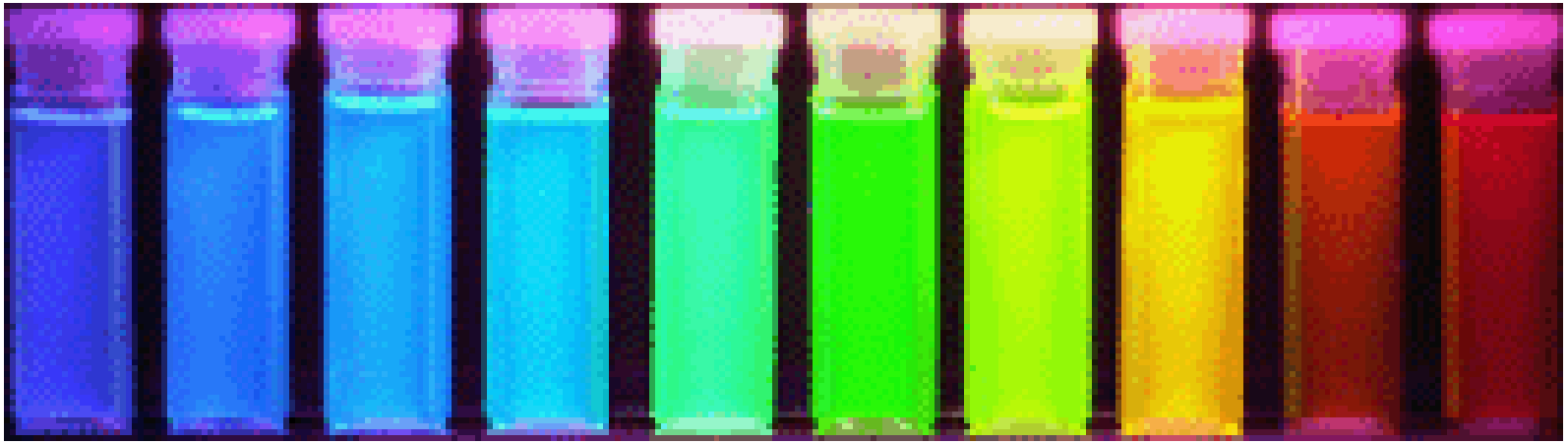


Normalized fluorescence spectra of CdSe-TOPO (dotted line) and CdSe@ZnS (solid line) with 470 nm excitation

J. Phys. Chem. **1996**, *100*, 468

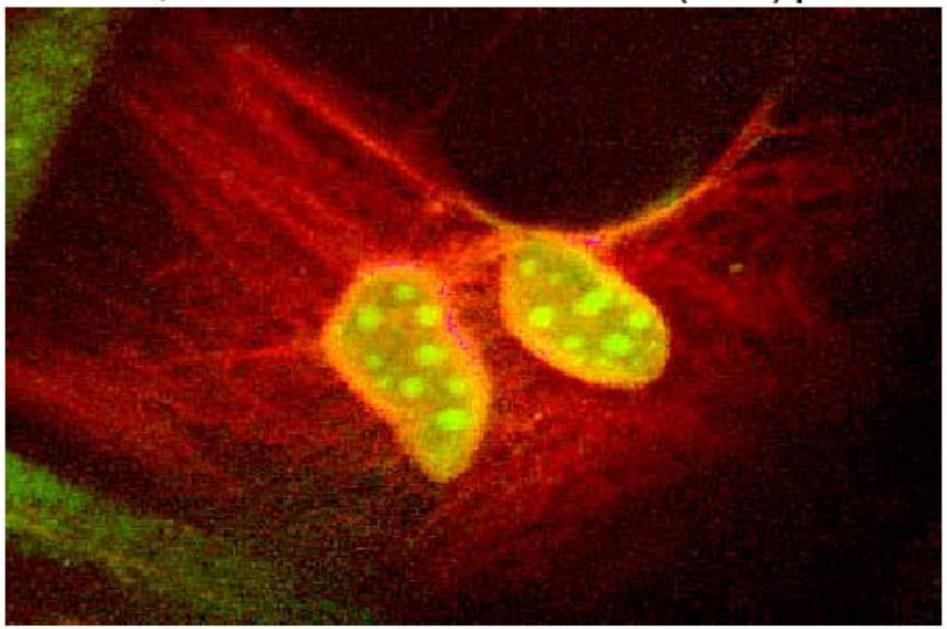
Nanoparticles

- 奈米粒子的價電子經由照光激發至能量狀態較高的傳導帶之後，會自發性地將能量釋放回到較穩定的價帶，而這能量釋放的途徑是以光的型式進行。因為粒徑的不同而造成奈米粒子具有不同的能隙大小。相對地，其放光的波長亦會因為粒徑的增大，而釋放出波長較長的光。



Engineered Nanostructures and Cells

Bruchez, Alivisatos et al Science 281 (1998) p. 2013



10 nm particles, inside cell

- **Receptor mediated endocytosis**
  - o d > 100 nm colloids don't
  - o d < 50 nm do
- **High reactivity of nanoparticle surfaces**
  - o Strong oxidizing/reducing agents
  - o Free radical activity

奈米無敵?

- 美國自然保育委員會（The Natural Resources Defense Council）提到，對於奈米產品以及生產的製造商，其所可能產生的潛在健康以及環境威脅，我們所瞭解的並不多。

都是奈米產品 超過350種

伍德羅威爾遜中心新興奈米科技計畫的首席科學顧問梅納（Andrew Maynard），2006/11/15在《Nature》期刊上刊出奈米科技所產生的一些風險。

毒藥非“毒”

- 追溯到遠古神農時代，《淮南子·修務訓》中這樣記載：「神農……嘗百草之滋味，水泉之甘苦，令民知所避就。當此之時，一日而遇七十二毒。」由此，古代把所有治病的藥物泛稱「毒藥」。

毒藥非“毒”

- 要有療效, 一定是毒藥
- 無毒:中醫本草中的上品藥 人蔘, 黃耆, 當歸等可久服無害等

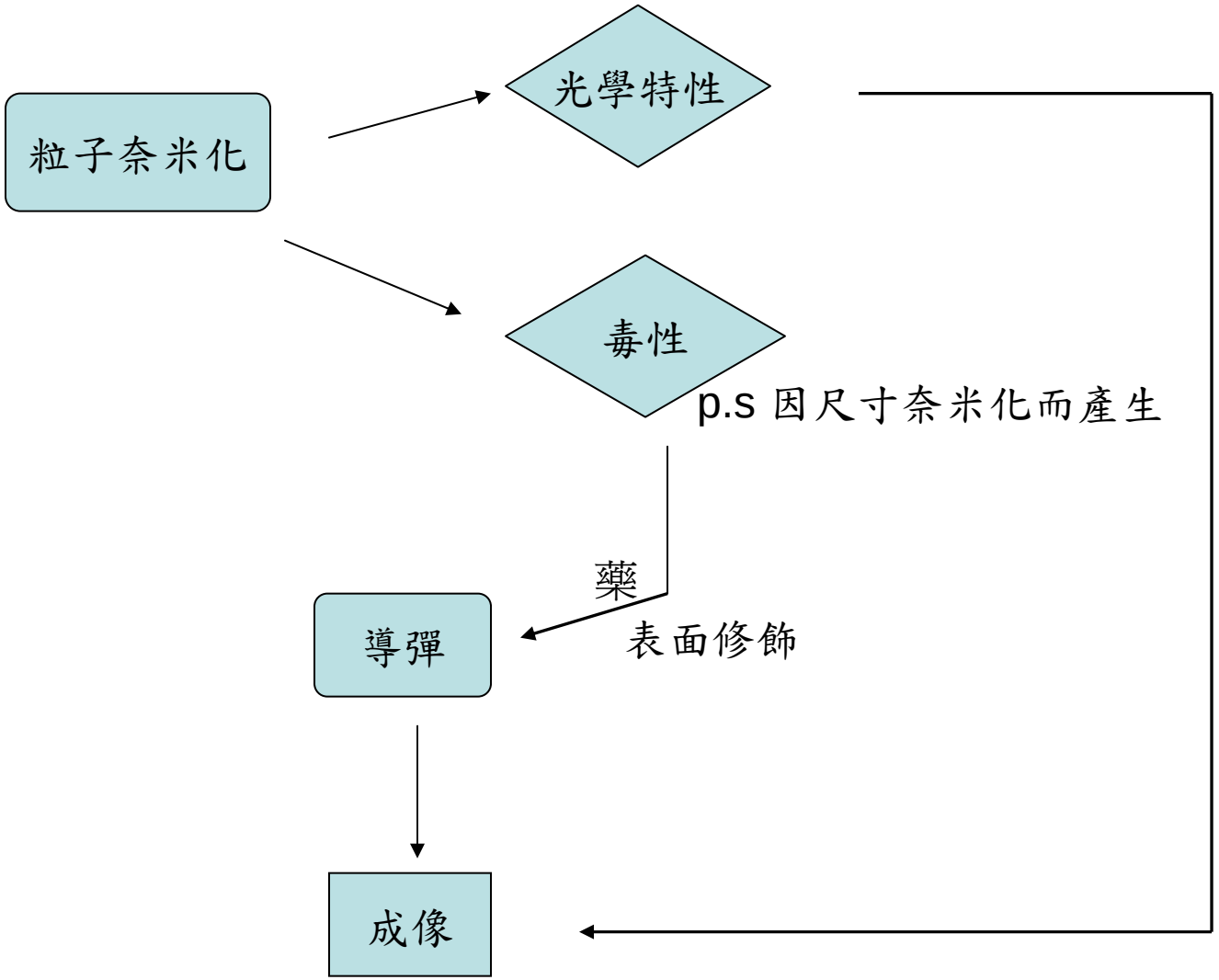
有療效 一定是毒

- 良藥:殺病不傷身
- 一般藥:殺病也傷身
- 毒藥:殺病也殺身
- 終極毒藥:只殺身

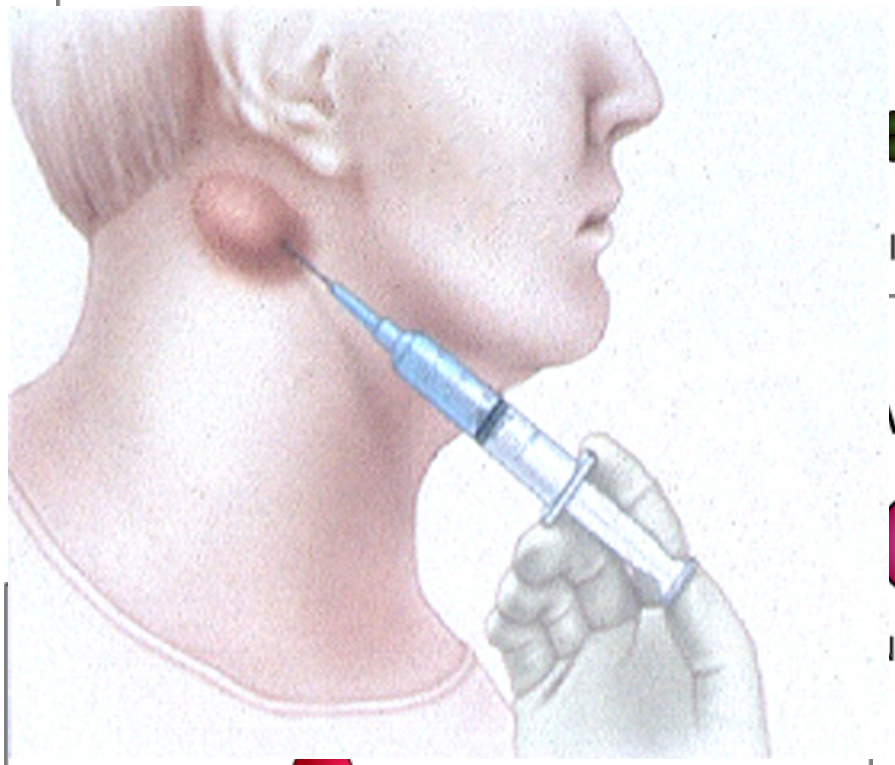
粒子奈米化

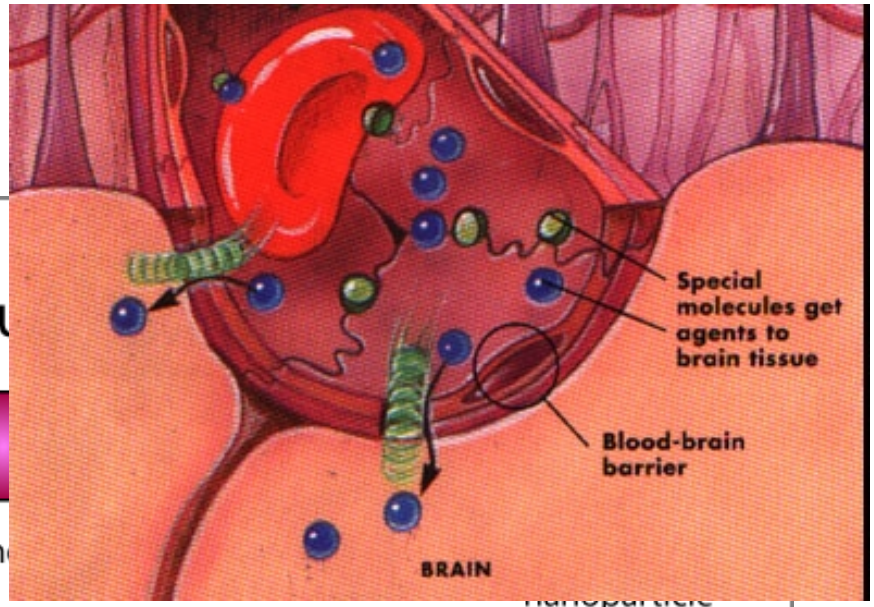
奈米X檔案

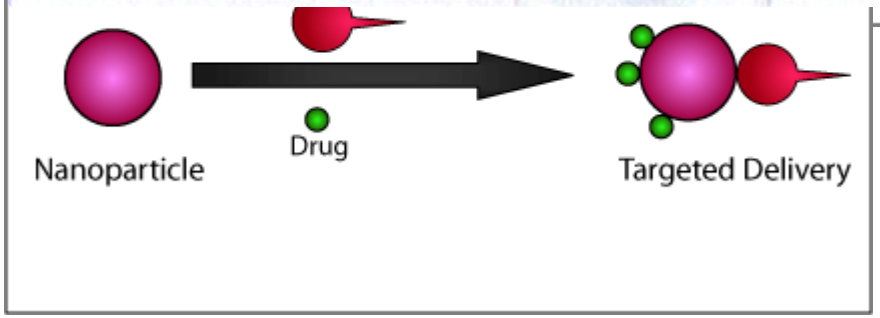
奈米粒子 + γ射線= **X**


粒子奈米化
光學特性
毒性
p.s 因尺寸奈米化而產生
藥
表面修飾
導彈
成像

Drug delivery system

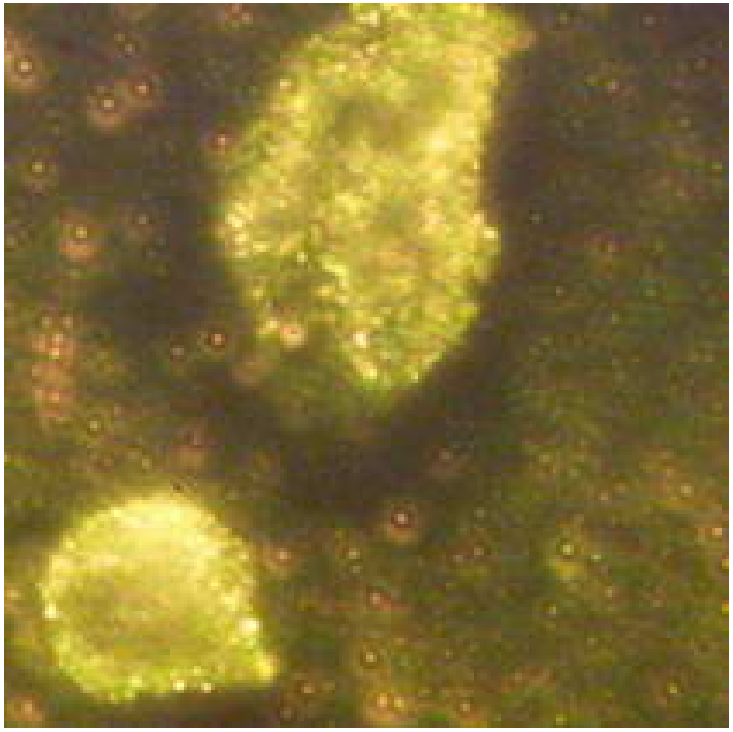






Gold Nanoparticles and Cancer Cell Detection

- Using gold nanoparticles to target EGFR on cancer cells for easy detection



工作原理

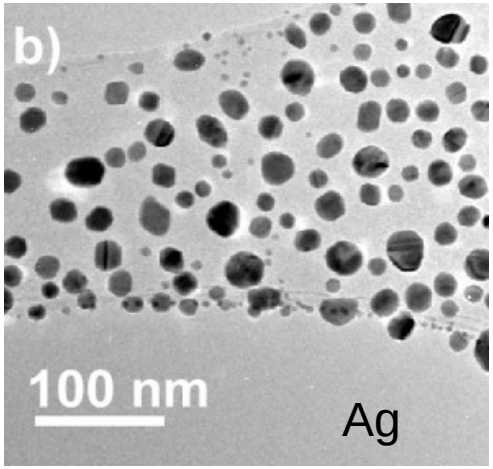
- 癌細胞表面經常背覆一層生長激素的受體蛋白質：Epidermal Growth Factor Receptor (EGFR).
- 正常細胞較少表現表現這個蛋白質.
- 在奈米金表面接上可以認識EGFR的抗體，這個複合體便可以在人體內找到癌細胞並黏貼在癌細胞表面

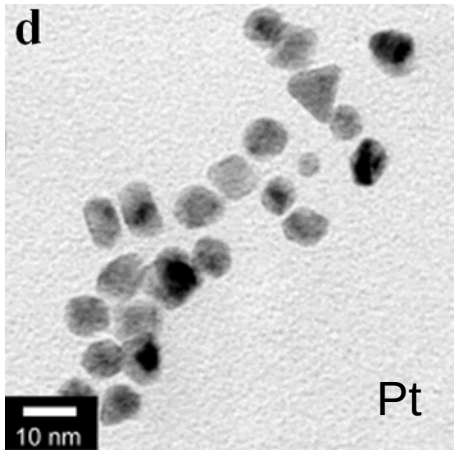
呈像

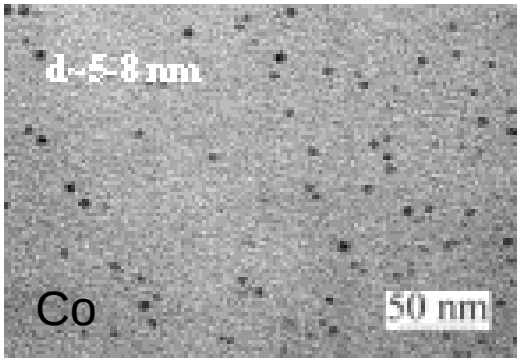
微波治療

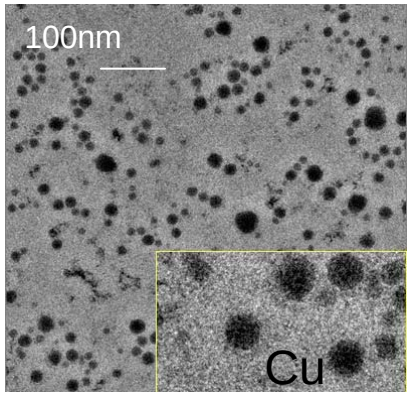
奈米金

Other Metal nanoparticles



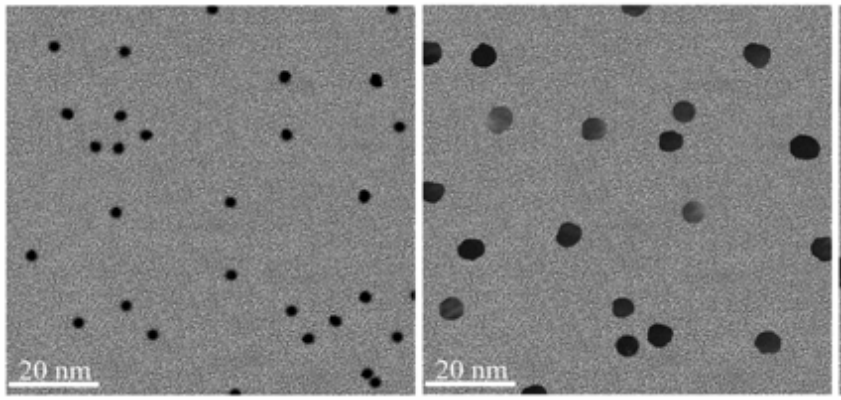


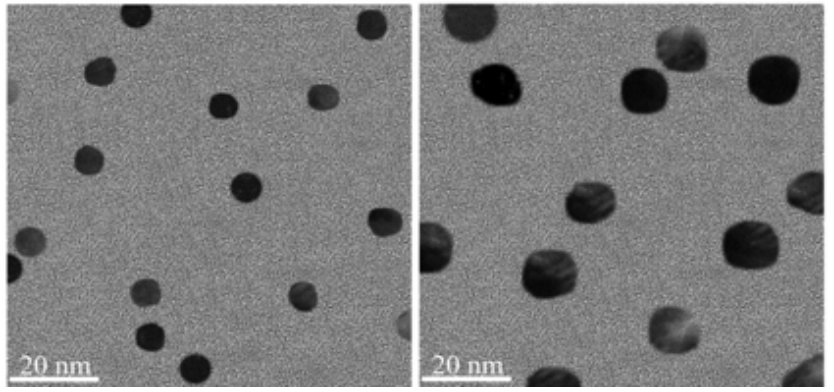




1.粒徑普遍太大
2.粒徑均勻性不足
3.生物相容性不良

Gold nanoparticles

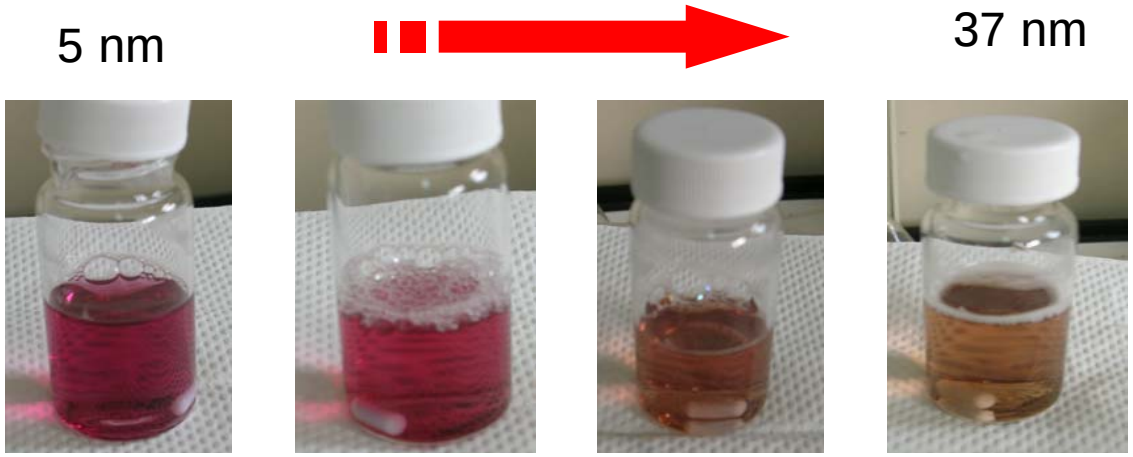




1.2-100 nm皆可合成
2.可控制大小均勻度佳
3.生物相容性好

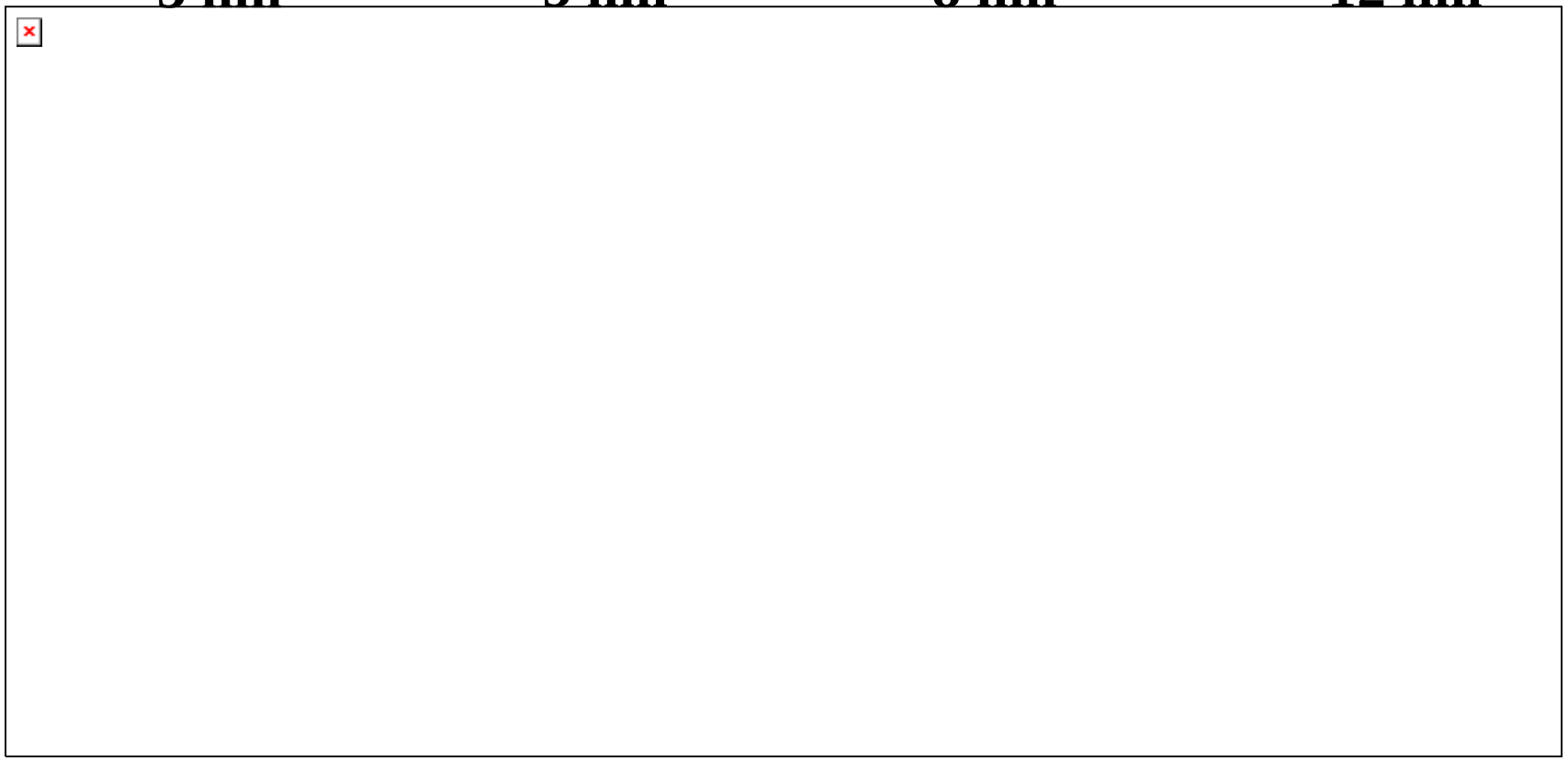
Gold Nanoparticle

- $HAuCl_4 \cdot 3H_2O$
- Trisodium citrate
- Ascobic acid ， $NaBH_4$
- Cetyltrimethylamonium bromide (CTAB)



Gold Nanoparticle

3 nm 5 nm 8 nm 12 nm



17 nm 37 nm 50 nm 100 nm

TEM(穿遂式電子顯微鏡)

奈米金粒子毒性

- 生物相容性最好的金屬 :金(Gold)
- Gold Nanoparticles

奈米表面

奈米生物材料

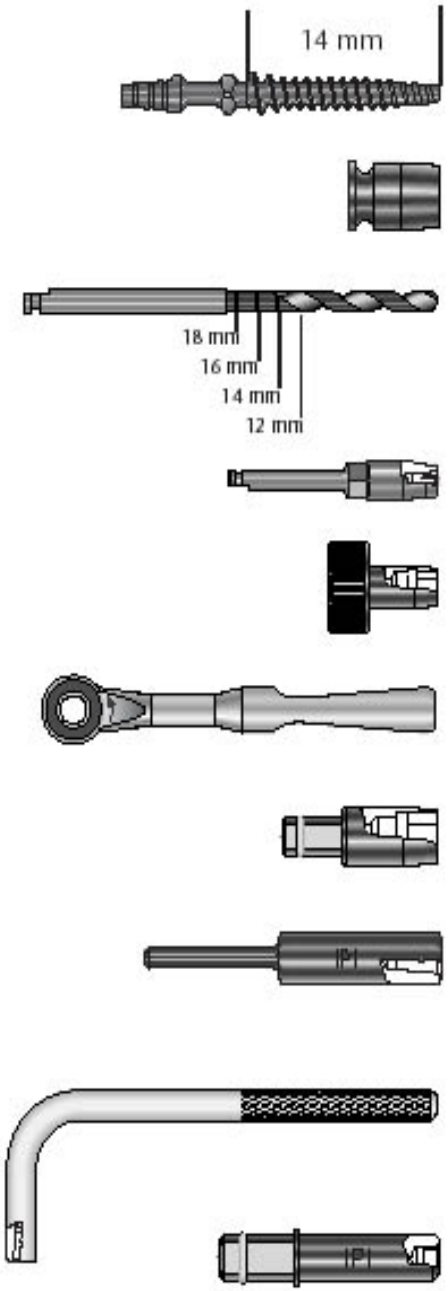
- 適合於生物體內應用的奈米材料，易於被生物體接受，且不引起不良反應，這類奈米生物材料主要有

  高分子奈米微粒

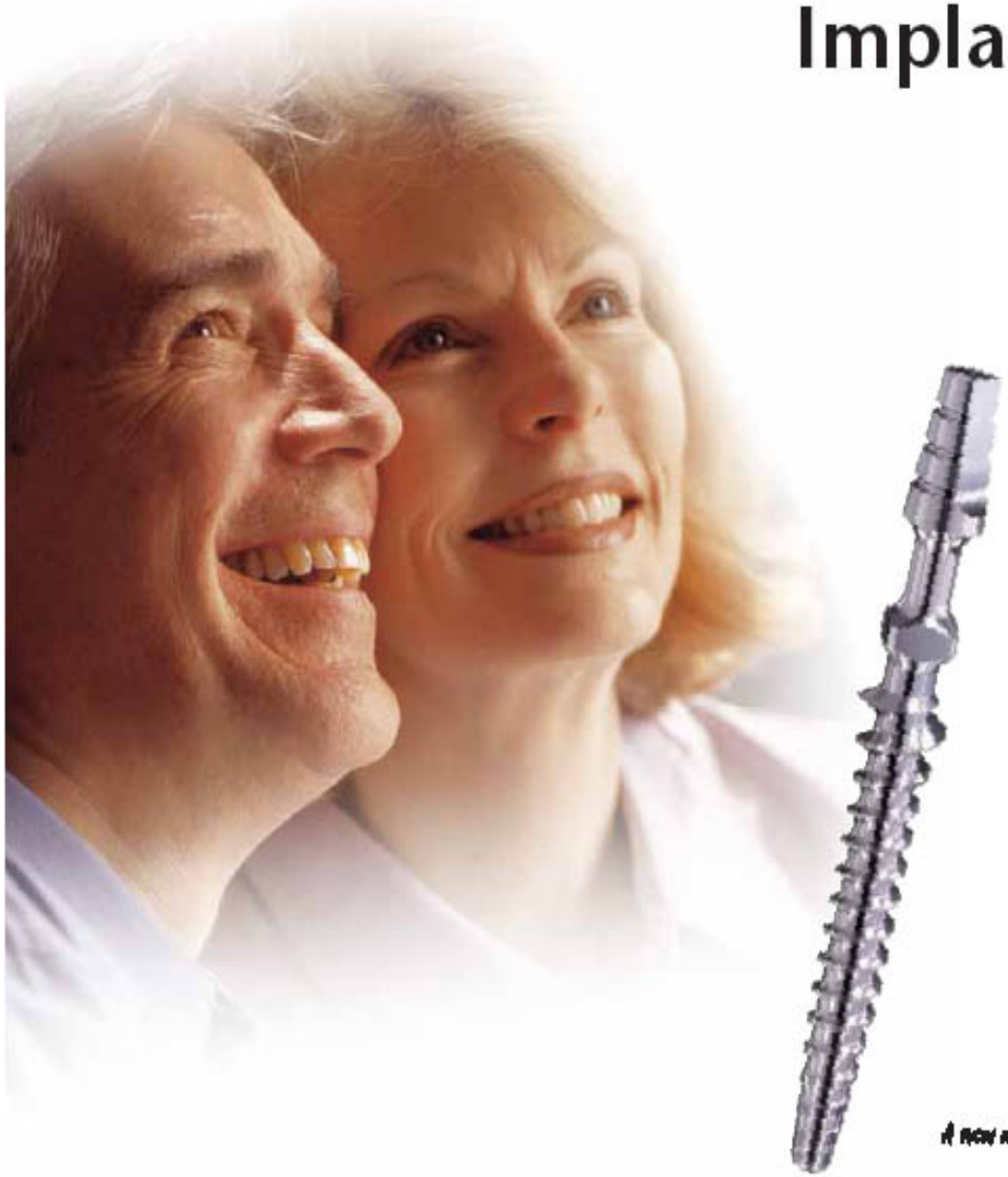
  無機奈米微粒

  奈米結構生物材料等等

- 植牙


14 mm
18 mm
16 mm
14 mm
12 mm

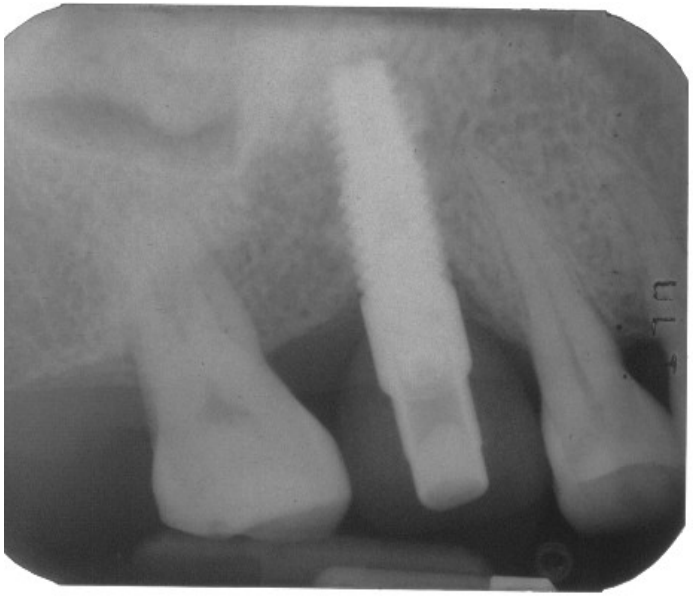
Immediate Provisional Implant



NICAL PROCEDURE & PRODUCT CATALOG

C-B-I Nobel Biocare

A new way to think...and act!



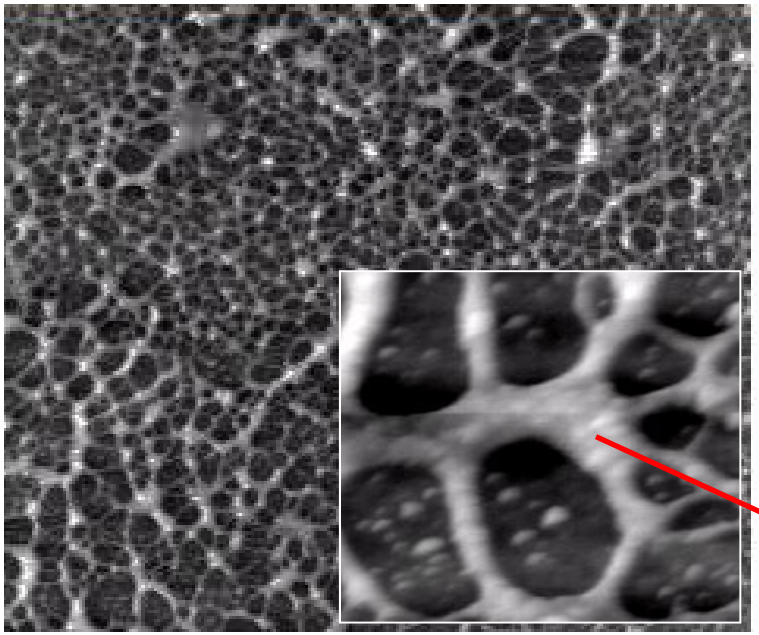
表面奈米化 → 人工植體

EX:人工植牙, 關節, 心臟支架

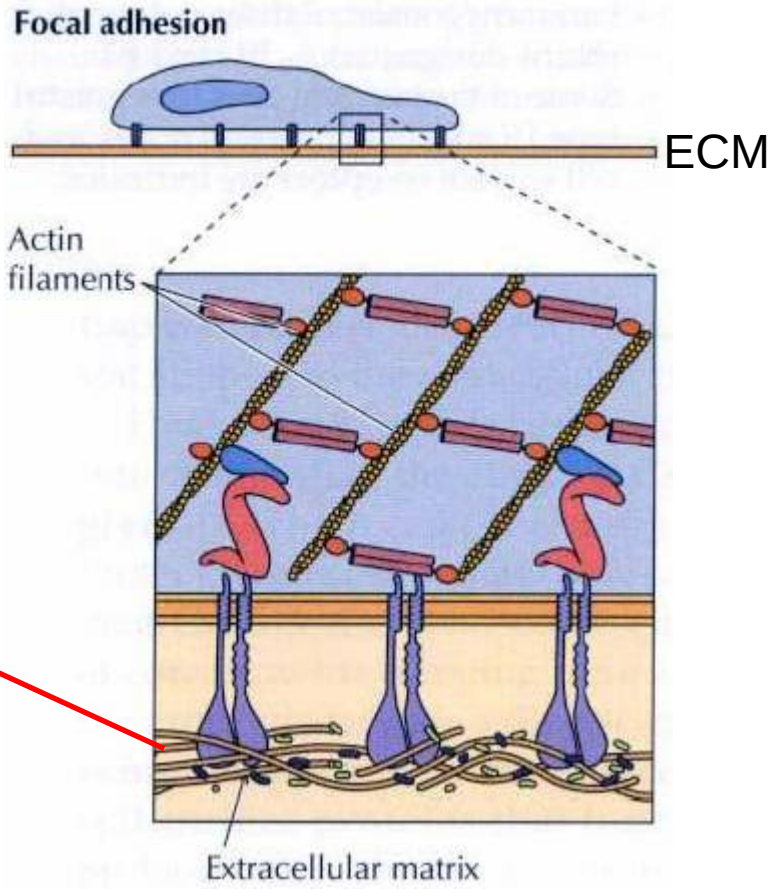
奈米化表面 → 控制細胞 → 成長移動

Cellular attachment & Extracellular matrix(ECM)

細胞外基質 (ECM)



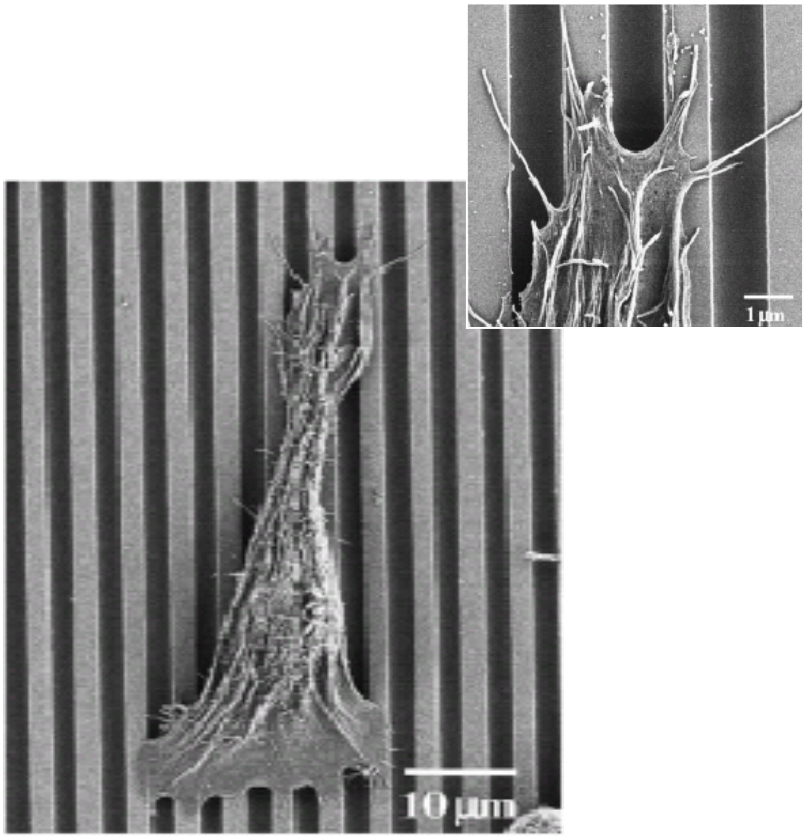
5 x 5 um



微結構表面應用於細胞生長與分化

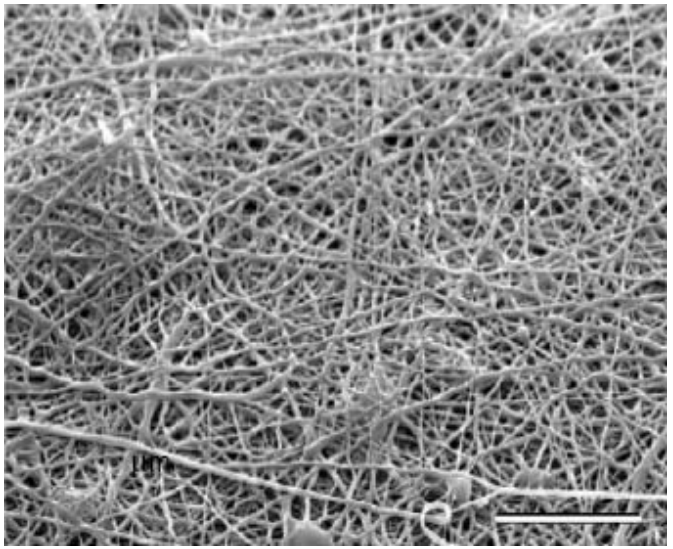
半導體製程

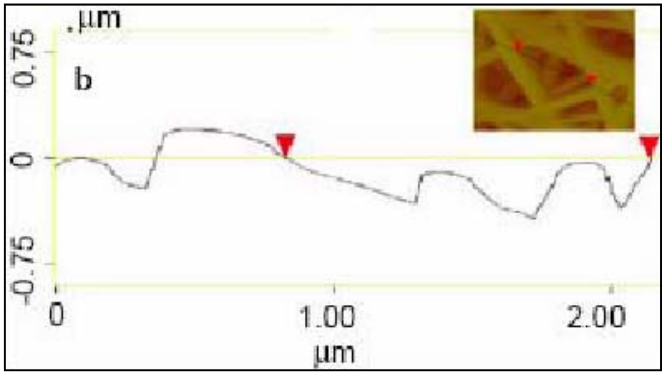
pattern of nanoscale



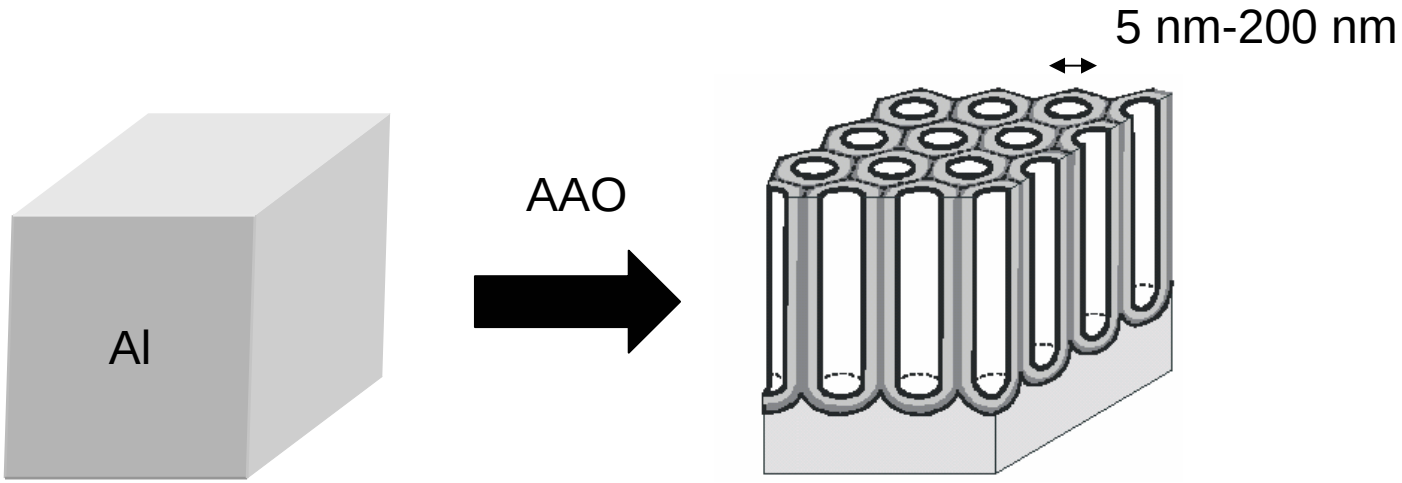
化學聚合製程

nanofibers (polymer)



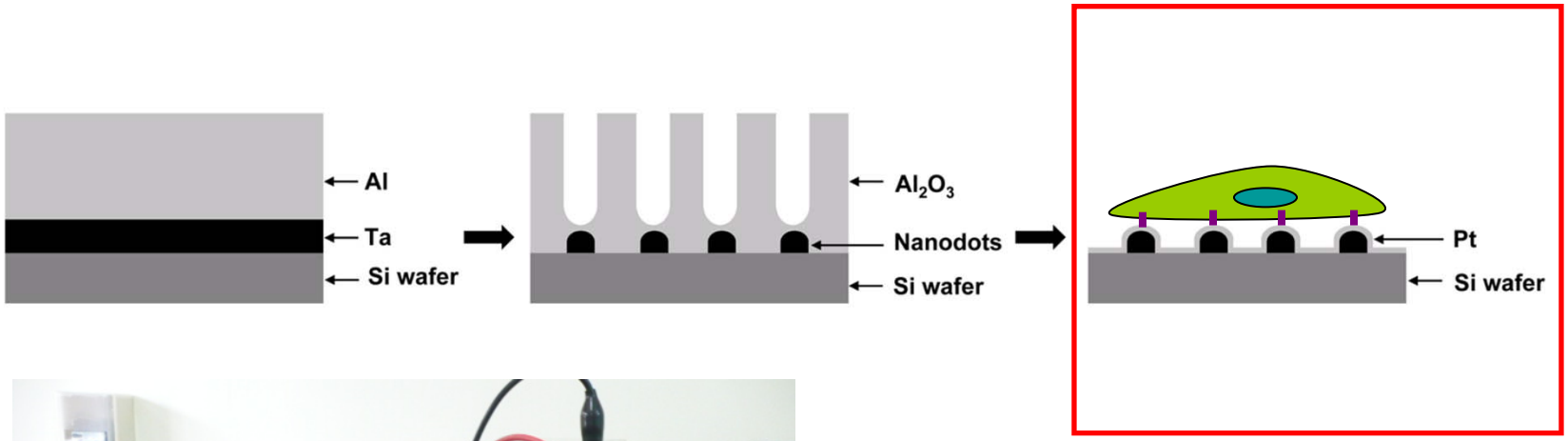


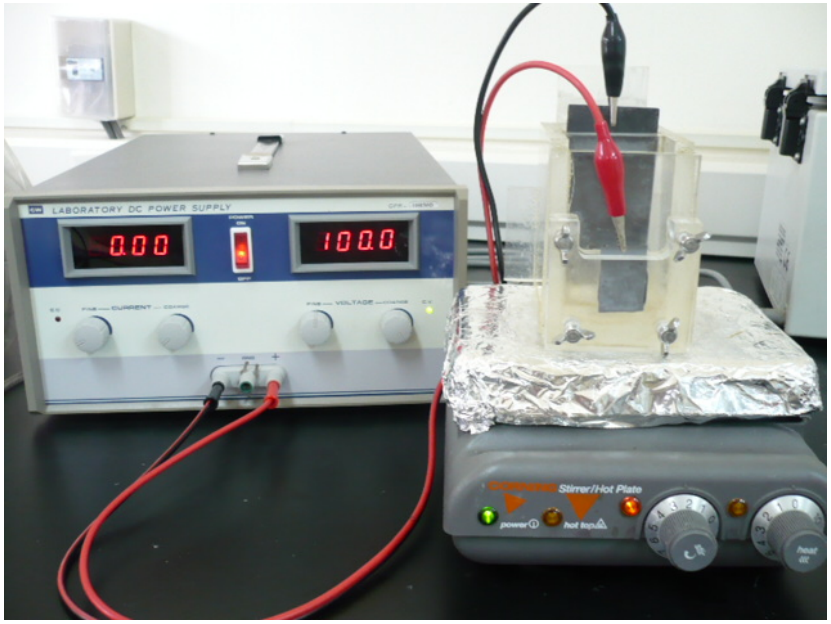
AAO流程圖



Anodic Aluminum Oxide (AAO)

陽極氧化鋁



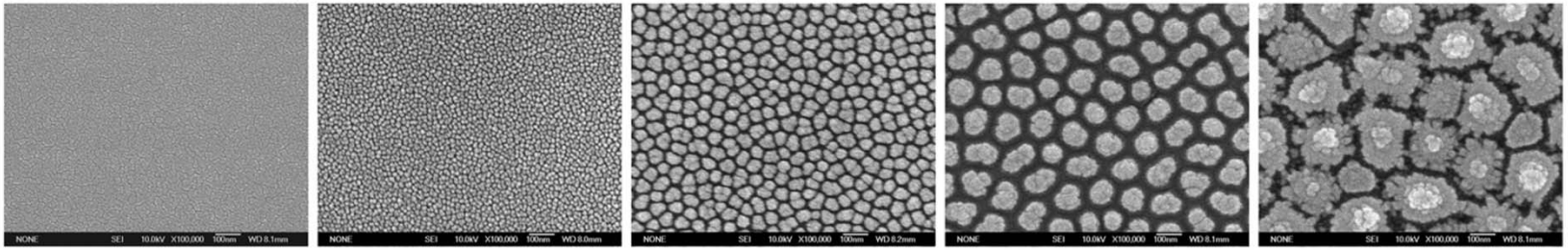


$2H^+ + 2e^- \rightarrow H2\uparrow$ (陰極)

$Al \rightarrow Al^{3+} + 3e^-$ (陽極)

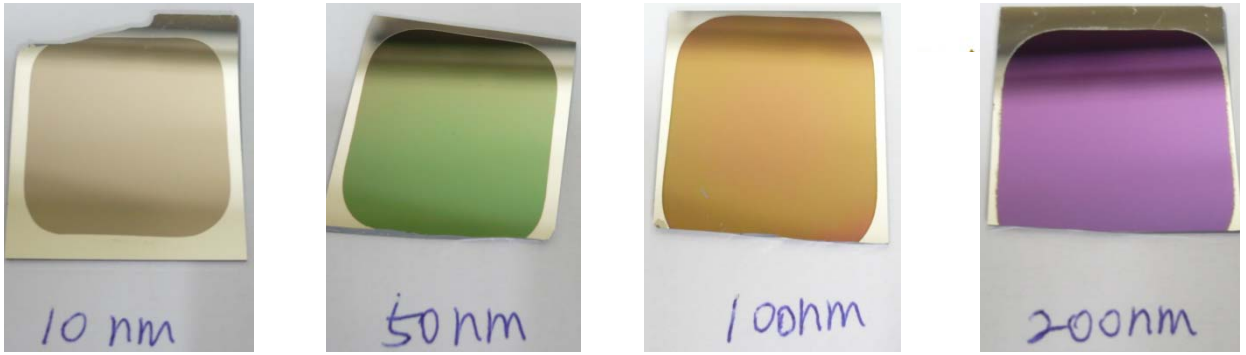
$2Al^{3+} + 3O^{2-} \rightarrow Al_2O_3$

各尺寸奈米點細胞培養表面 (SEM)

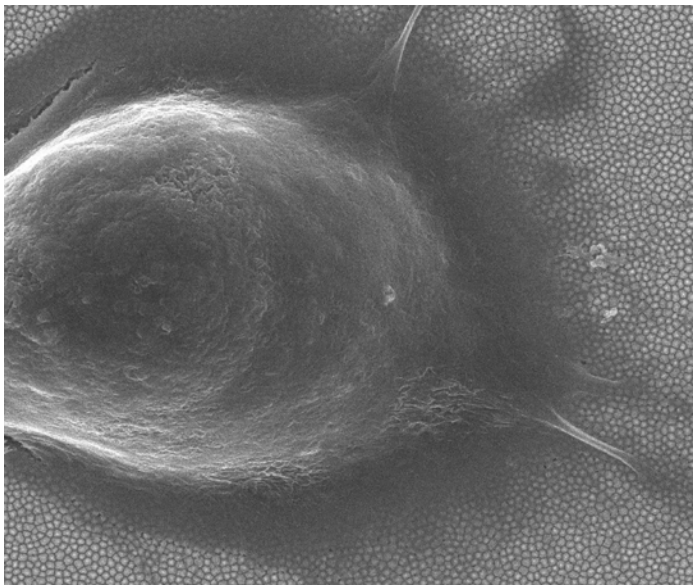


flat　10nm　50nm　100nm　200nm

100nm

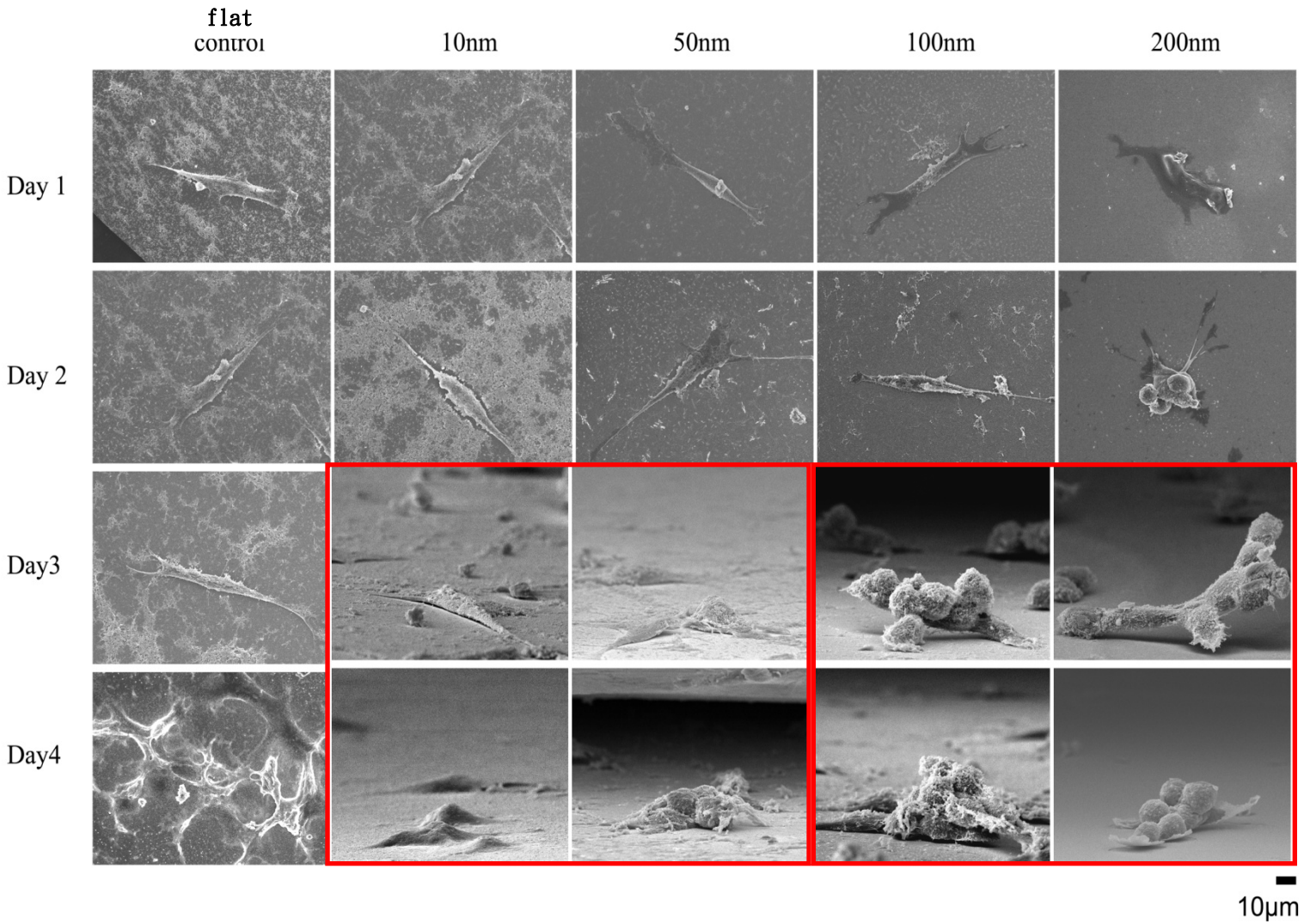


3T3 Fibroblast



- 貼附型細胞
- 與上皮、內皮細胞相似之纖維母細胞

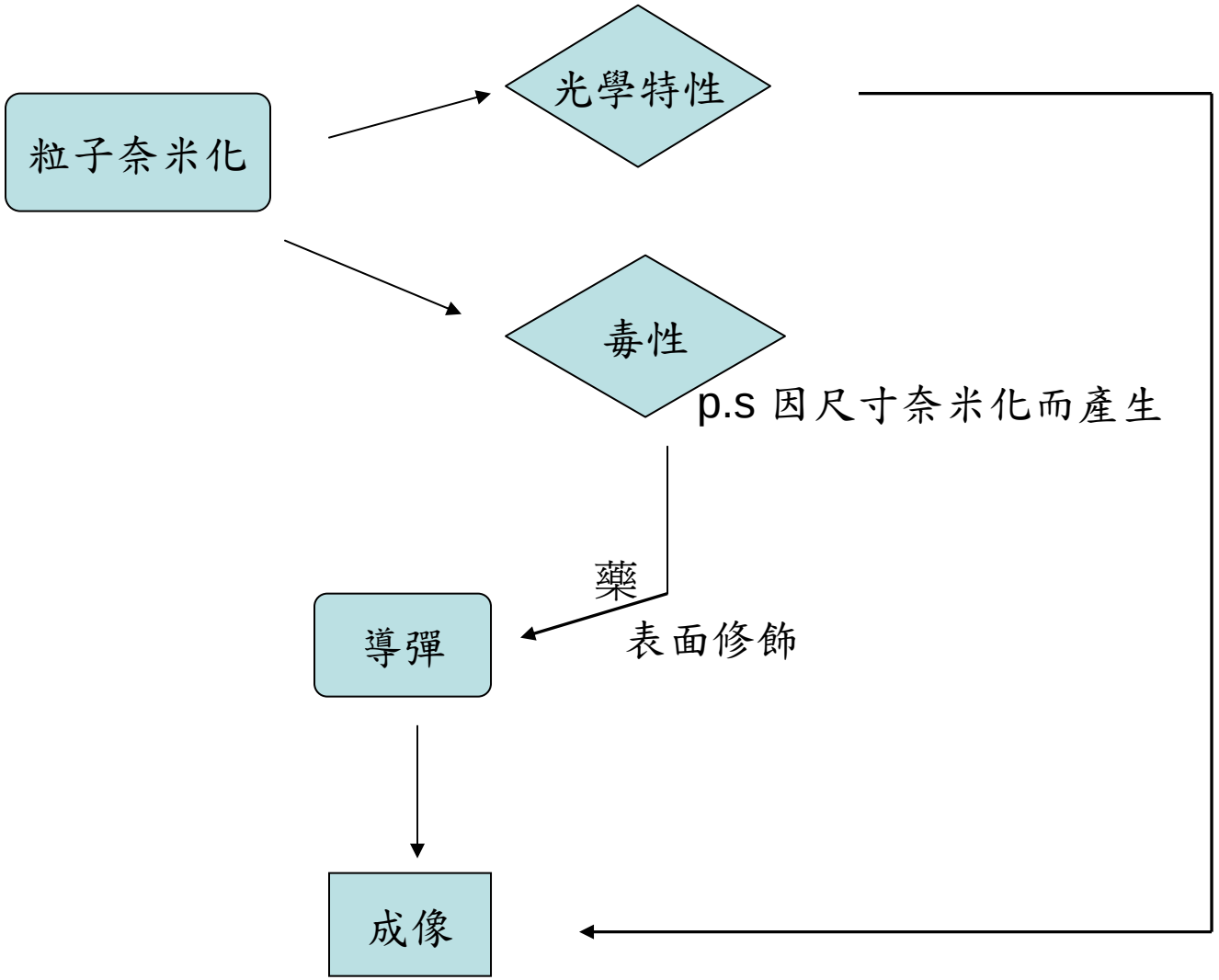
奈米表面對細胞貼附性之影響 (SEM)



Cellular response to Nano-surface

1.50 nm 以上奈米點表面可以造成細胞自然凋亡

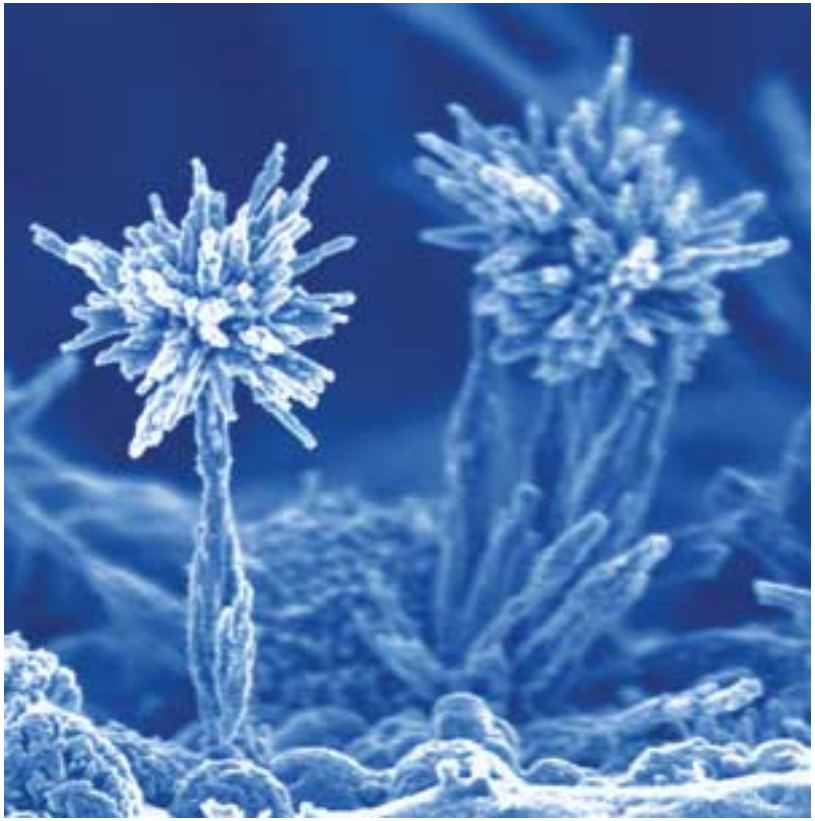
2.藉由操控奈米表面尺寸將可控制細胞的生長


粒子奈米化
光學特性
毒性
p.s 因尺寸奈米化而產生
藥
表面修飾
導彈
成像

總結

奈米醫學

未來的醫學



致謝

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- 交通大學應用化學系
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  葉孝蔚 博士(生物TEM成像)

國科會與農委會計畫補助

Thank you for your attention