聯合縮小軍－奈米材料在生醫上的應用

牟 中 原

國立臺灣大學化學系

97年 3月 2日

National Taiwan University

奈米科技

A World in a Word

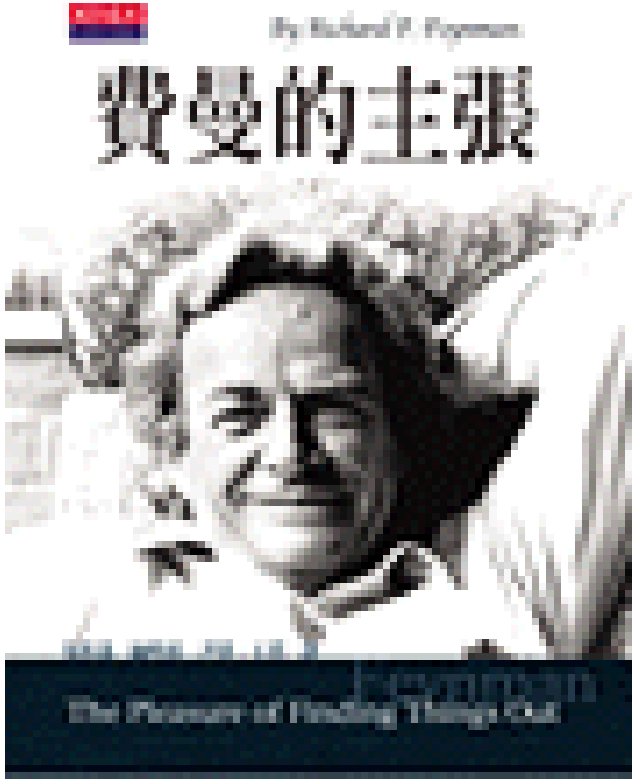
Make It Small !
Make It Small !
Make It Small !
Make It Small !
Make It Small !
Make It Small !
Make It Small !
Make It Small !
Make It Small !
Make It Small !
Make It Small !
Make It Small !

FEYMANFEYMAN FEYMANFEYMAN
FEYMANFEYMAN FEYMANFEYMAN
FEYMANFEYMAN FEYMANFEYMAN
FEYMANFEYMAN FEYMANFEYMAN
FEYMANFEYMAN FEYMANFEYMAN
FEYMANFEYMAN FEYMANFEYMAN

奈米有多小?
nm

- 10^{-9}米**(m)**
- O.000000001米 **(沒感覺)**
- 姚明 身高 =2260000000 nm(還是沒感覺)
- 水分子直徑 = 0.28 nm

There is plenty of room down the bottom (1959)



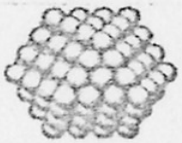
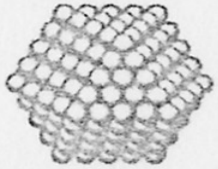
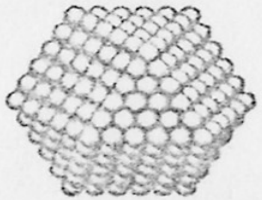
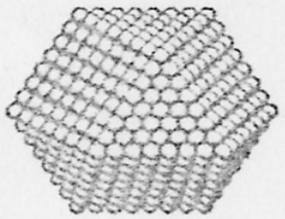
尺寸 與 技術

農業時代(2000 BC)	**cm**	**農具**
工業革命(1750)	**mm**	**機械**
微電子時代(1960)	**μm**	**CMOS**
21世紀	**nm**	**分子**

東西切小 後有甚麼好處?

- 變軟
- 表面/體積比增大
- 顏色改變
- 熔點降低
- 磁性
- 單電子傳導性
- 催化活性

TABLE 2.1 The relation between the total number of atoms in full shell clusters and the percentage of surface atoms

Full-shell Clusters		Total Number of Atoms	Surface Atoms (%)
1 Shell		13	92
2 Shells		55	76
3 Shells		147	63
4 Shells		309	52
5 Shells		561	45
7 Shells		1415	35

奈米光觸媒

TiO_2

鈦白粉

防紫外線

光觸媒

紙填充料

白色顏料

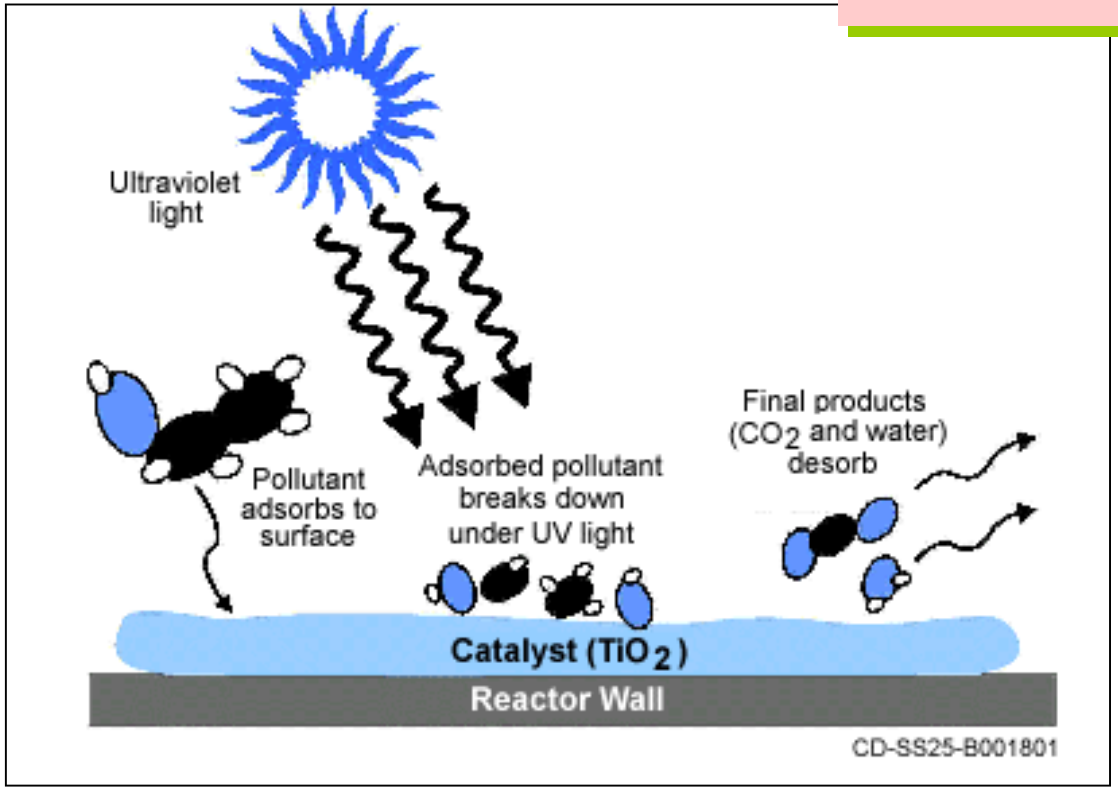
太陽能電池

處理/修補

光催化劑

✸銀/金@二氧化鈦 移除髓中的環境污染物.
✸使用可見太陽光的能量行光化學反應.

George Chumanov, Clemson University



✸生化引出奈米尺寸催化劑
✸在水中或土中的化學降解過程.

Daniel Strongin, Temple U

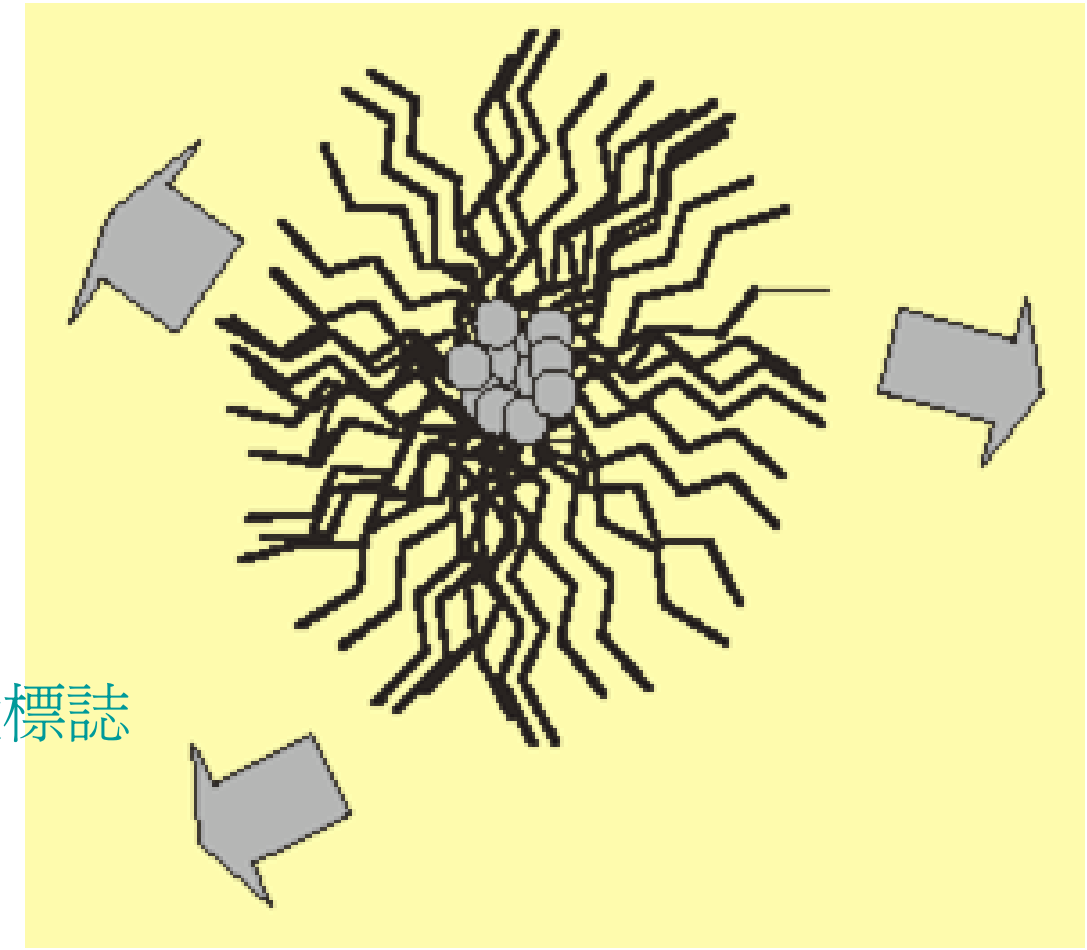

本班已完成
“奈米光觸媒”
抗SARS消毒
使用與總統府同等級

化學:

催化劑

化學感應器

奈米反應器



材料

薄膜

奈米電子元件

濾光器

生物

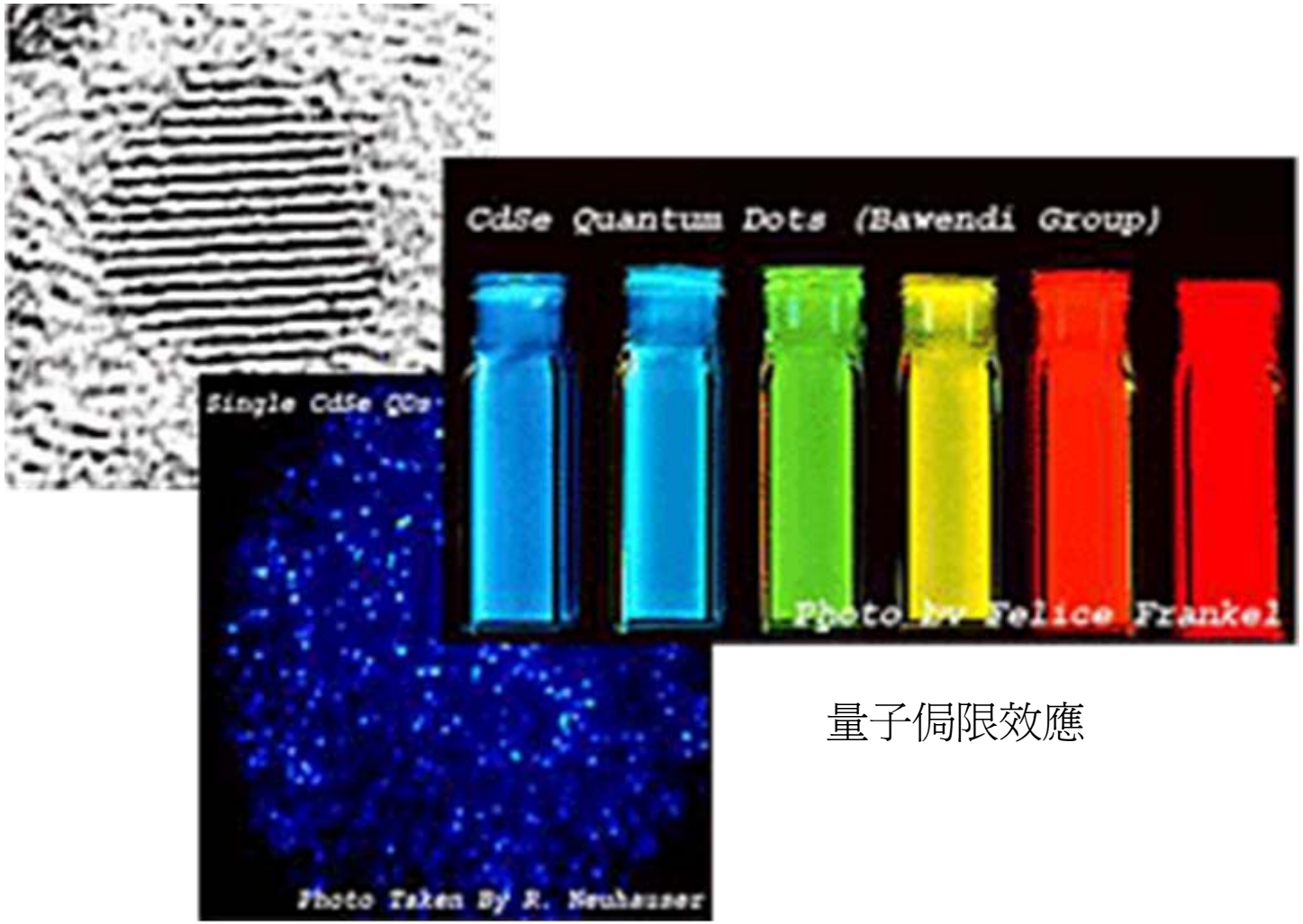
電子顯微鏡標誌

藥物輸送

DNA輸送

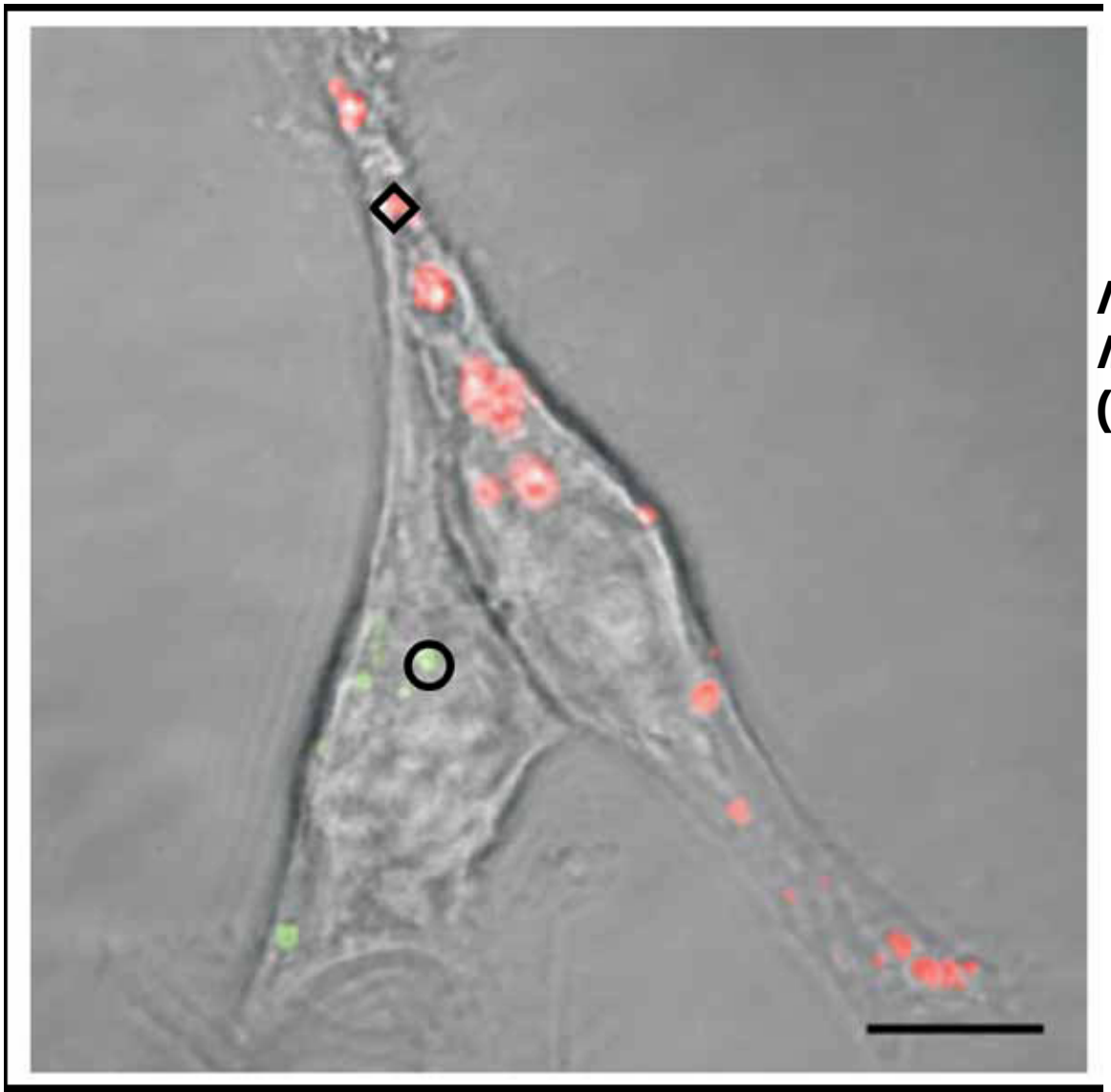
生物感應

介面活性劑保護的硒化鎘量子點



量子侷限效應

追蹤癌細胞轉移



Nature Medicine **10, 993 (2004)**

奈米金

顏 料

催化劑

蛋白質晶片

藥物及DNA輸送

黄金與永恆

小金人

世界杯

金閣寺

法老王

黃金

黃金是一種最早被植入人體的物質，根據中國醫藥學記載『黃金是一種固有成方，是人體最不排斥的物質之一』明朝藥聖李時珍，對黃金做了精闢的解說。

24K金離子可滲透深層肌膚，以強大負離子的吸引力，加速正離子的運行，衝破阻塞的微細血管。

這些年輕的血液循環帶給肌膚大量的氧氣、水分、胺基酸、維他命及礦物質，製造足量新細胞代替老死細胞，同時帶走多餘脂肪、色素、毒物、雜質、廢水及二氧化碳等，如此一來取得健康與平衡，身體毒素亦可即時清除，這是恆久持有無暇肌膚的最佳方法。

金鑽全系列體驗價

NT796

金鑽淨C精華液

NT199

市價 NT1800元 30ml

金鑽保濕潔顏膠

NT199

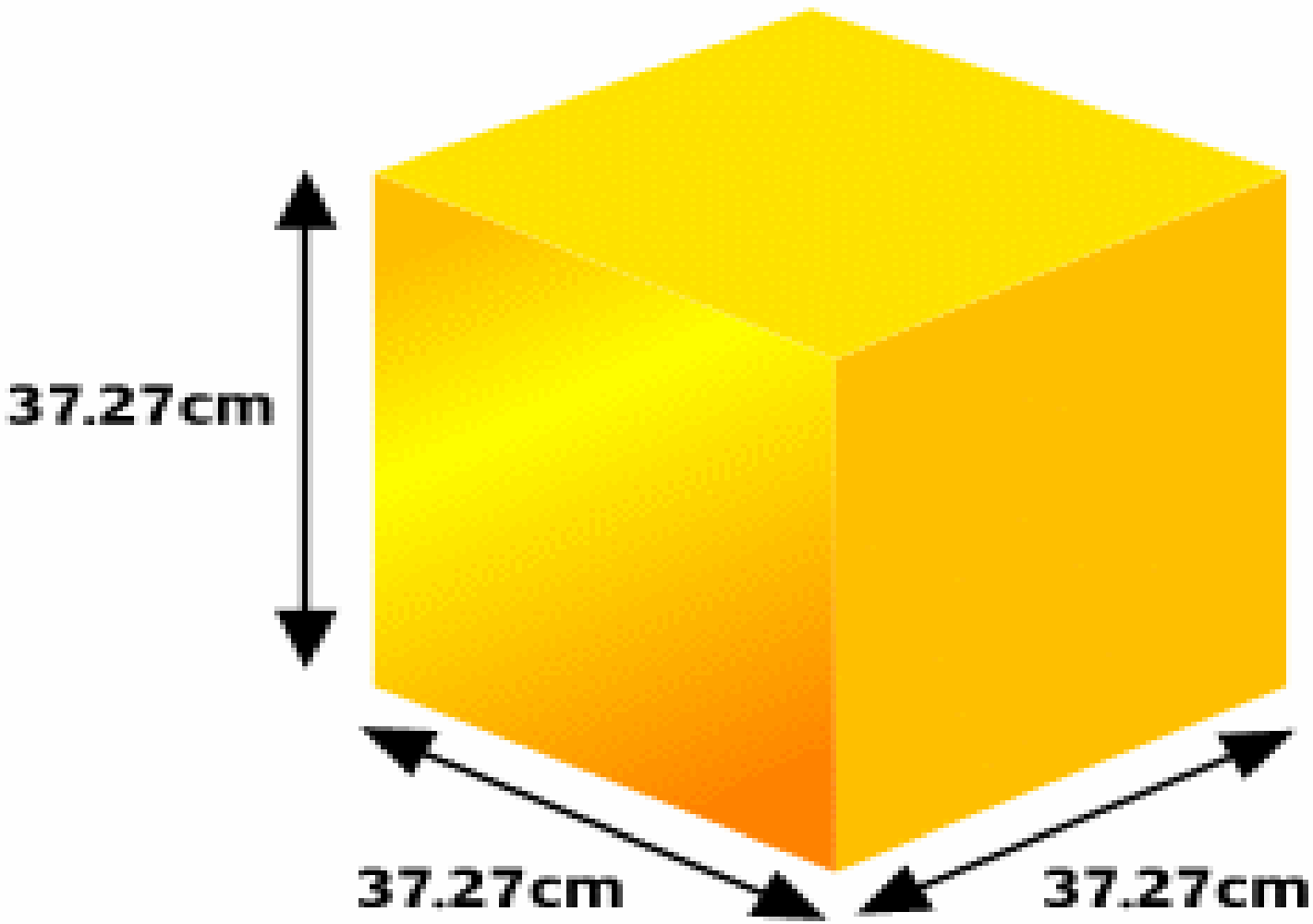
市價 NT1200元 130ml

搶購中

1. 加贈現金紅利796點
2. 累積晉升MVP會員消費額
3. 限線上刷卡付款宅即便出貨

- 大家談到——　　現代日本人，很會創新，出奇招，在日本清酒內，置入純金的金箔小片，金光閃閃，美其名「純金箔酒」。　　在「懷石料理」的米飯上，也撒了黃金箔片，是金飯，或在龍蝦上，洒金片。 我說：「可以確定，吃黃金，一定會拉黃金。」…

一噸黃金 (19.32 g/cm^3)



變軟

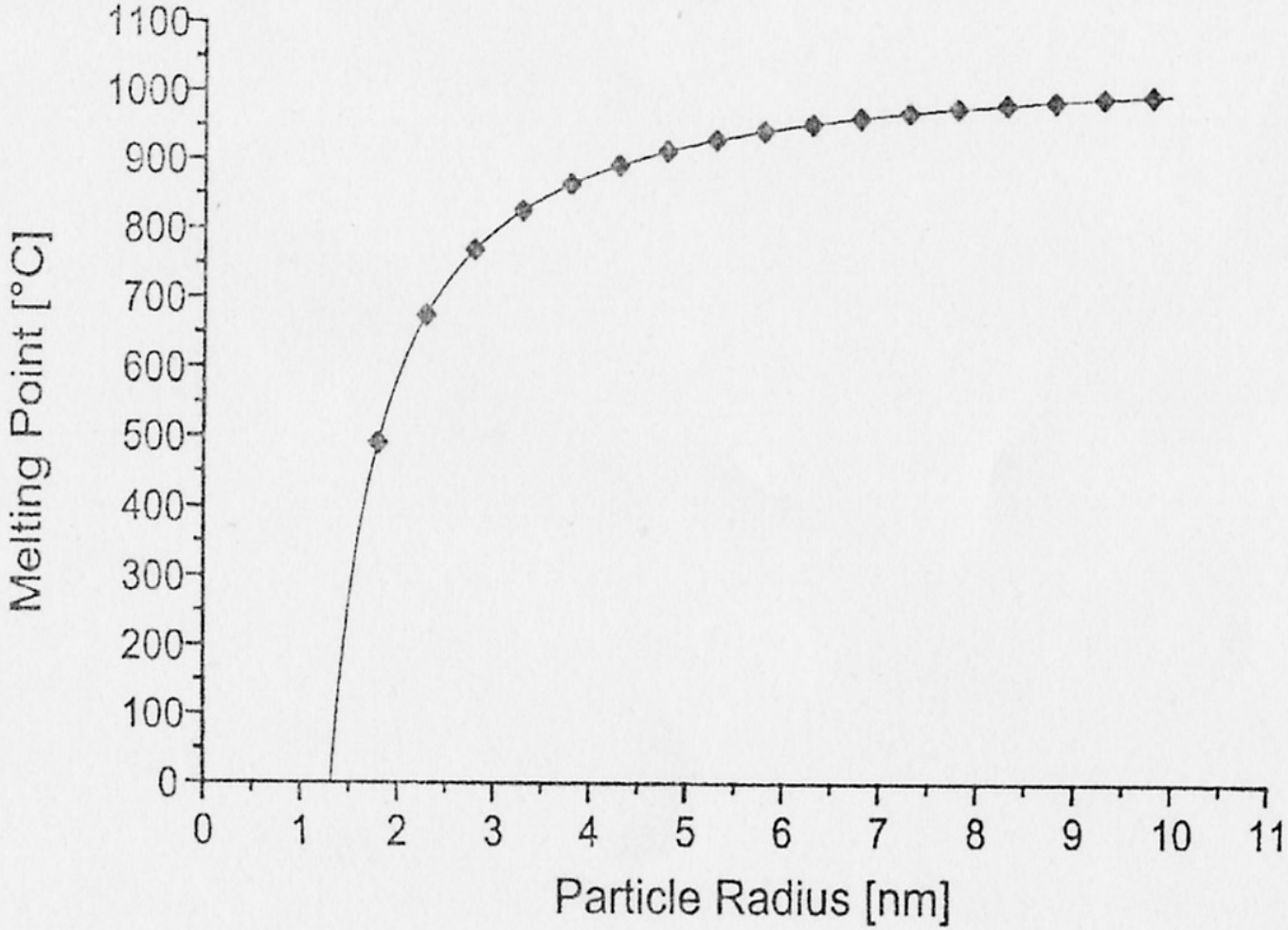
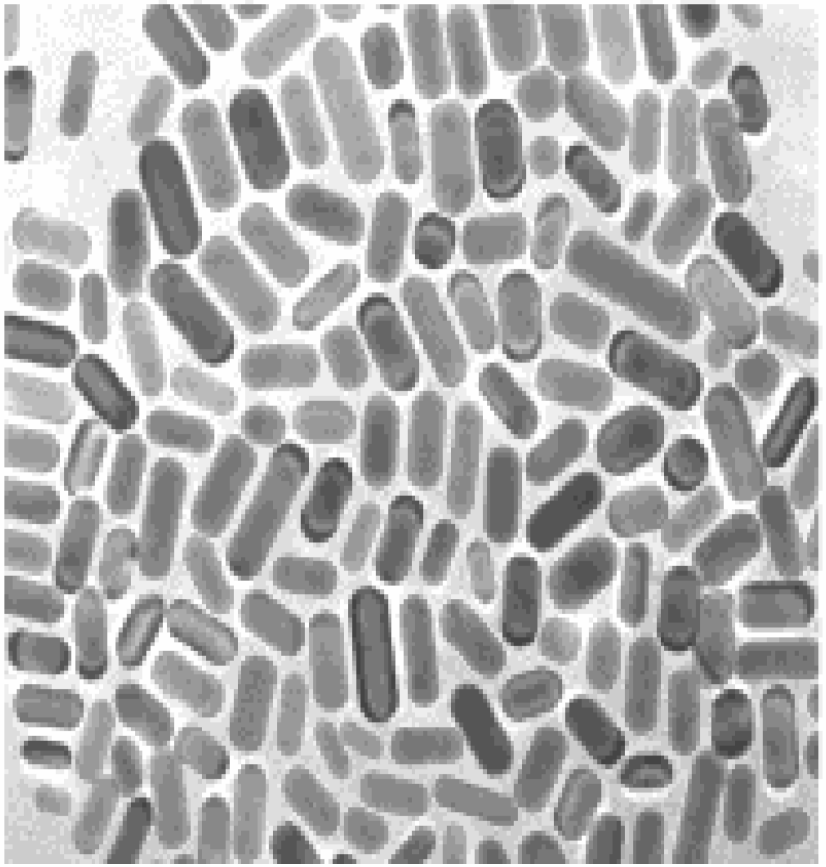


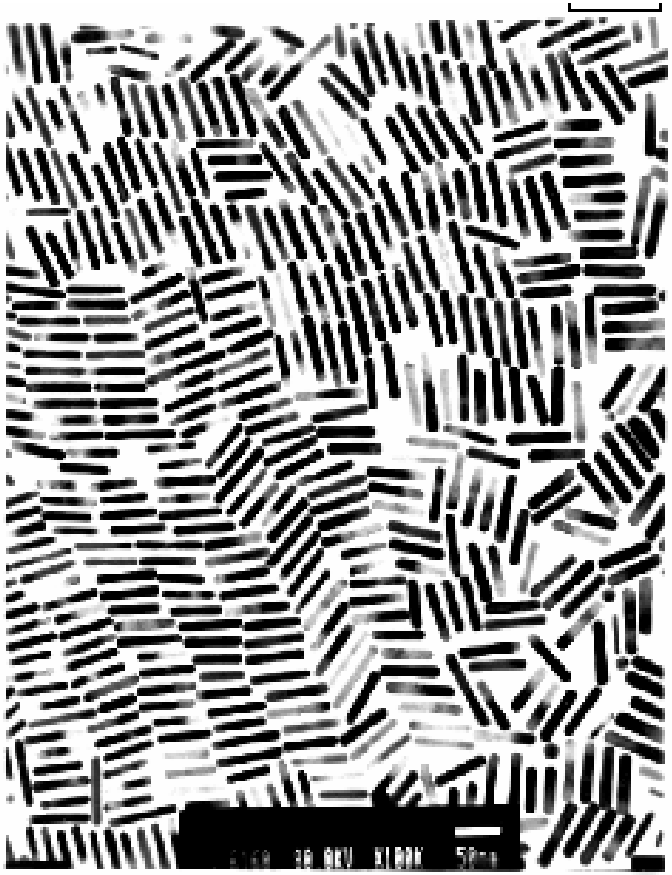
FIGURE 2.6 Relation between the size of gold particles and their melting point.

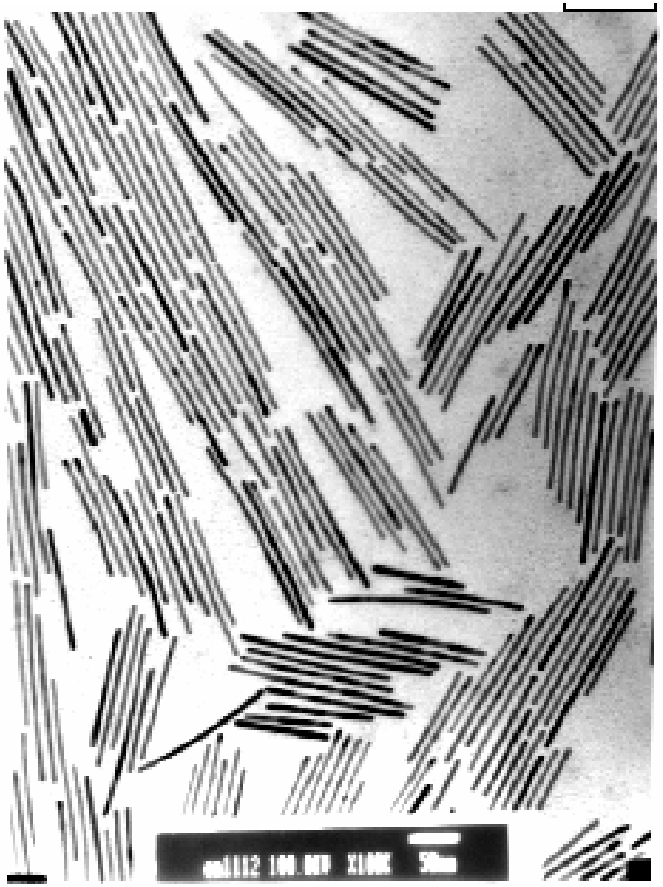
尺寸效應



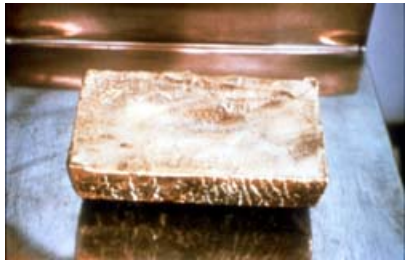
金奈米線

中正大學化學系王崇人教授提供





舉例來說:



塊材金

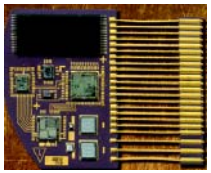
金奈米顆粒

珠寶

電子

勳章與錢幣

牙科術用

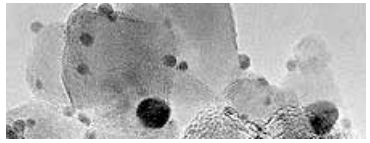


Pregnant

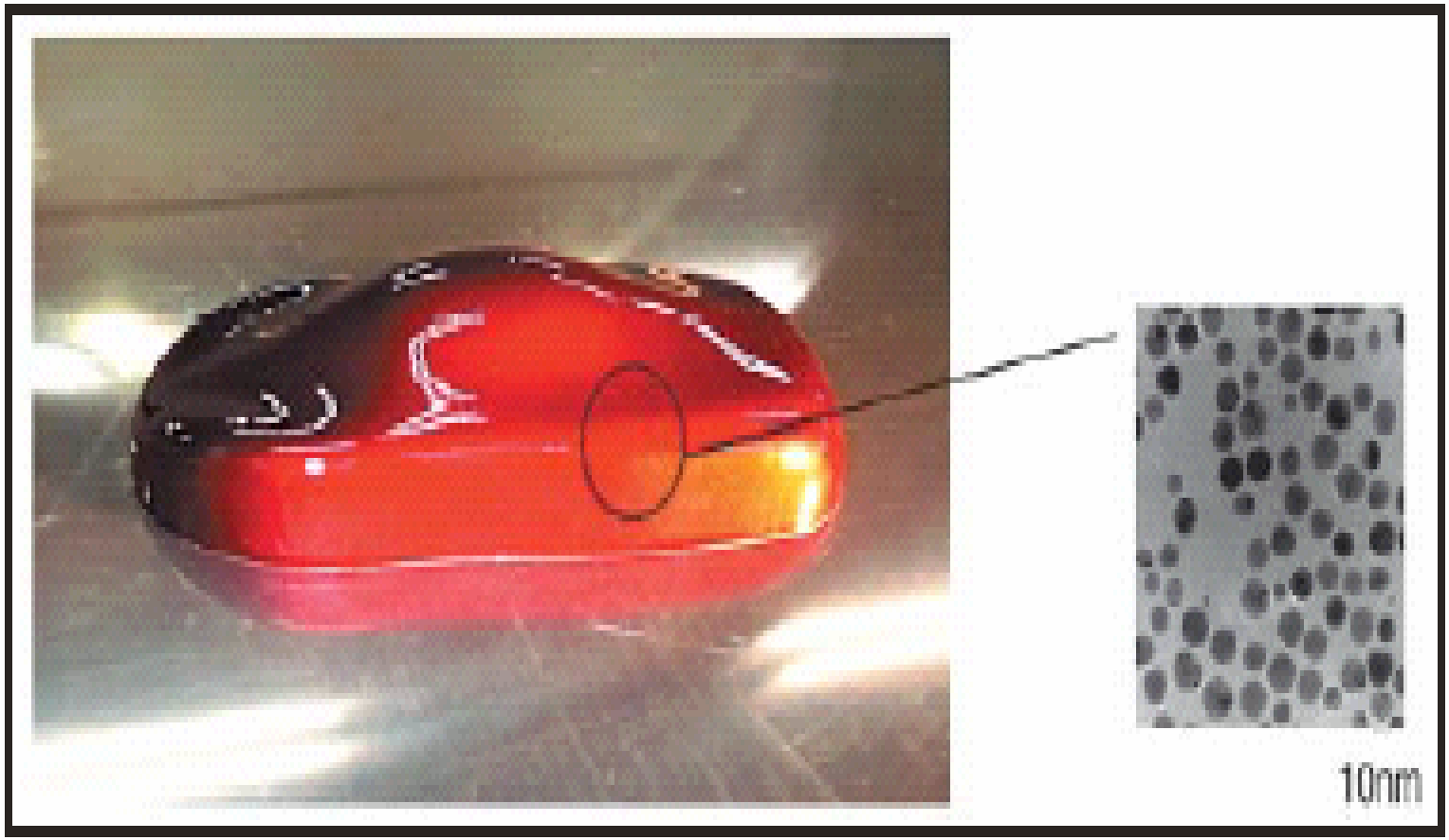
Not Pregnant

生物化學

金催化



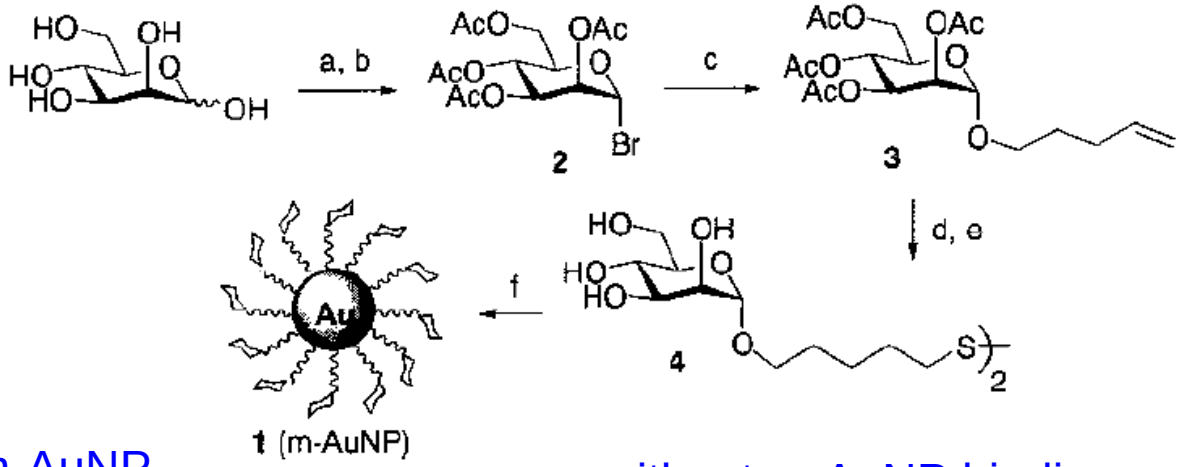
高分子穩定之膠體金
可產生動態染料效果



- 金薄膜/奈米顆粒做爲蛋白質晶片的平台

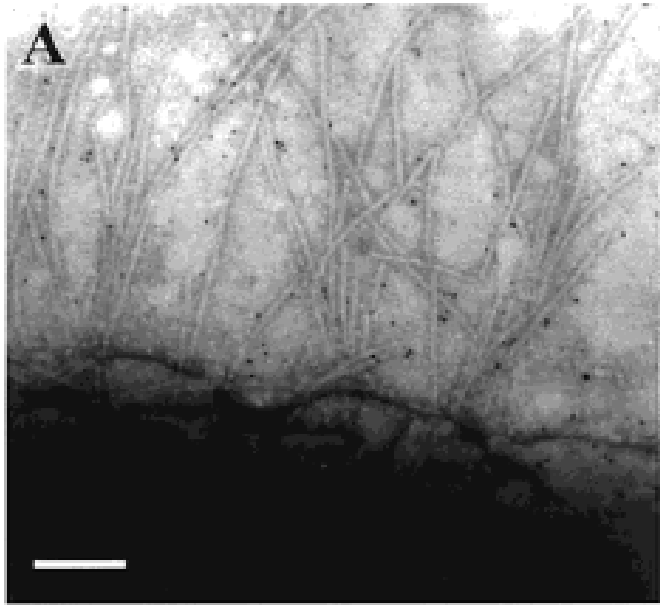
Selective Binding of Mannose-Encapsulated Gold Nanoparticles to Type 1 Pili in Escherichia coli

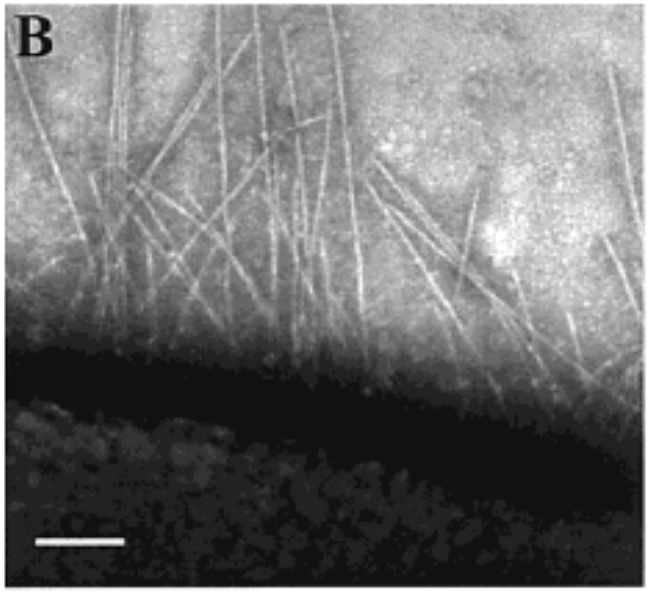
Scheme 1. Synthesis of m-AuNP **1**[a]



bound with m-AuNP

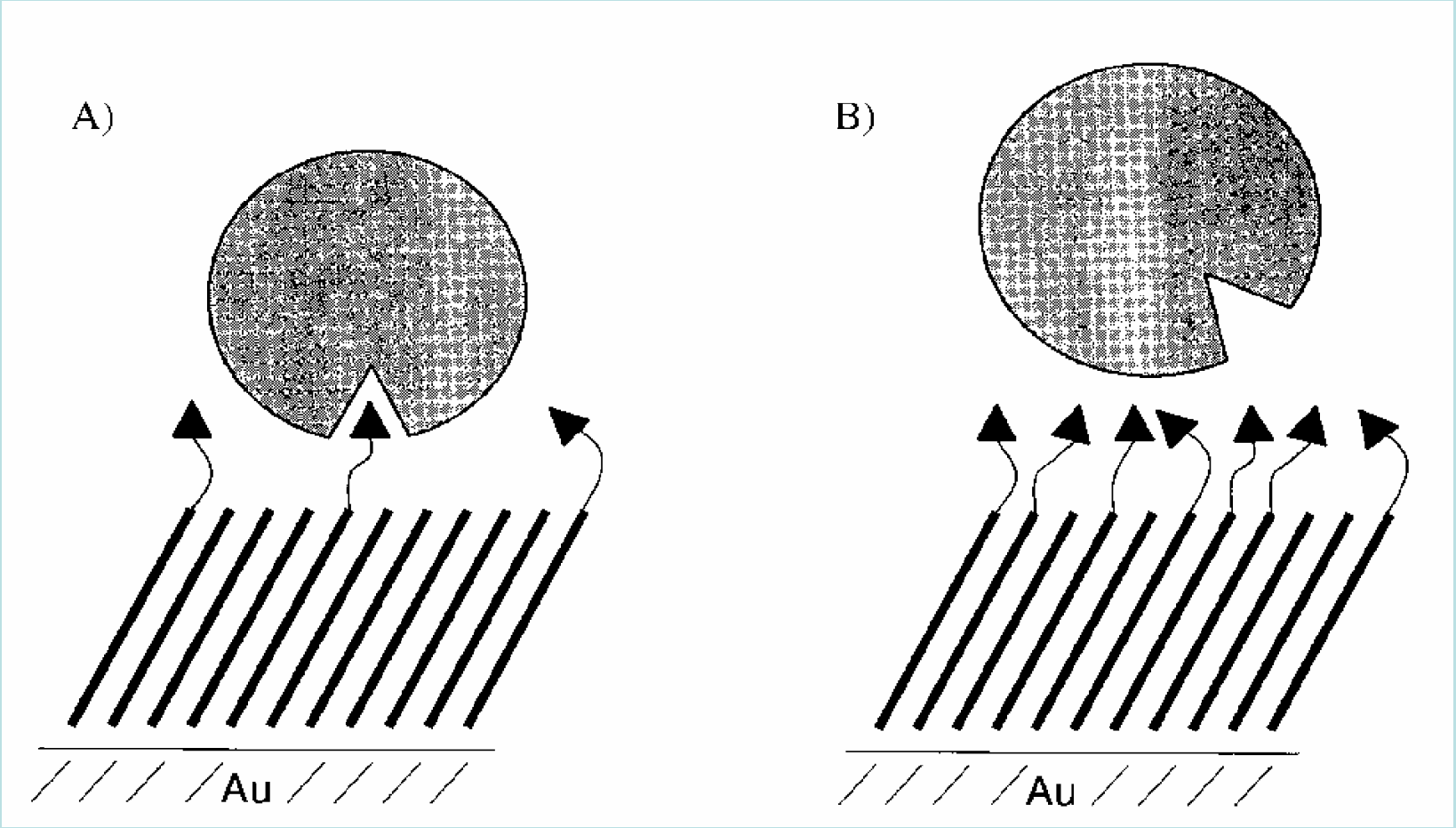
without m-AuNP binding.



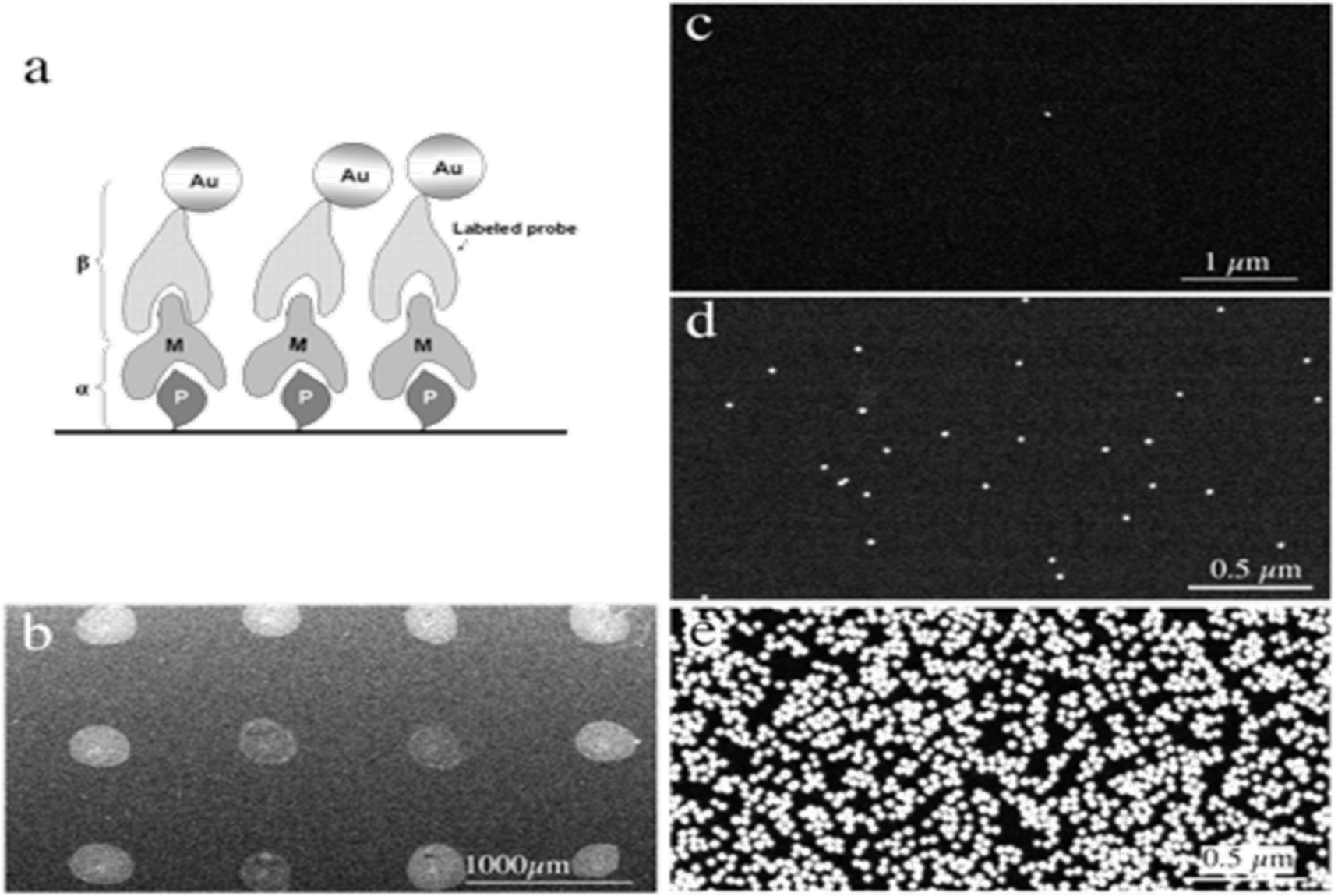


Ref: *Chen, C. C. J. AM. CHEM. SOC.* **2004**, *126*, 273.(台灣師範大學 陳家俊教授)

蛋白質-自組裝單層 作用

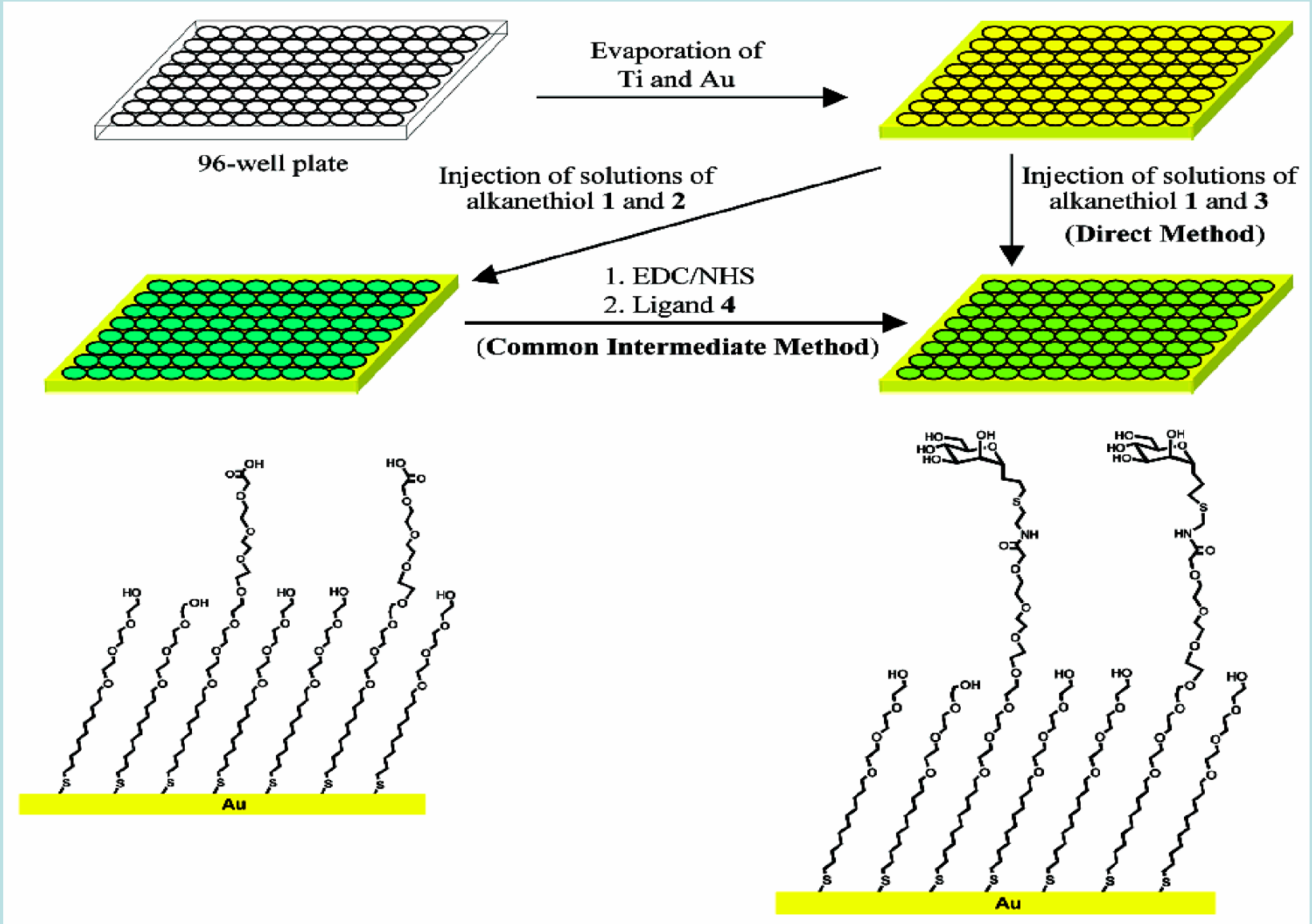


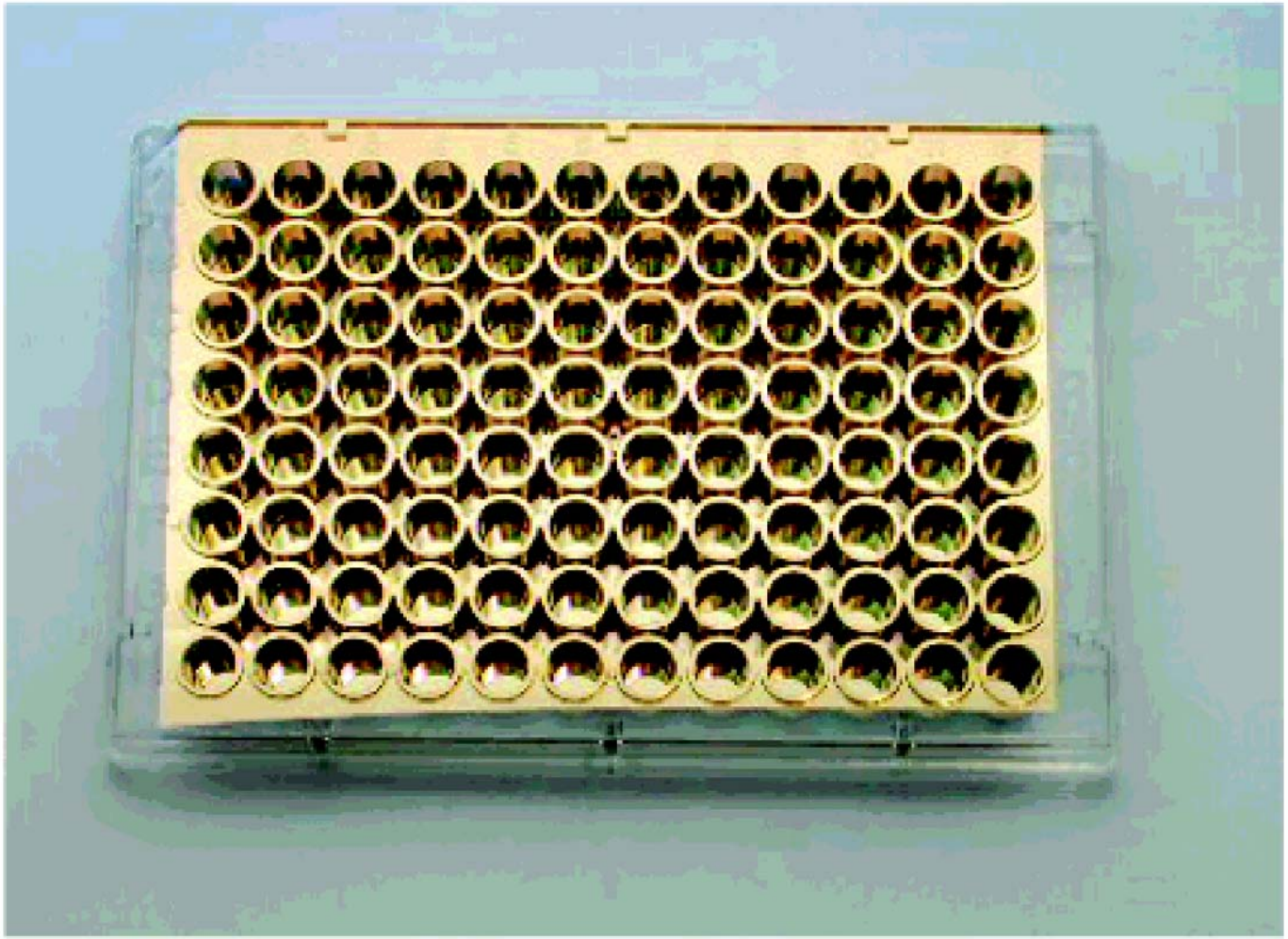
在低密度（A）固化上的配基應較在高密度（B）者容易與蛋白質形成鍵結



蛋白質陣列的定量偵測

Levit-Binnun et al., *Anal. Chem.*, **75** (6), 1436, 2003

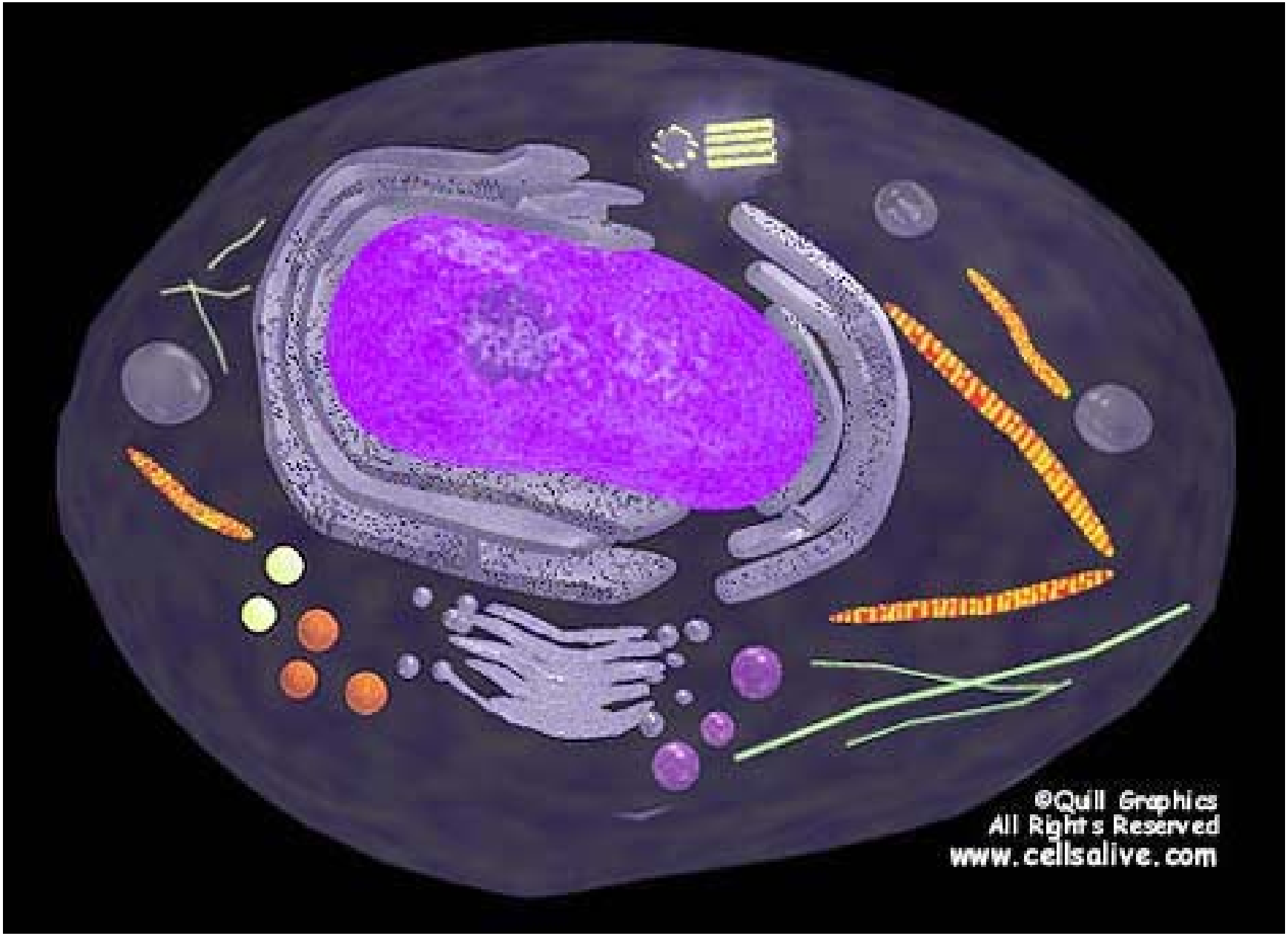

96-well plate
Evaporation of
Ti and Au
Injection of solutions of
alkanethiol 1 and 2
Injection of solutions of
alkanethiol 1 and 3
(Direct Method)
1. EDC/NHS
2. Ligand 4
(Common Intermediate Method)
Au
Au



金覆蓋96孔微滴定板的圖像.

師: .....連金子這樣安定的東西，切到奈米尺寸都變得這樣有用，你想想其他東西呢?

生: 嗯..... 我還是想要黃金，而且越大越好!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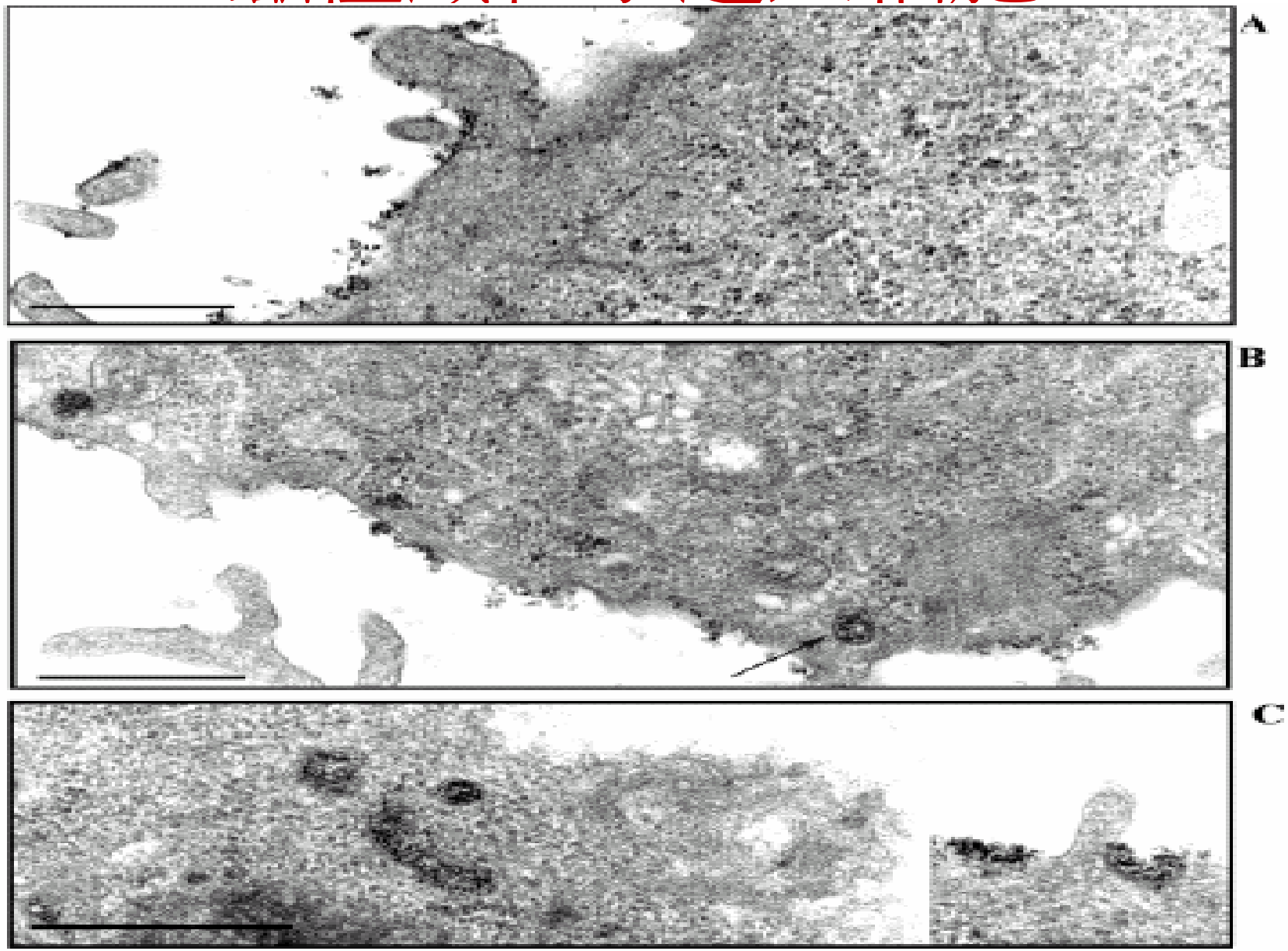
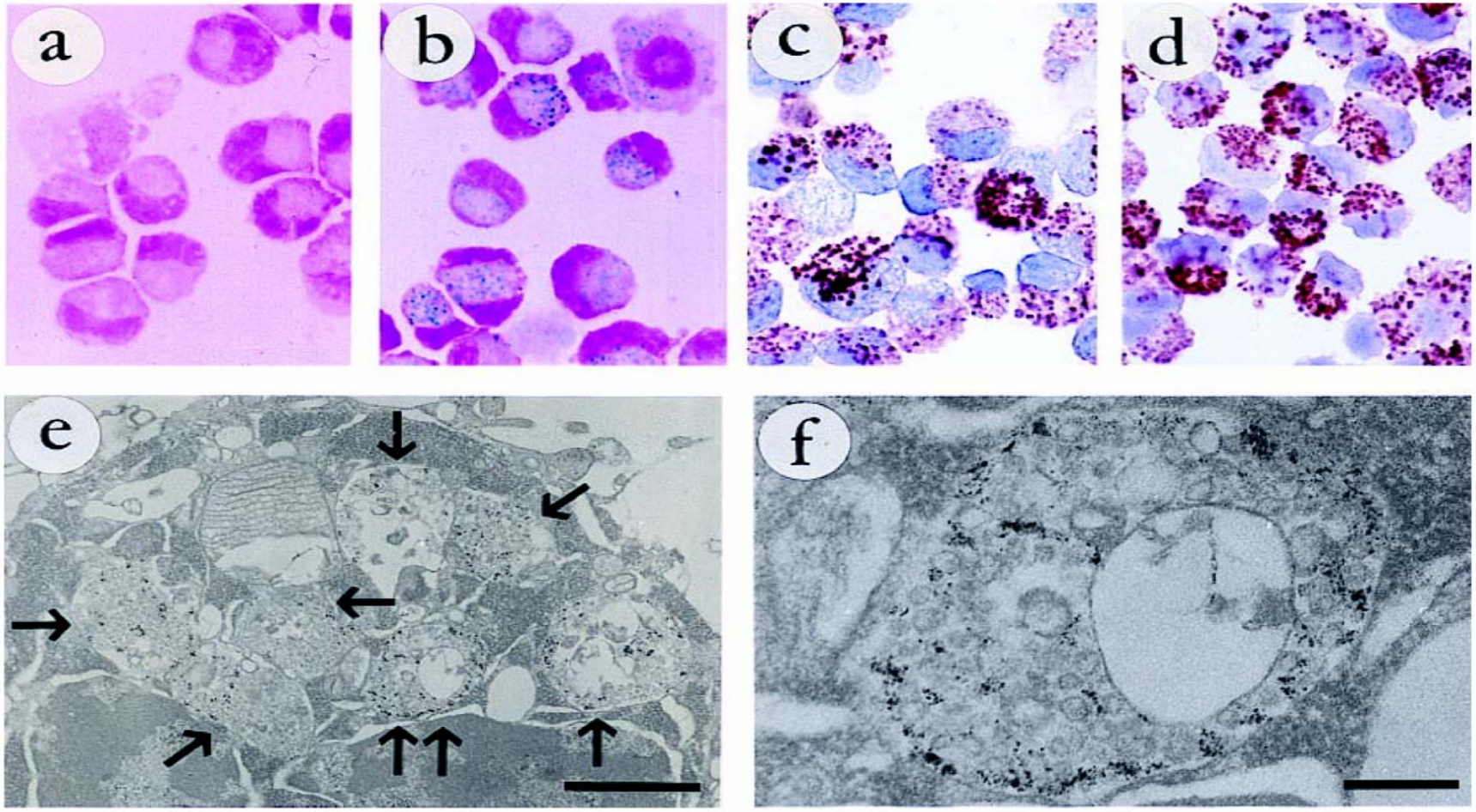
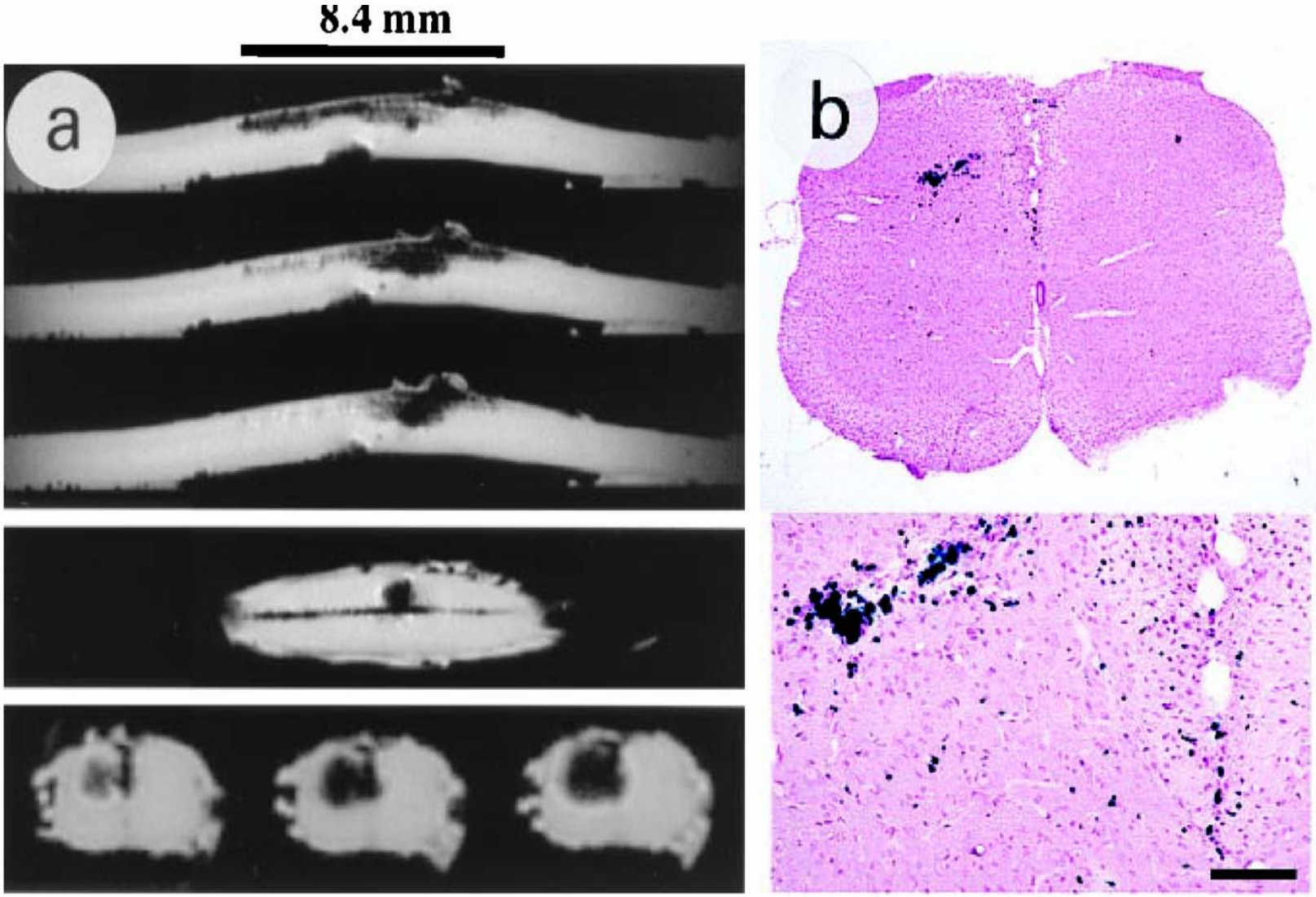
www.cellsalive.com

磁性鐵粒子進入細胞

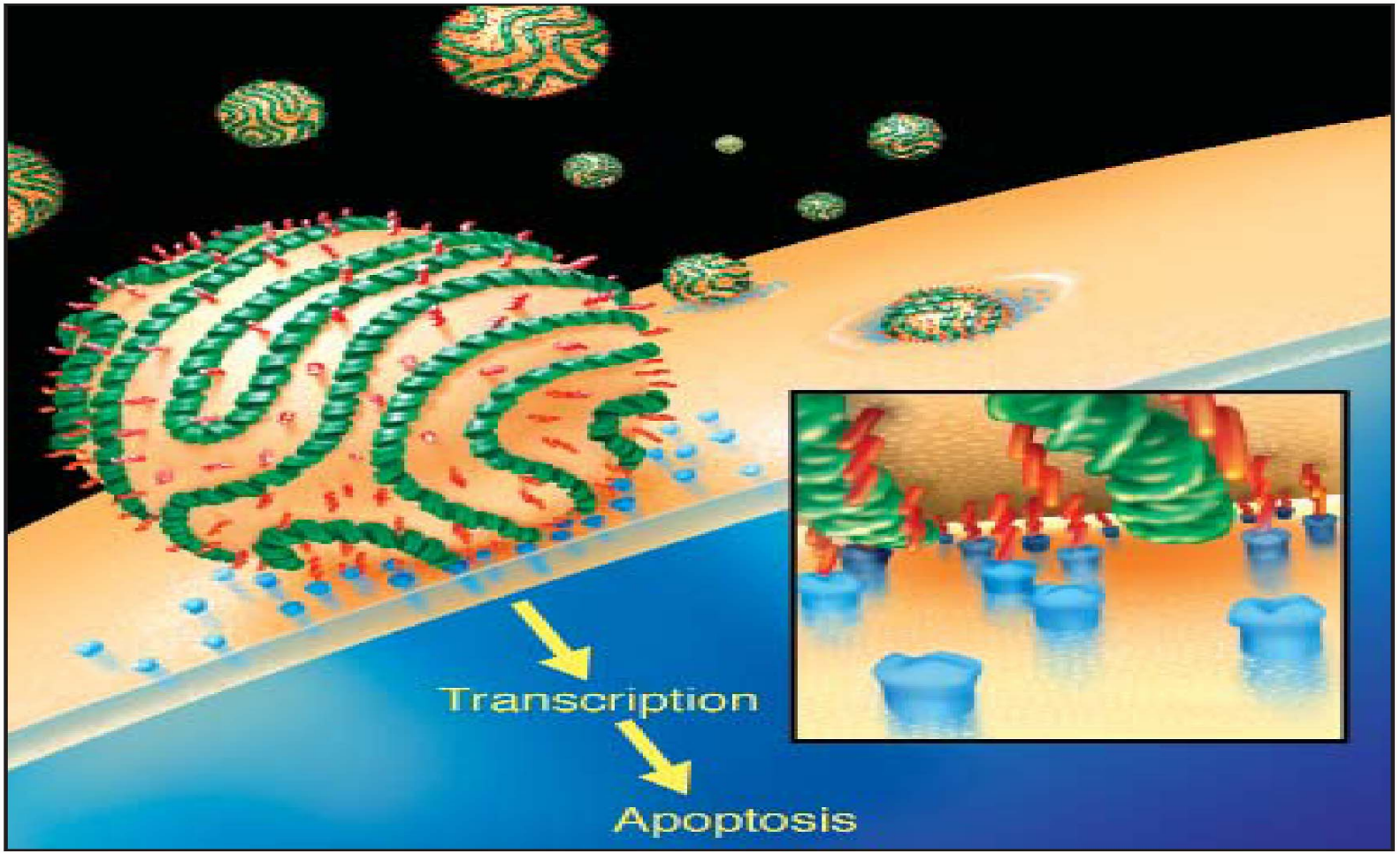


利用磁性奈米顆粒在磁共振中追蹤細胞遷移

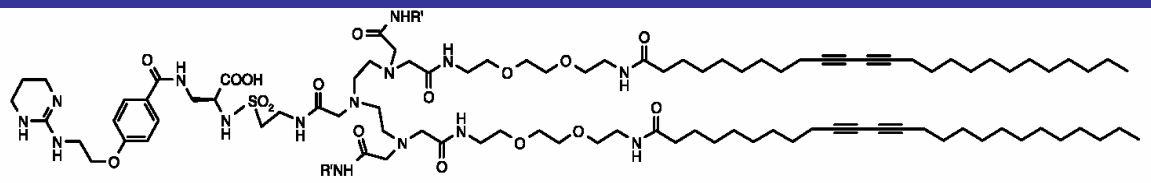



8.4 mm
a
b

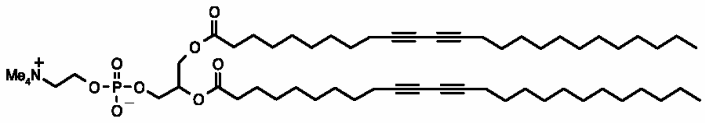
DNA 輸入細胞



Bull's-eye. Nanoparticles packed with targeting molecules (red) anchor to integrins (blue) on the outside of a tumor blood vessel cell before shuttling mutant DNA (green) inside.

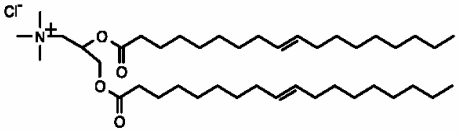


1
Integrin Antagonist Lipid



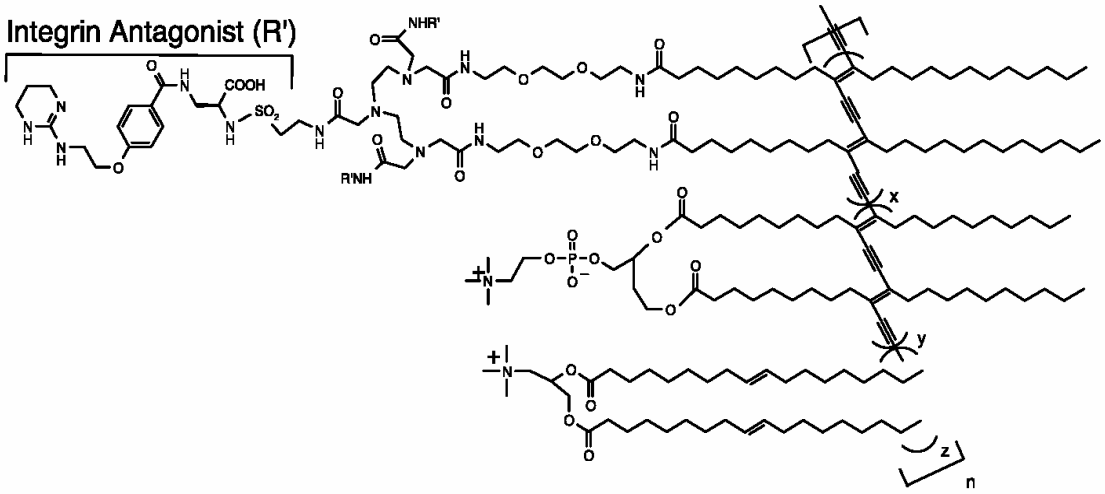
2
Base Lipid

+



3
Cationic Lipid

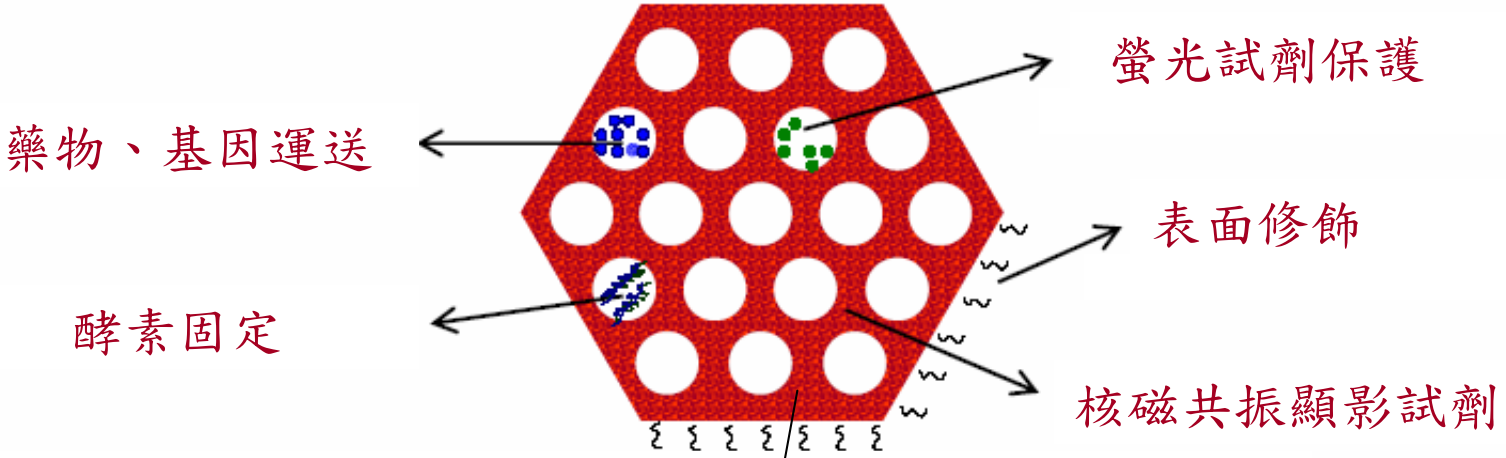
1. Sonication - H_2O
2. UV Irradiation, 0°C



4 αvβ3-NP

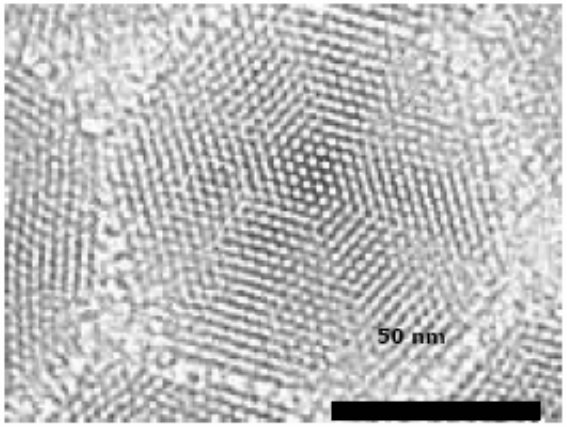
“奈米容器”在生物醫學上應用：

奈米中孔洞材料 MCM-41 於生物系統中扮演之攜帶角色



多功能的細胞追蹤、運送試劑

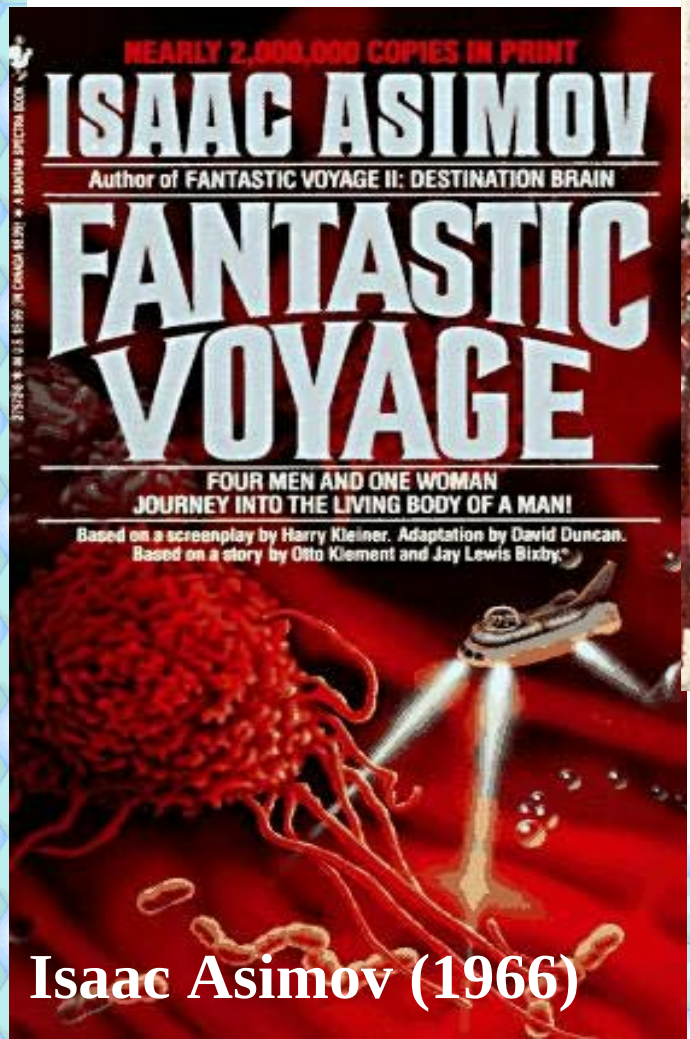
- 無生物毒性
- 高細胞滲透率
- 附以有機試劑保護
- 導引、判定、殲滅



The Plot: Fantastic voyage

聯合縮小軍

A 20th century Fox Film(1966)

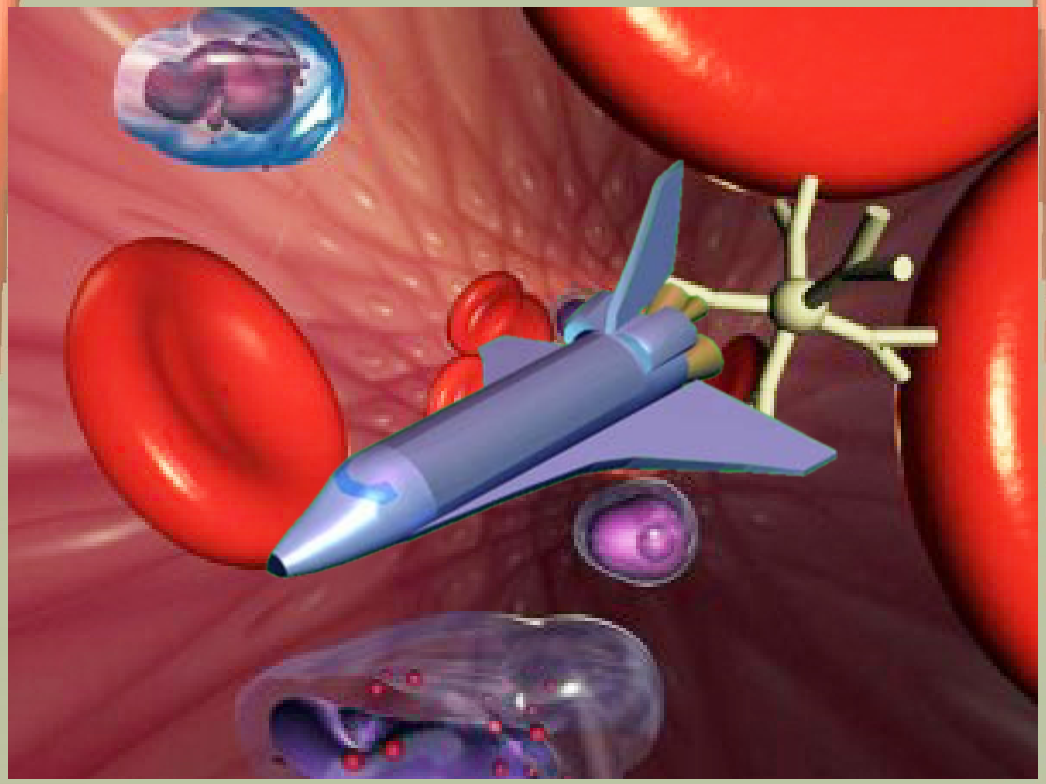


Isaac Asimov (1966)

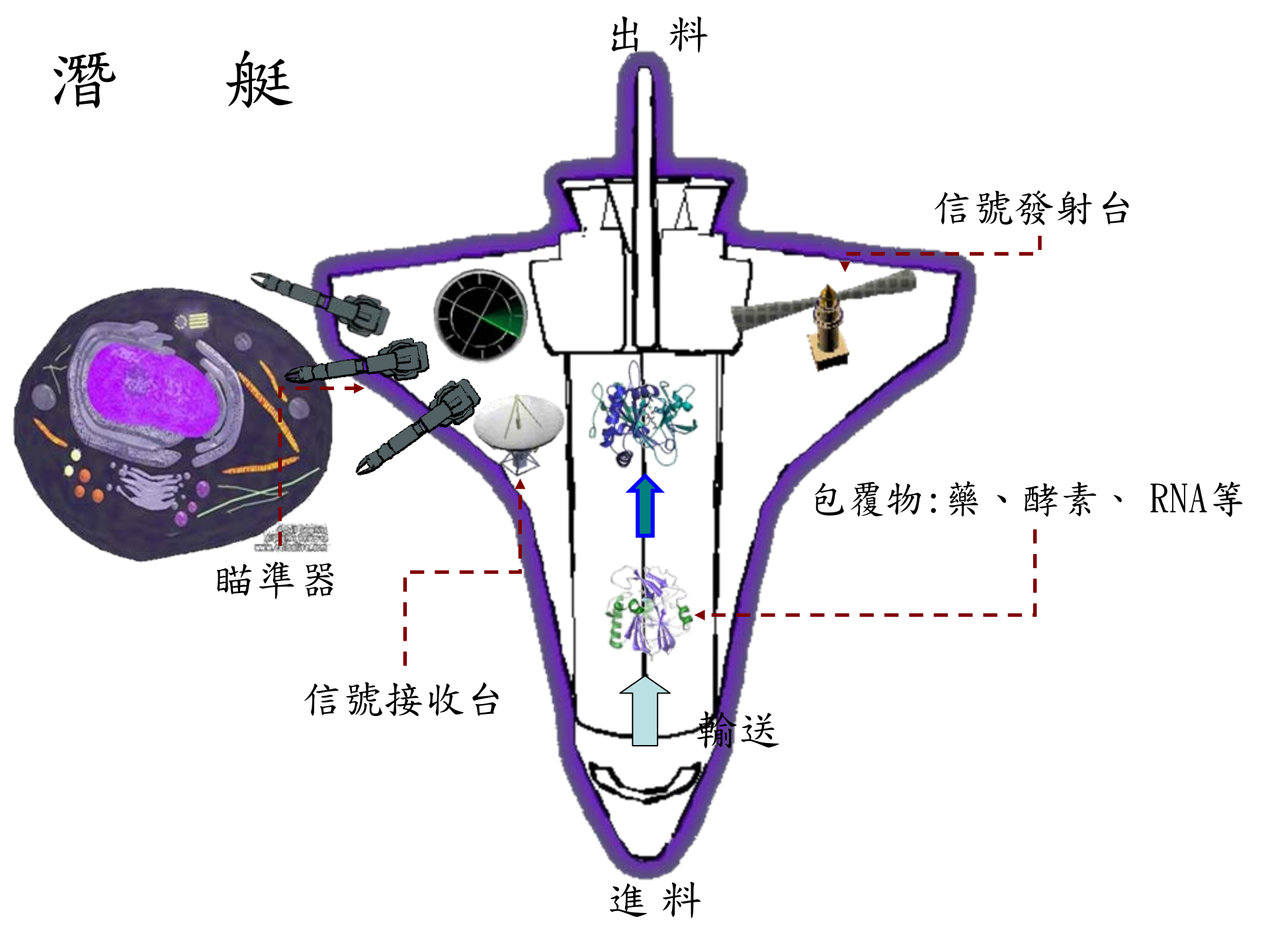
Salvador Dali (1965)

Christie's London (2007)
580,000 BP (1,141,732 US$)

“潛　艇”
--自　組　裝

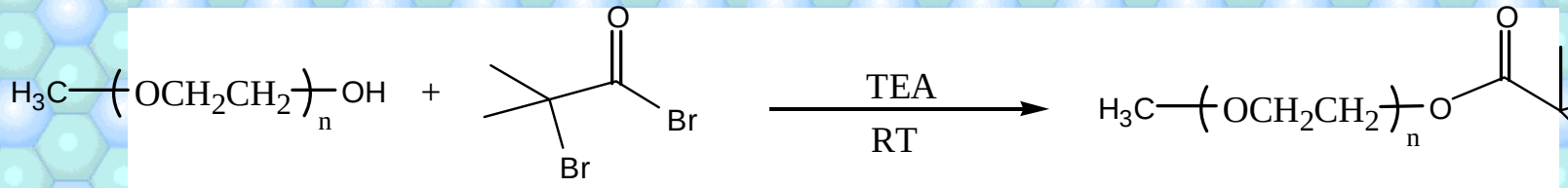


潛　　艇



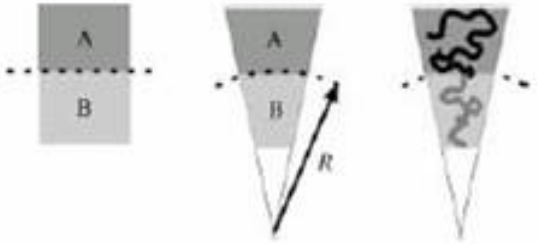
介面活性劑/水

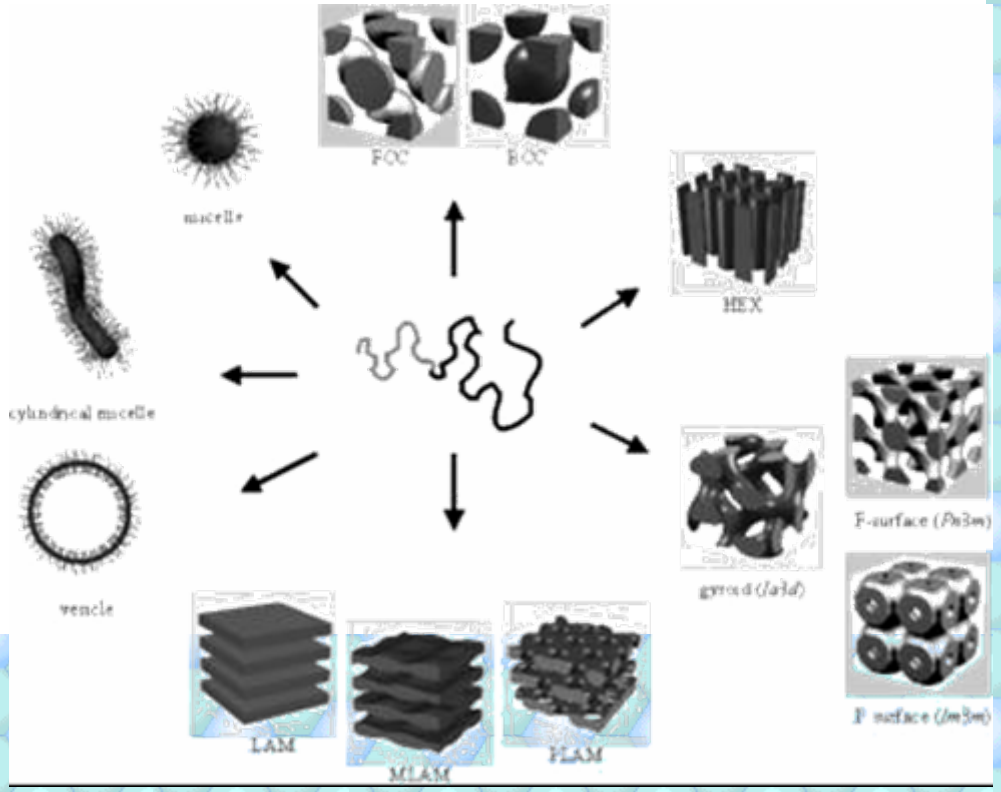
共聚化合物及介面活性劑的自組裝結構:



1. n=17
2. n=45
3. n=114

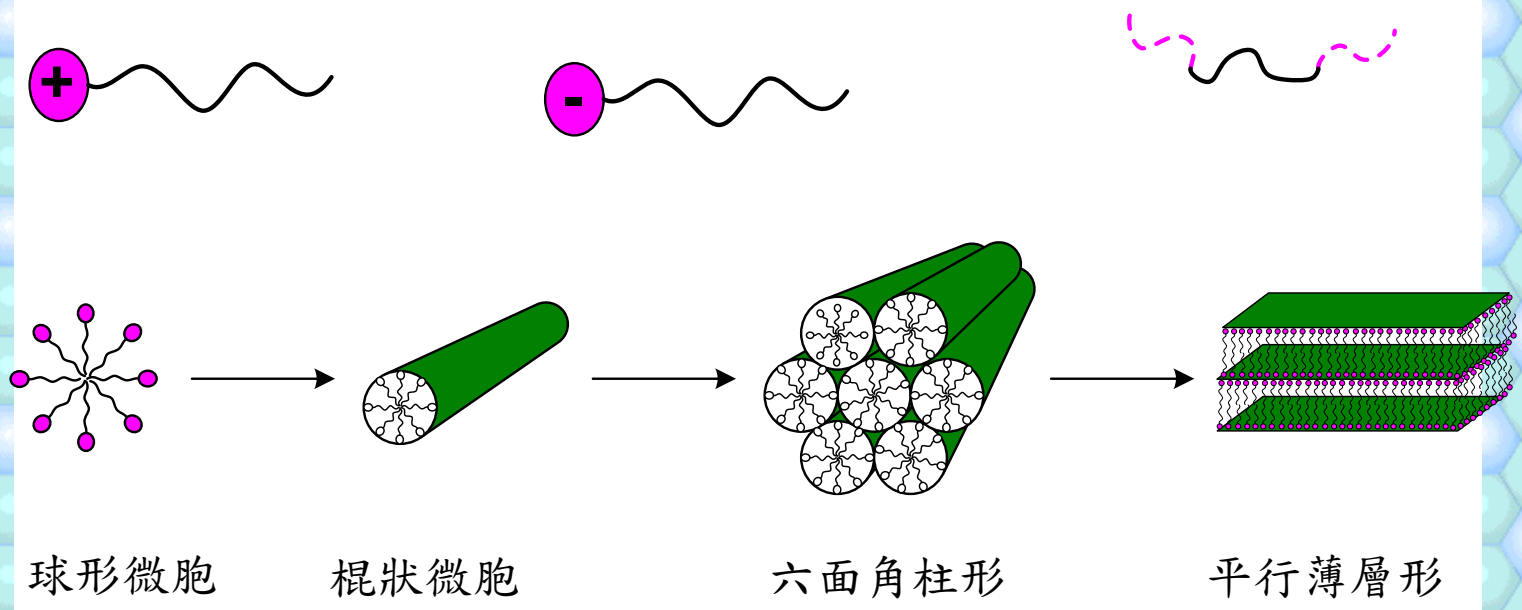
曲率控制



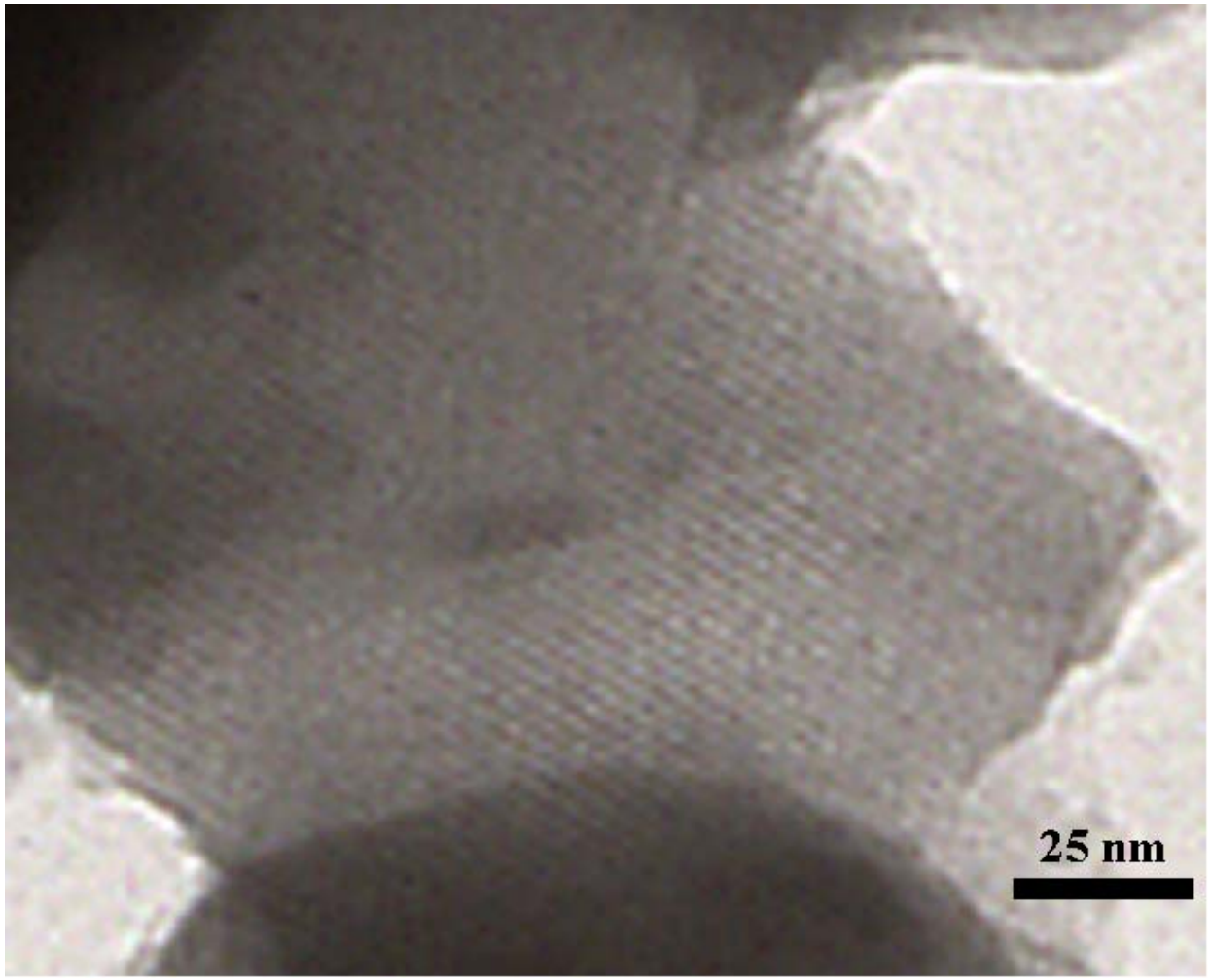


介面活性劑/水/矽酸鹽類

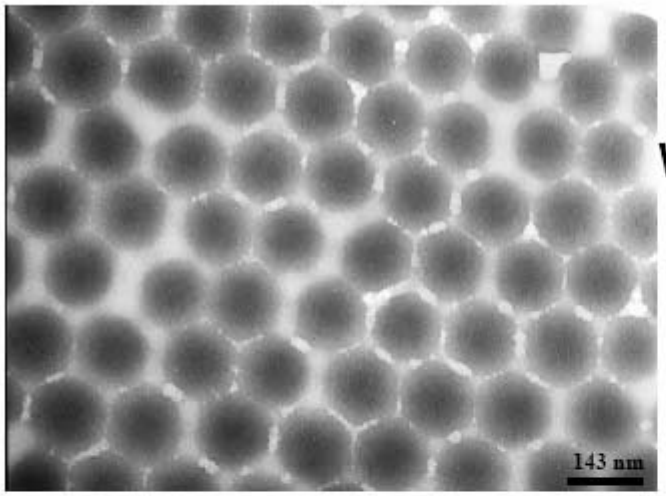
介面活性劑的自組裝過程



排列整齊的六面型結構



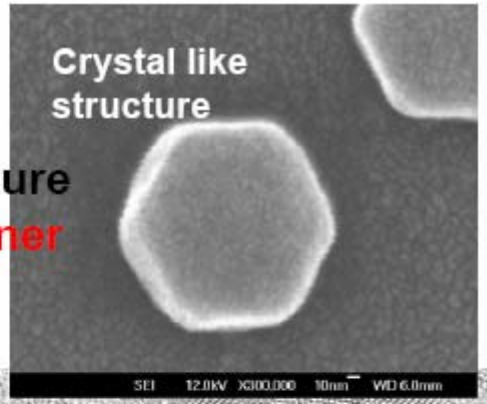
中孔洞矽奈米顆粒, MSN

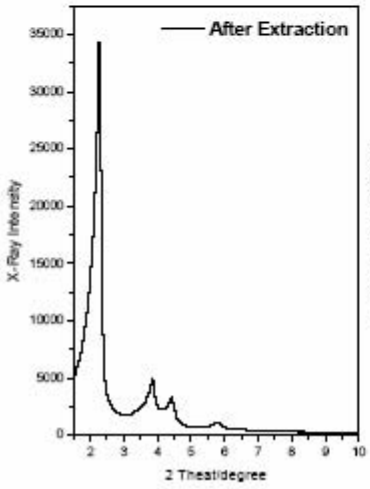


Homogeneous synthesis

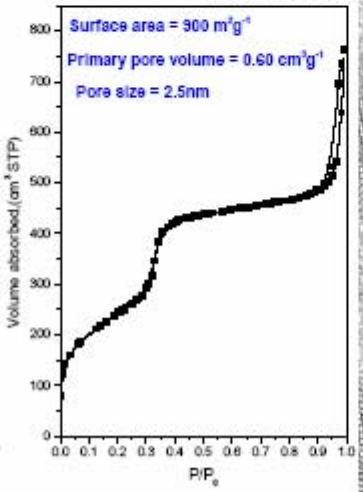
Well ordered structure

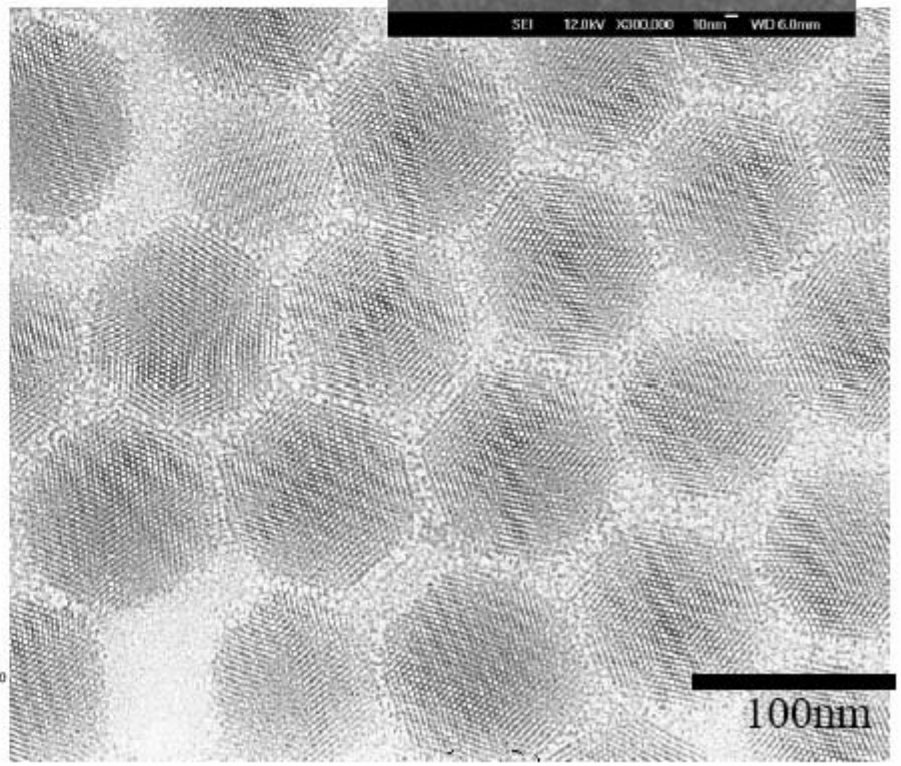
→ **excellent container**



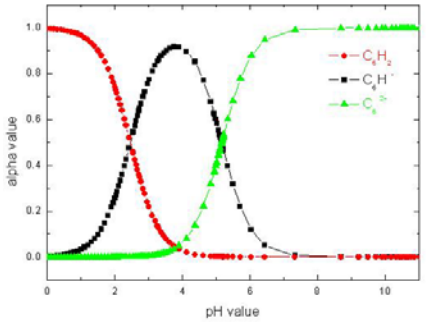


After extraction



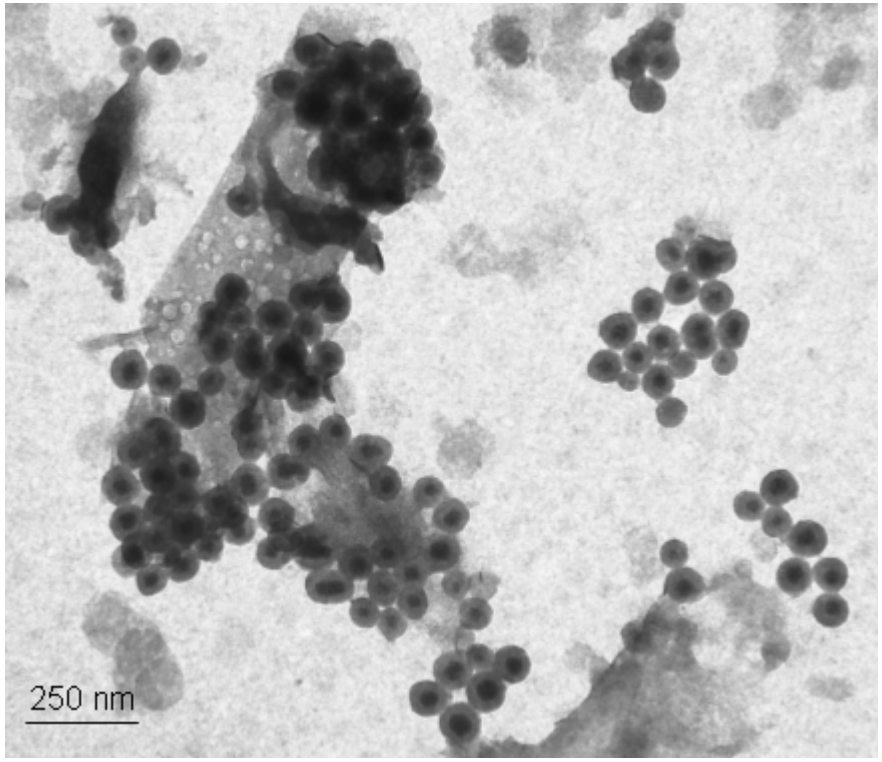


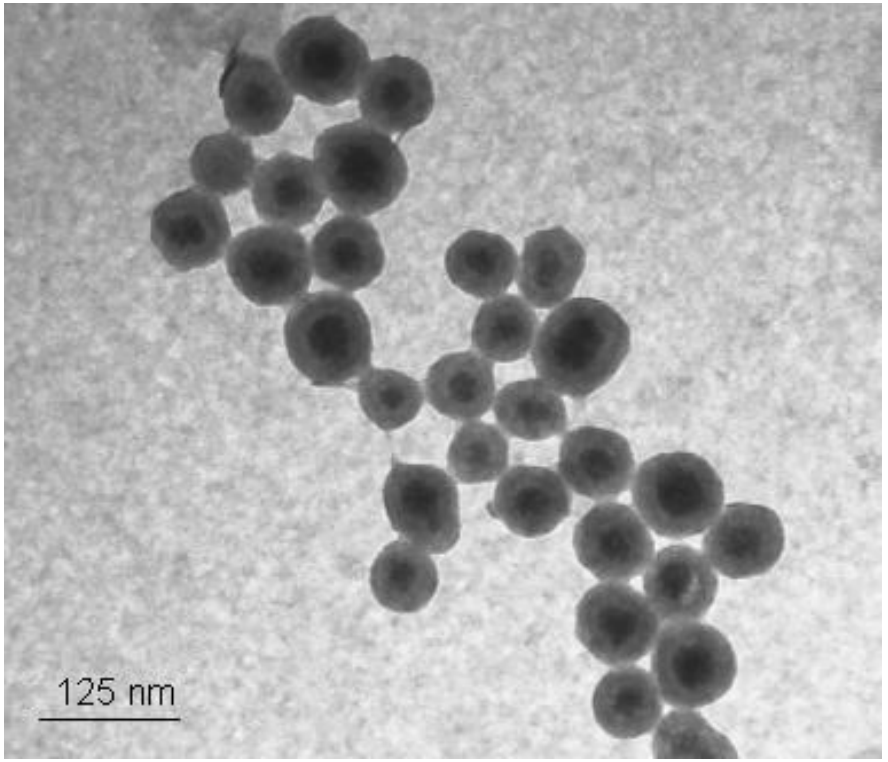
6 mM C_6Na_2 PBS at pH = 6.99



TEM

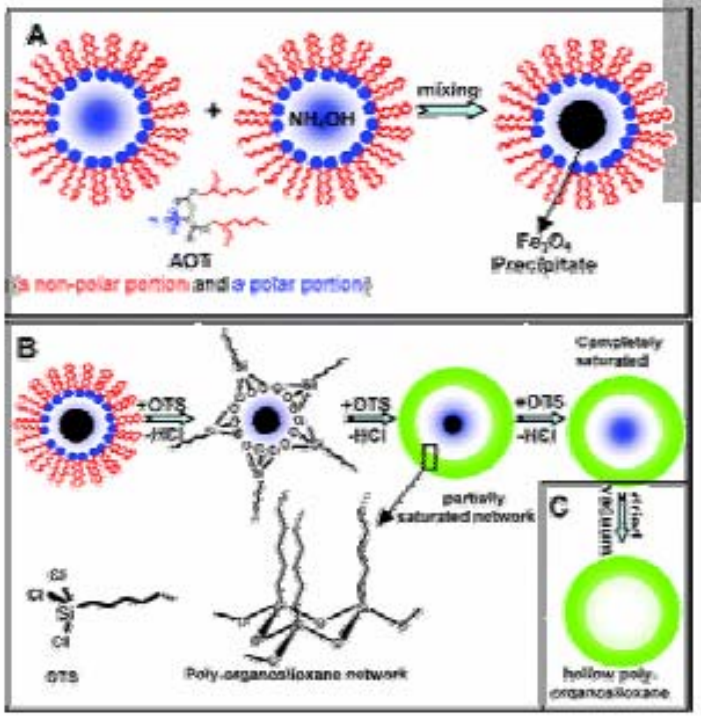
Incubate at 63 ^oC for 13 h

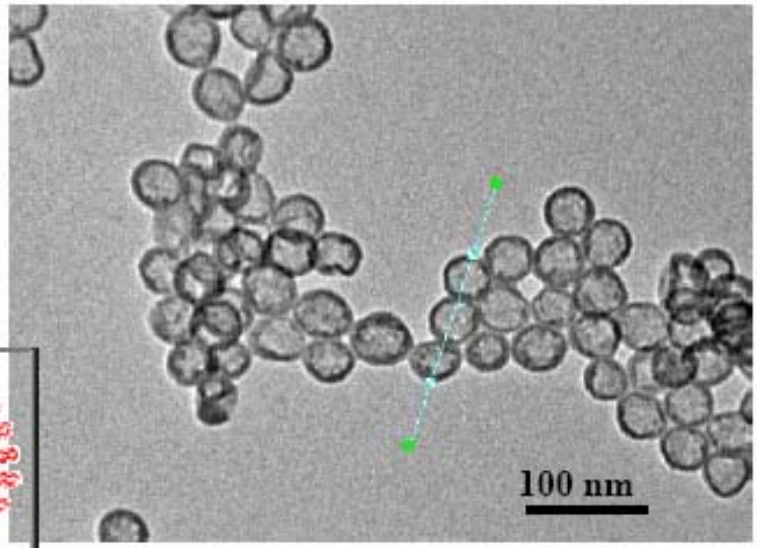


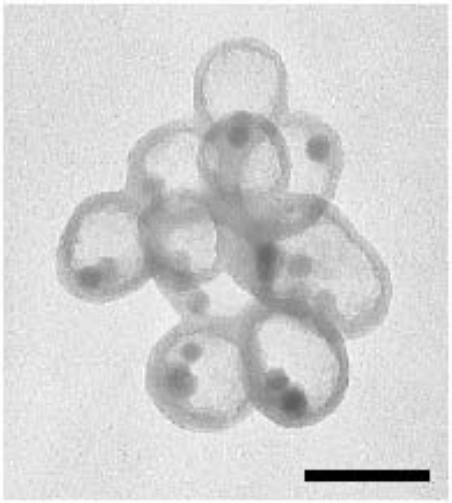


中空矽球體

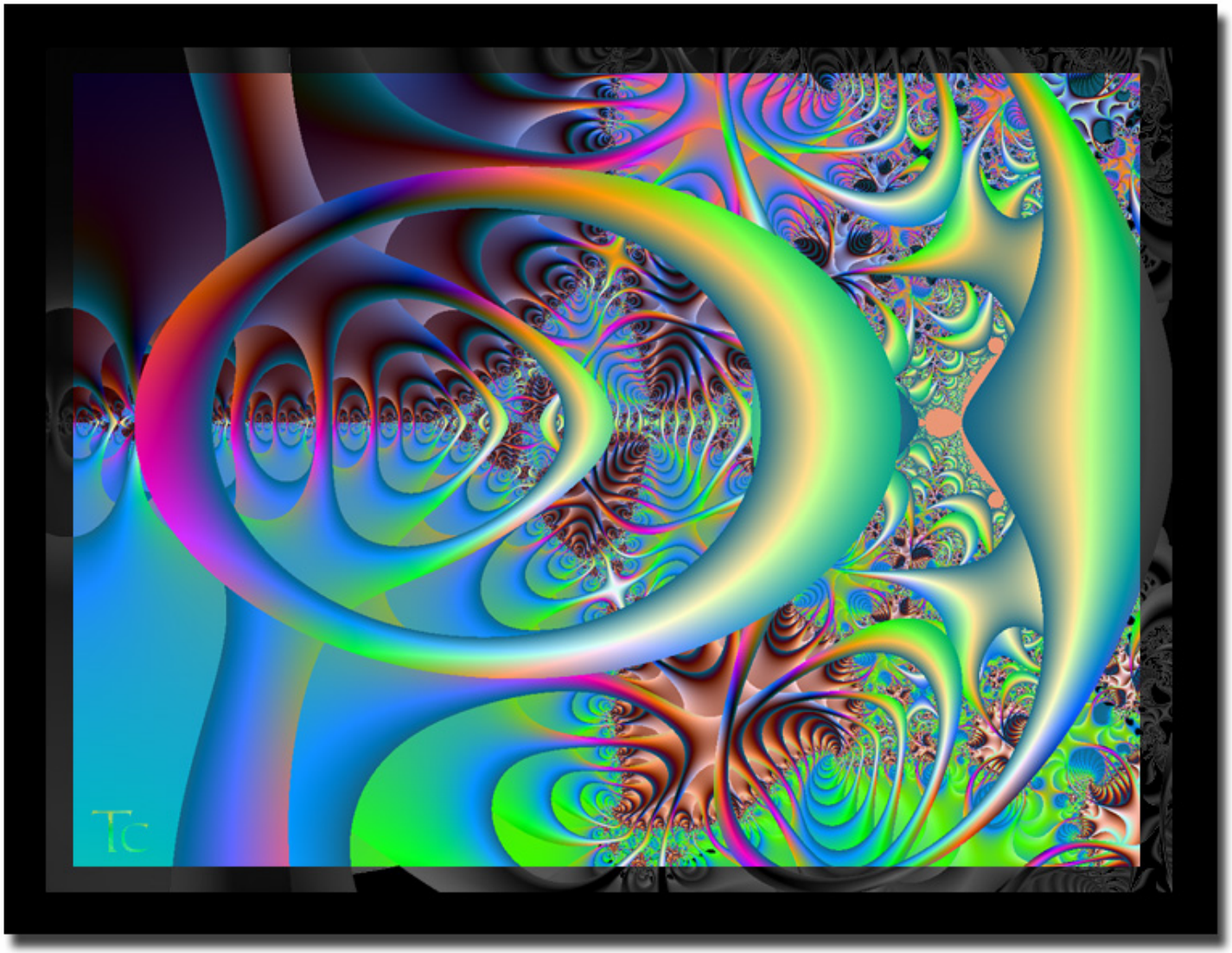
微 乳 液


A
mixing
AOT
Precipitate
B
+OTS
-HCl
Completely saturated
partially saturated network
C
dried
hollow poly-organosiloxane
OTS
Poly-organosiloxane network

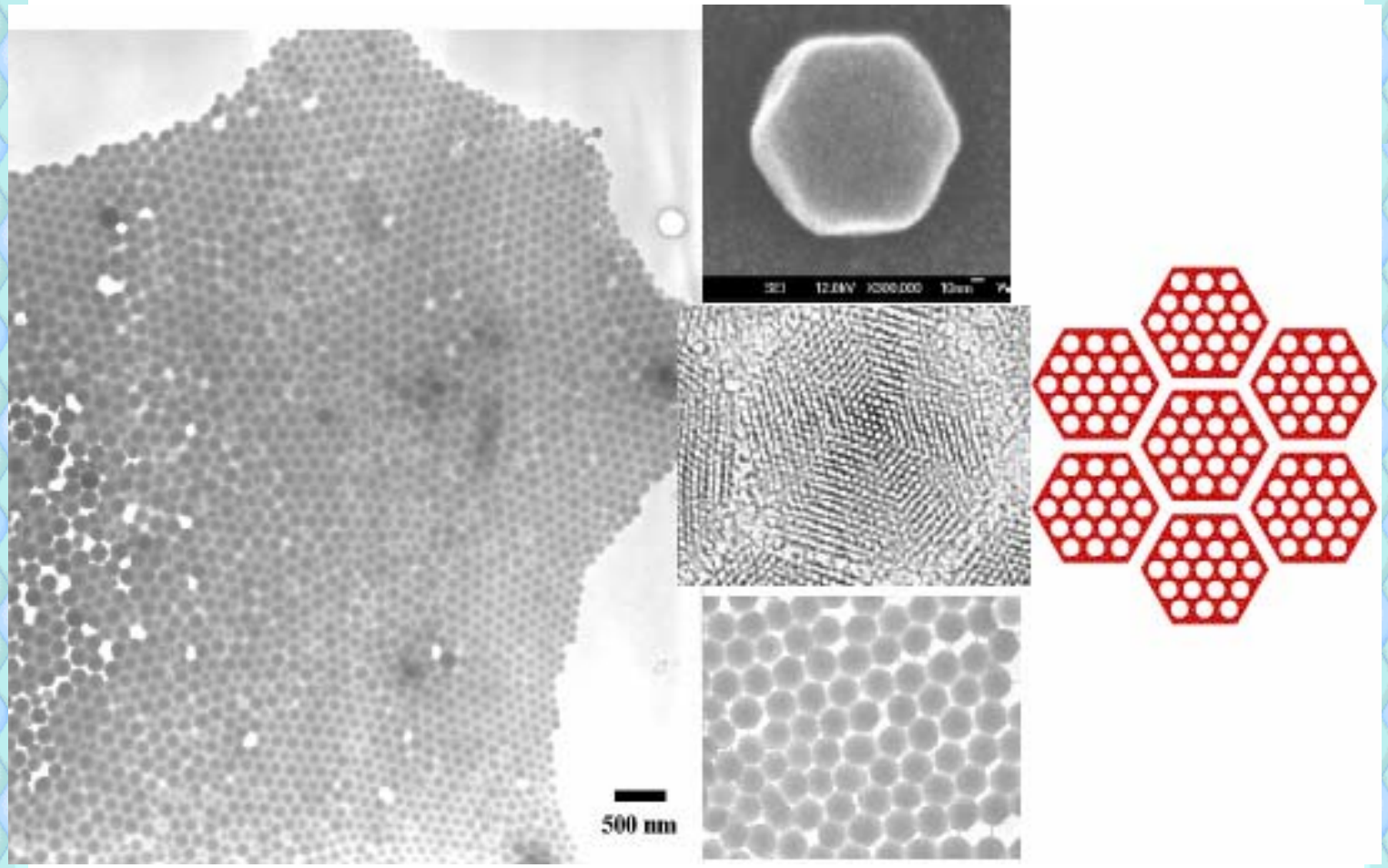

100 nm



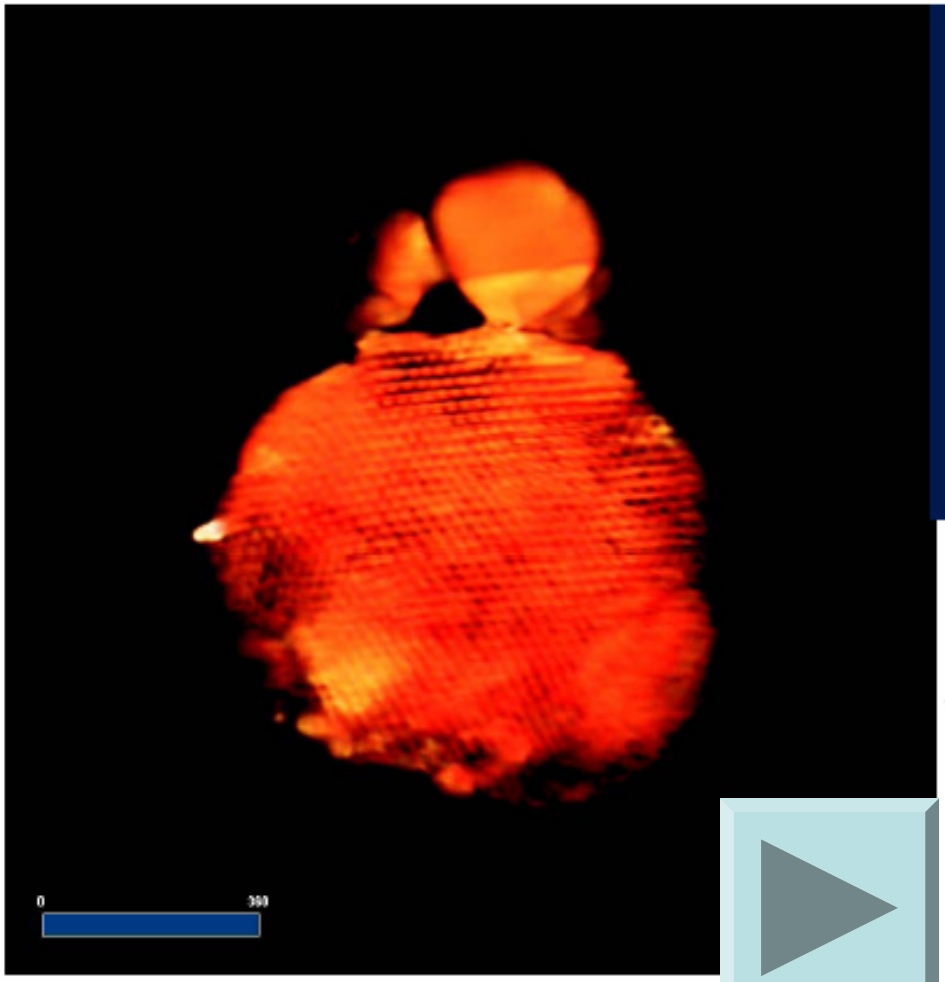
對於層級結構…

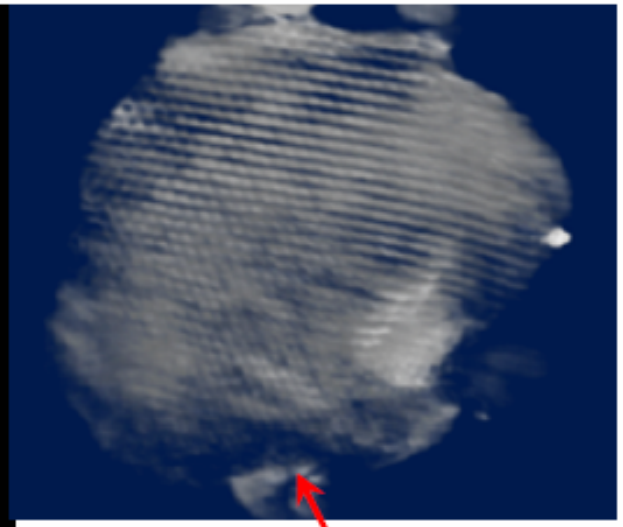


自相仿層級結構：MCM-41 奈米晶型晶體



掃瞄穿透式電子顯微鏡 STEM



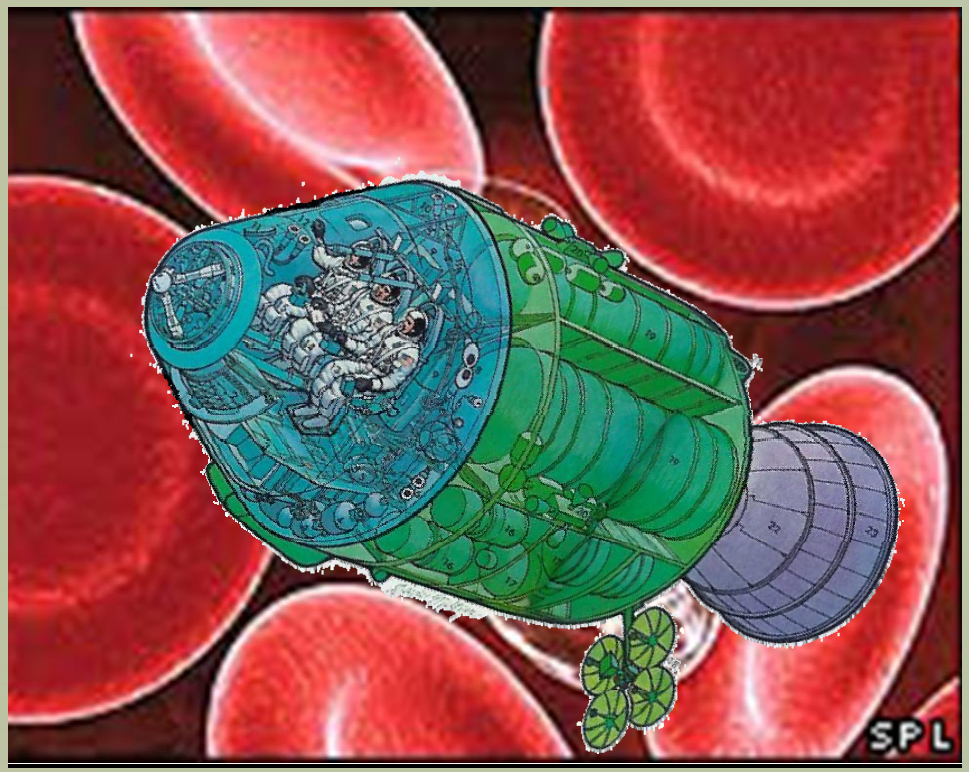


切片圖

SBA-15
三度空間形貌

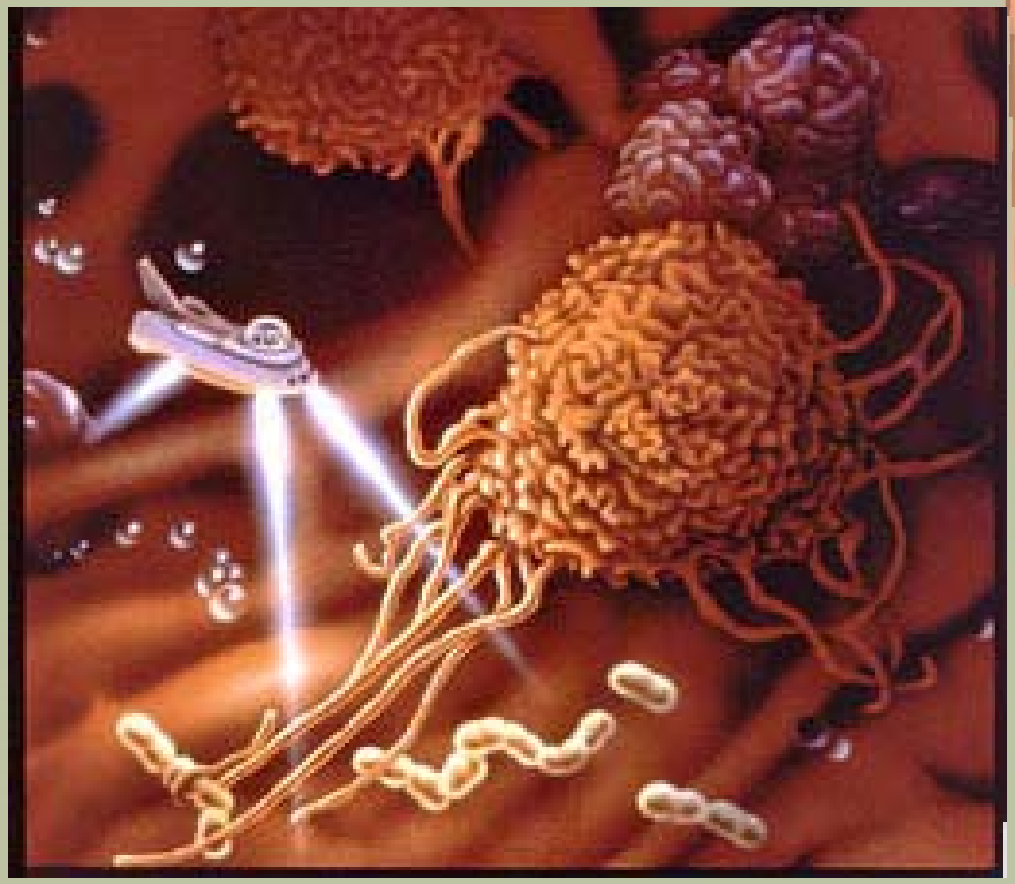
潛艇艙體：

限制空間效應



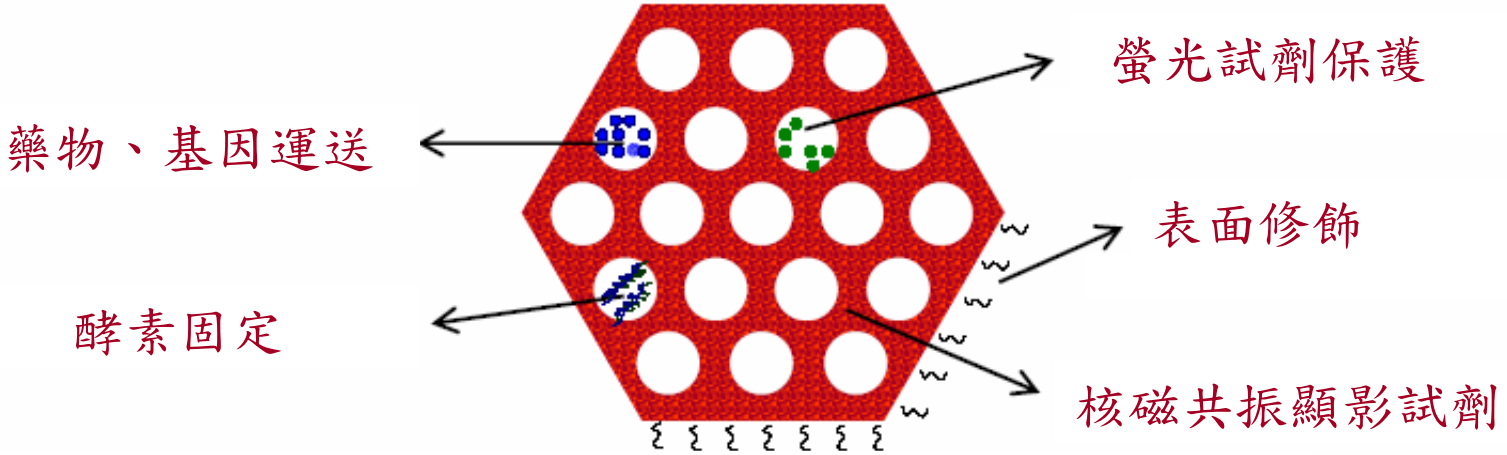
信號發射台:

追 蹤



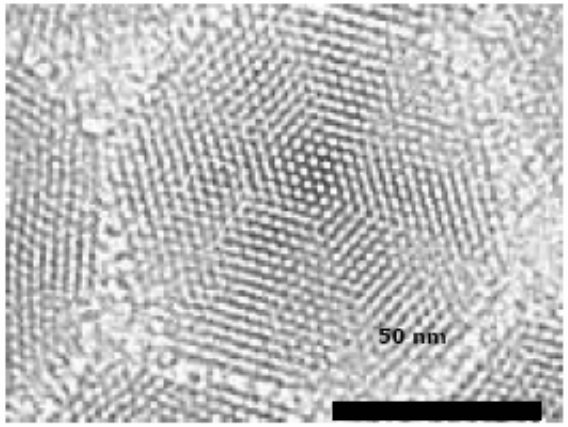
“奈米容器”在生物醫學上應用：

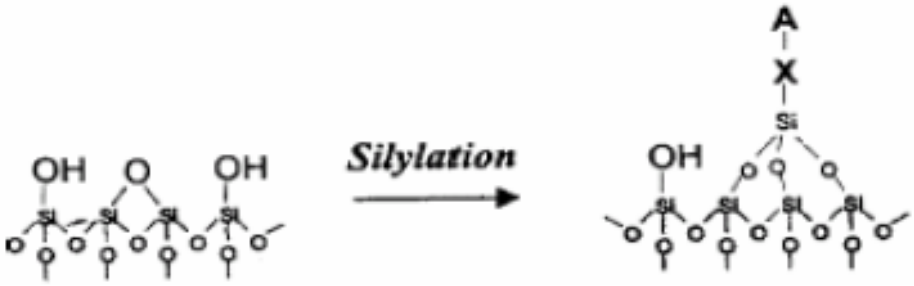
奈米中孔洞材料MCM-41於生物系統中扮演之攜帶角色



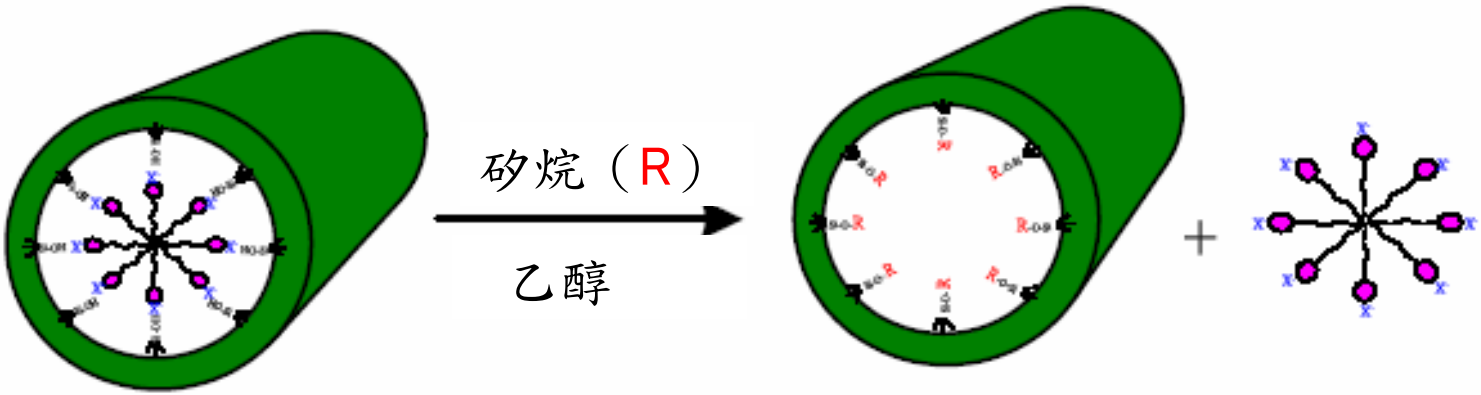
多功能的細胞追蹤、運送試劑

- 無生物毒性
- 高細胞滲透率
- 附以有機試劑保護
- 導引、判定、殲滅



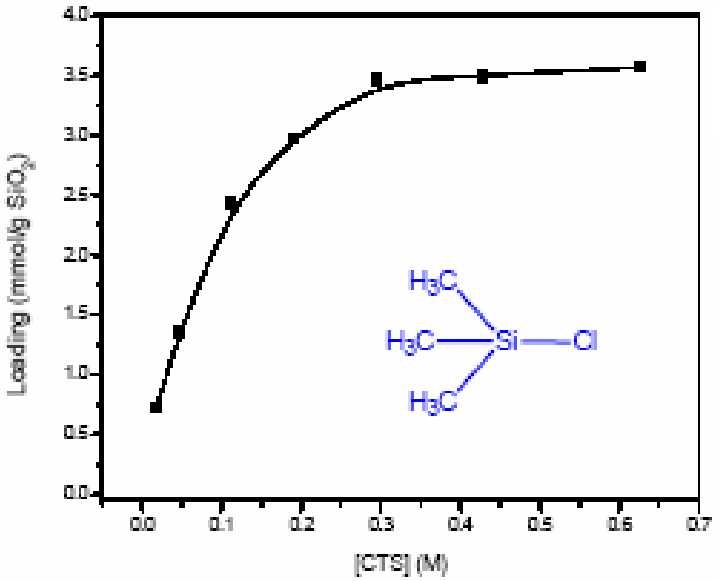


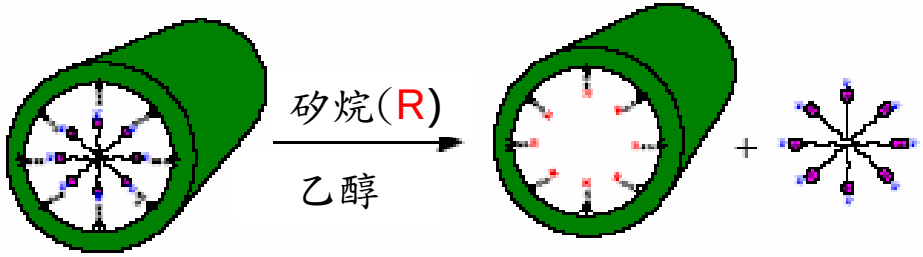
有機矽烷化合物直接修飾於中孔洞矽材



：介面活性劑　　矽烷　：$R_3Si\text{-}Cl$ or $R\text{-}Si(OR)_3$

吸附等溫曲線

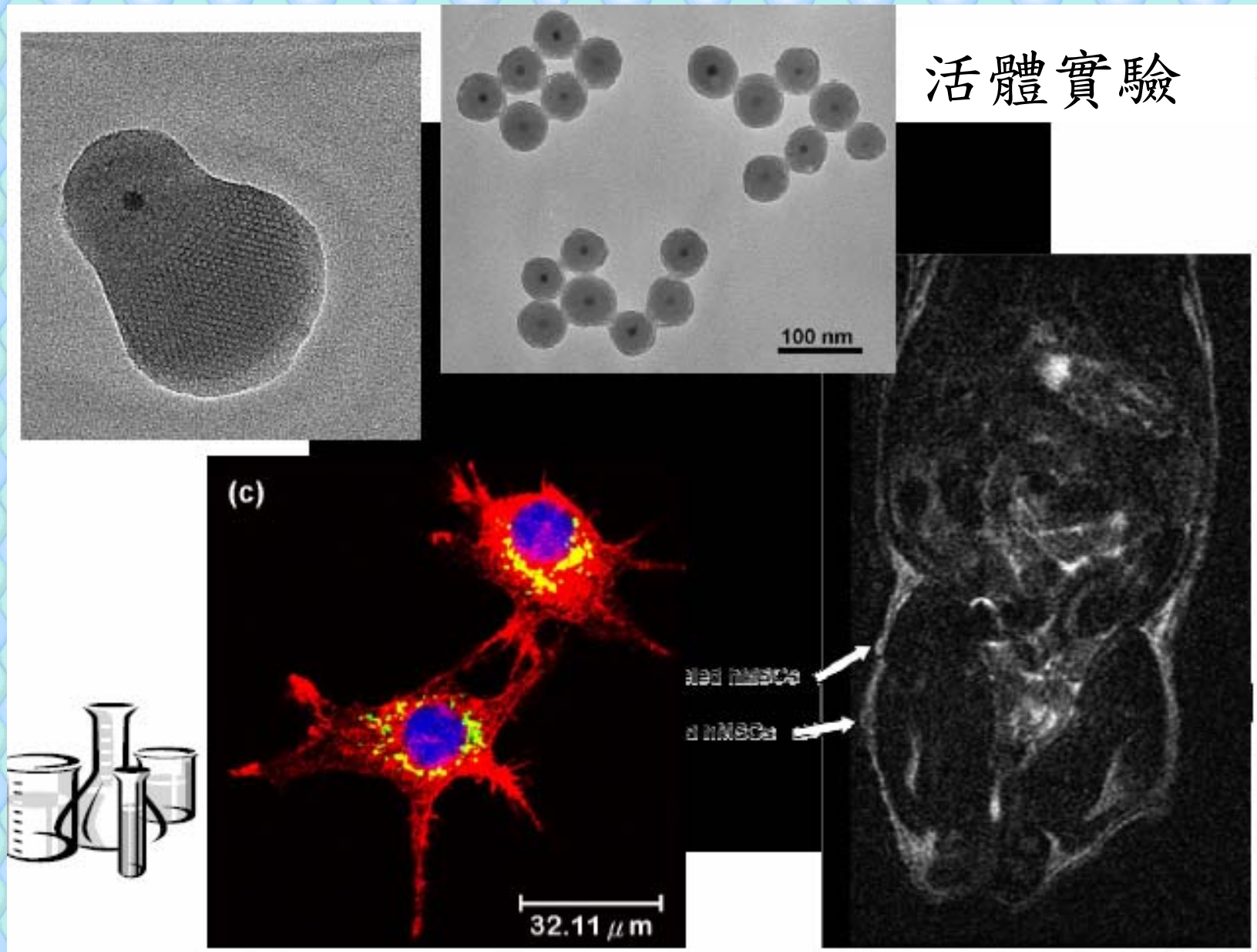




較弱的氫鍵
交互作用力

較強的化學共價鍵
交互作用力

活體實驗



Cell Uptake

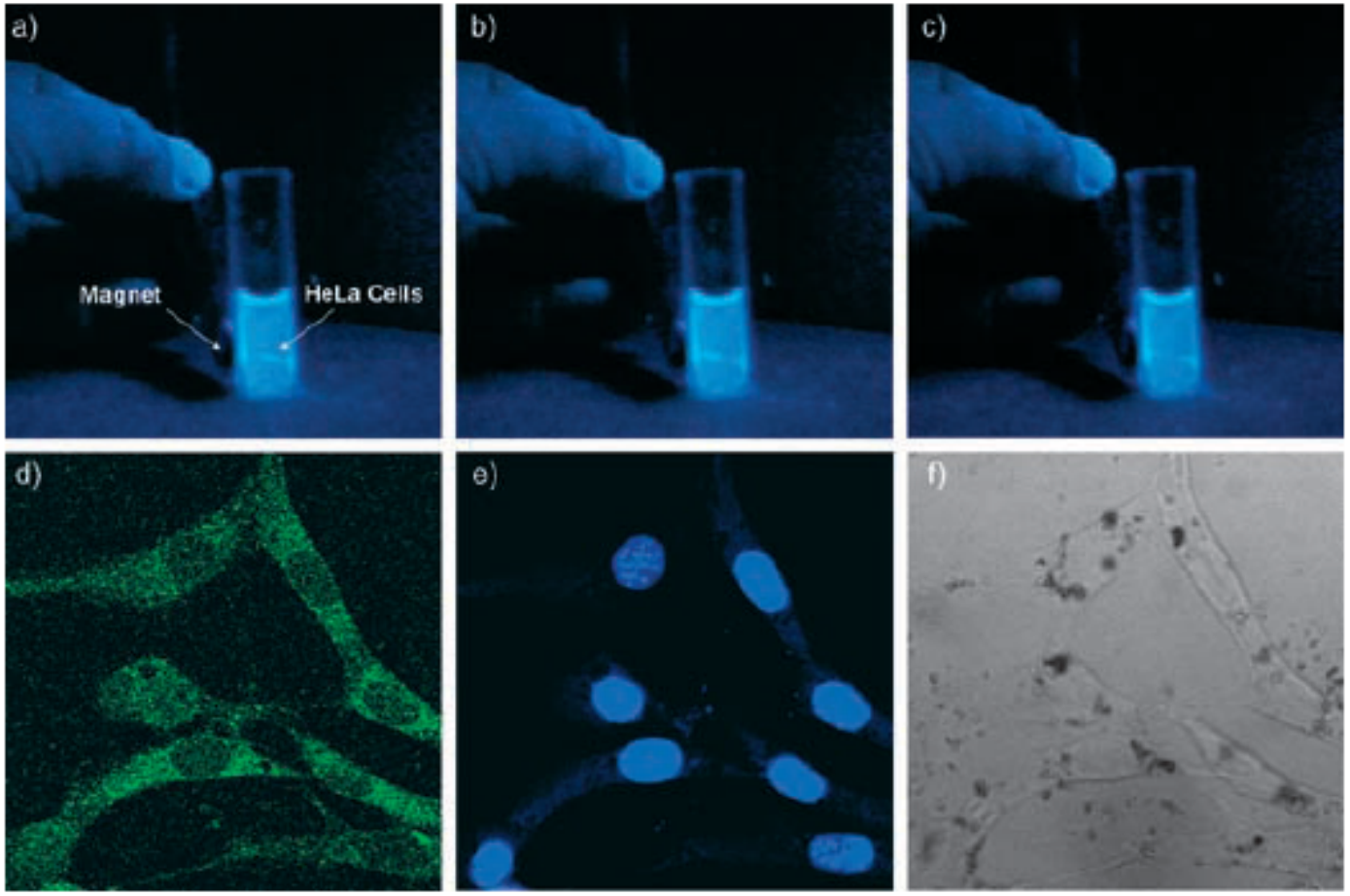
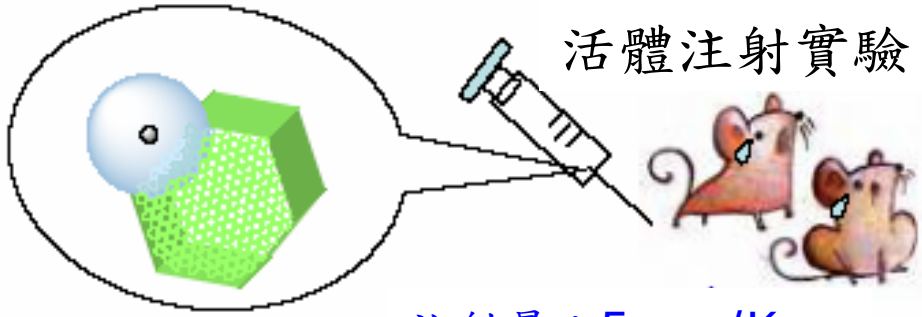


Figure 5. a–c) Single frames of photographs of HeLa cells with Fe_3O_4-capped fluorescein-loaded MSNs traveling across the cuvette, propelled by magnetic force. d–f) Fluorescence confocal micrographs of HeLa cells after 10 h incubation with Fe_3O_4-capped fluorescein-loaded MSNs: d) cells excited at 494 nm; e) cells excited in the UV region; f) a pseudo-brightfield image, where dark aggregations of magnet-MSNs can be clearly observed.

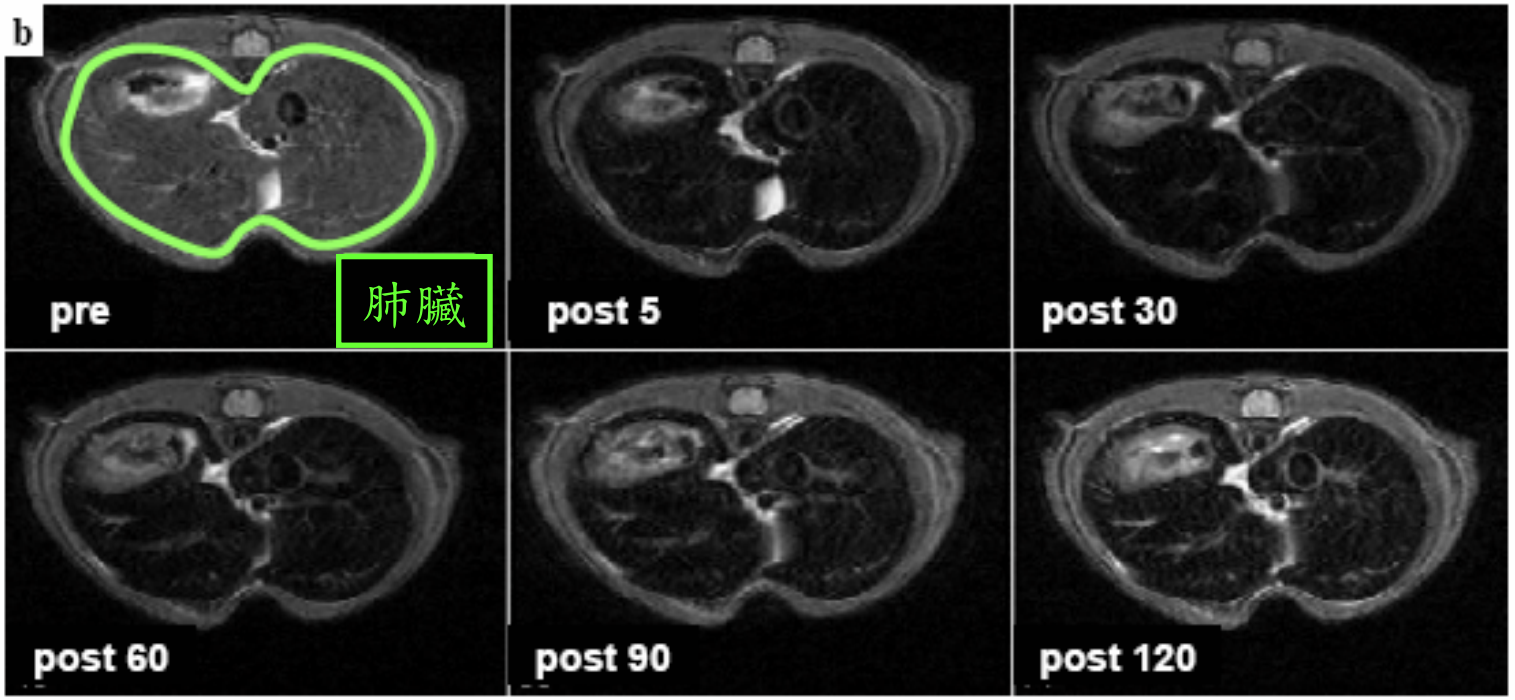
T_2 Weighted Imaging– 腎臟、脾臟、肺臟

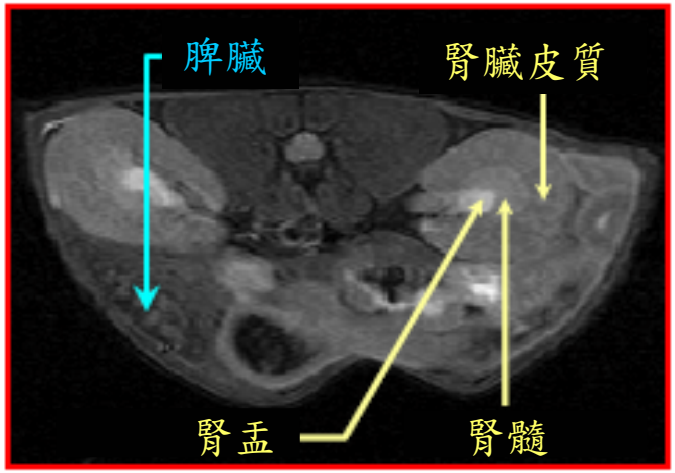


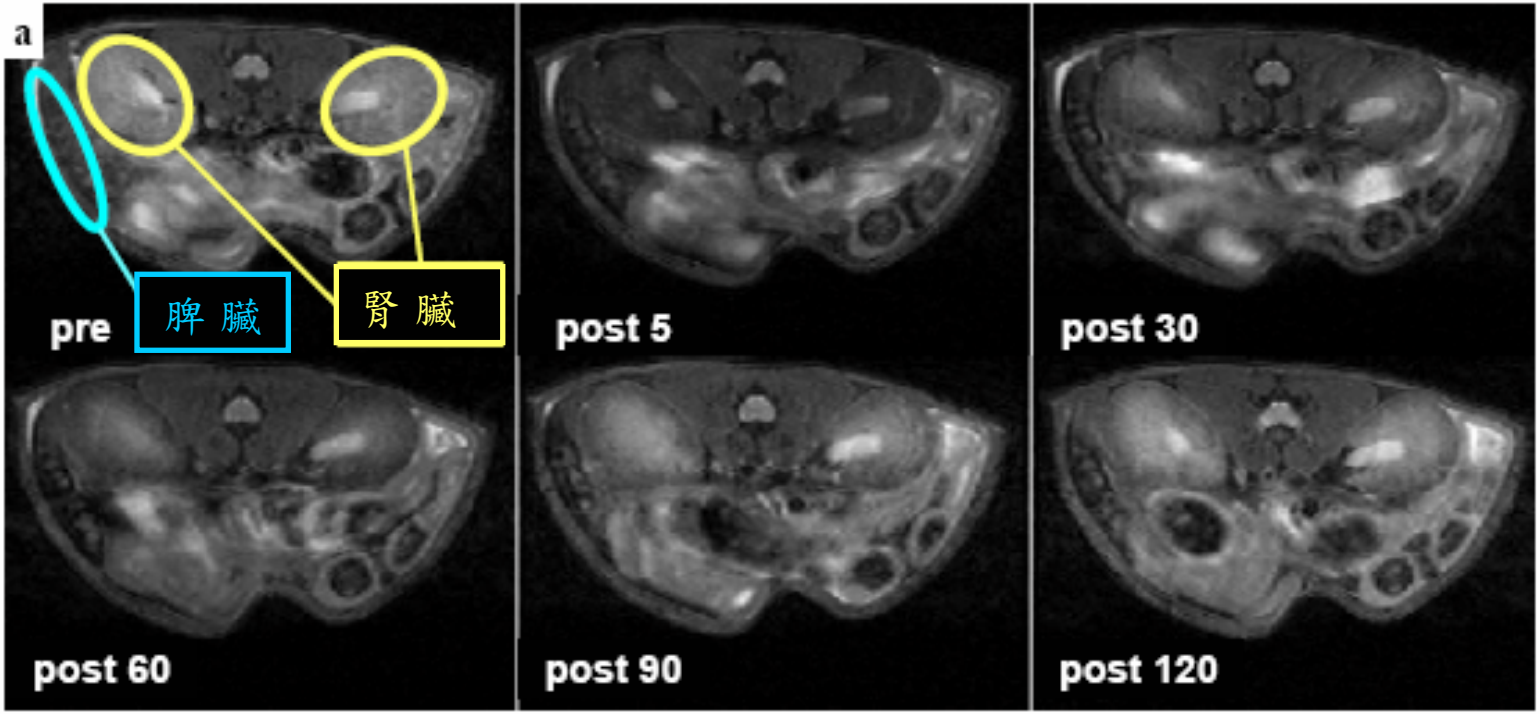
活體注射實驗

核磁共振顯影

注射量：5 mg/Kg

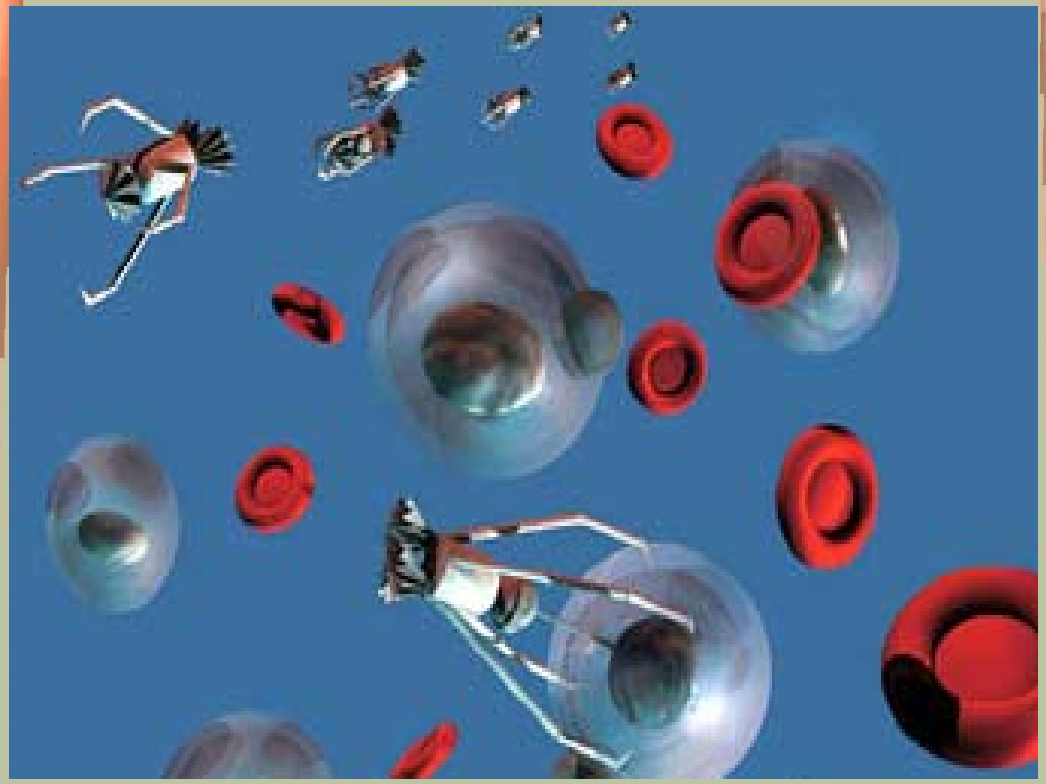


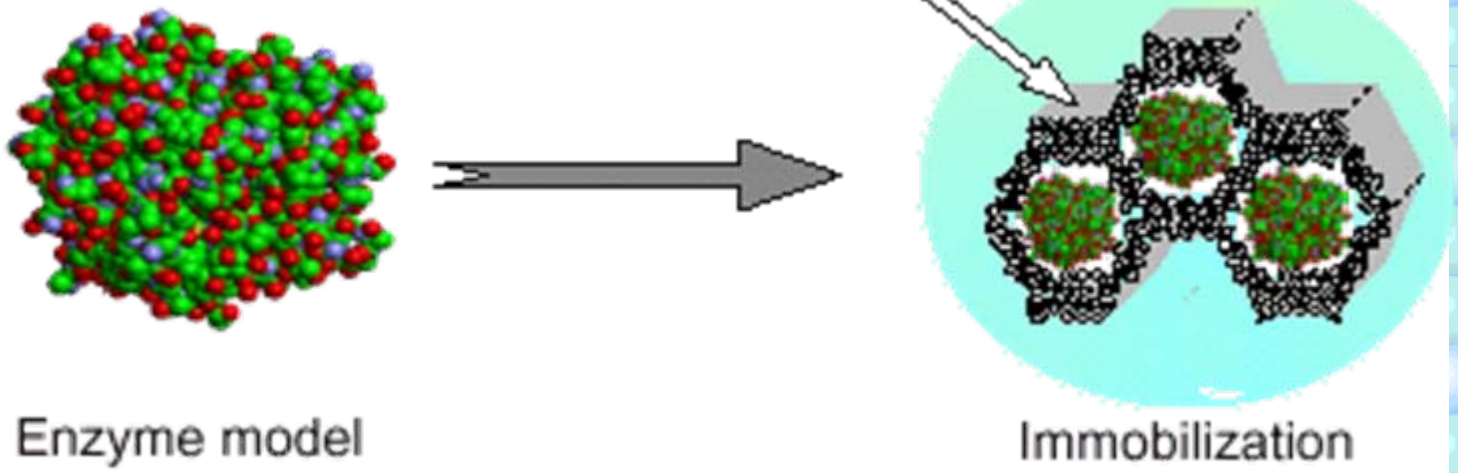

脾臟
腎臟皮質
腎盂
腎髓


a
脾 臟
腎 臟
pre
post 5
post 30
post 60
post 90
post 120

瞄準器：

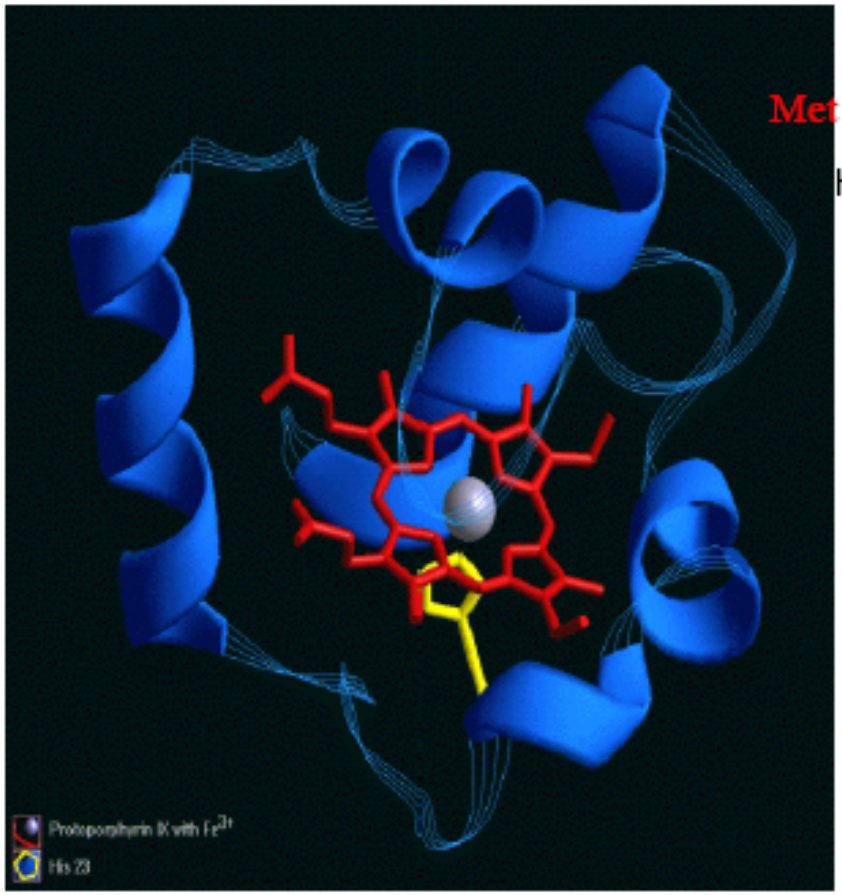
“細胞辨識”

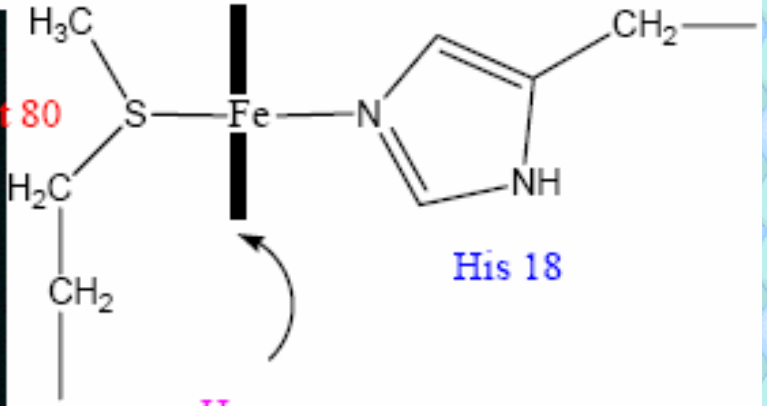




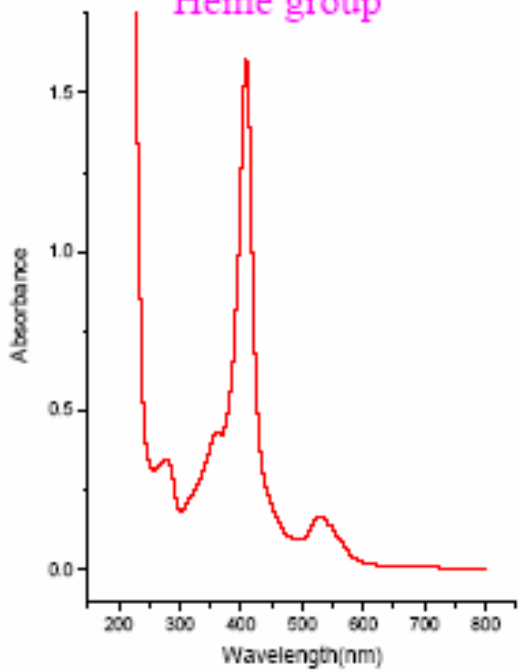
High Stable Biocatalyst by Mesoporous Silicate-Immobilized Cytochrome c for Polycyclic Hydrocarbon oxidation

Structure of cytochrome- C

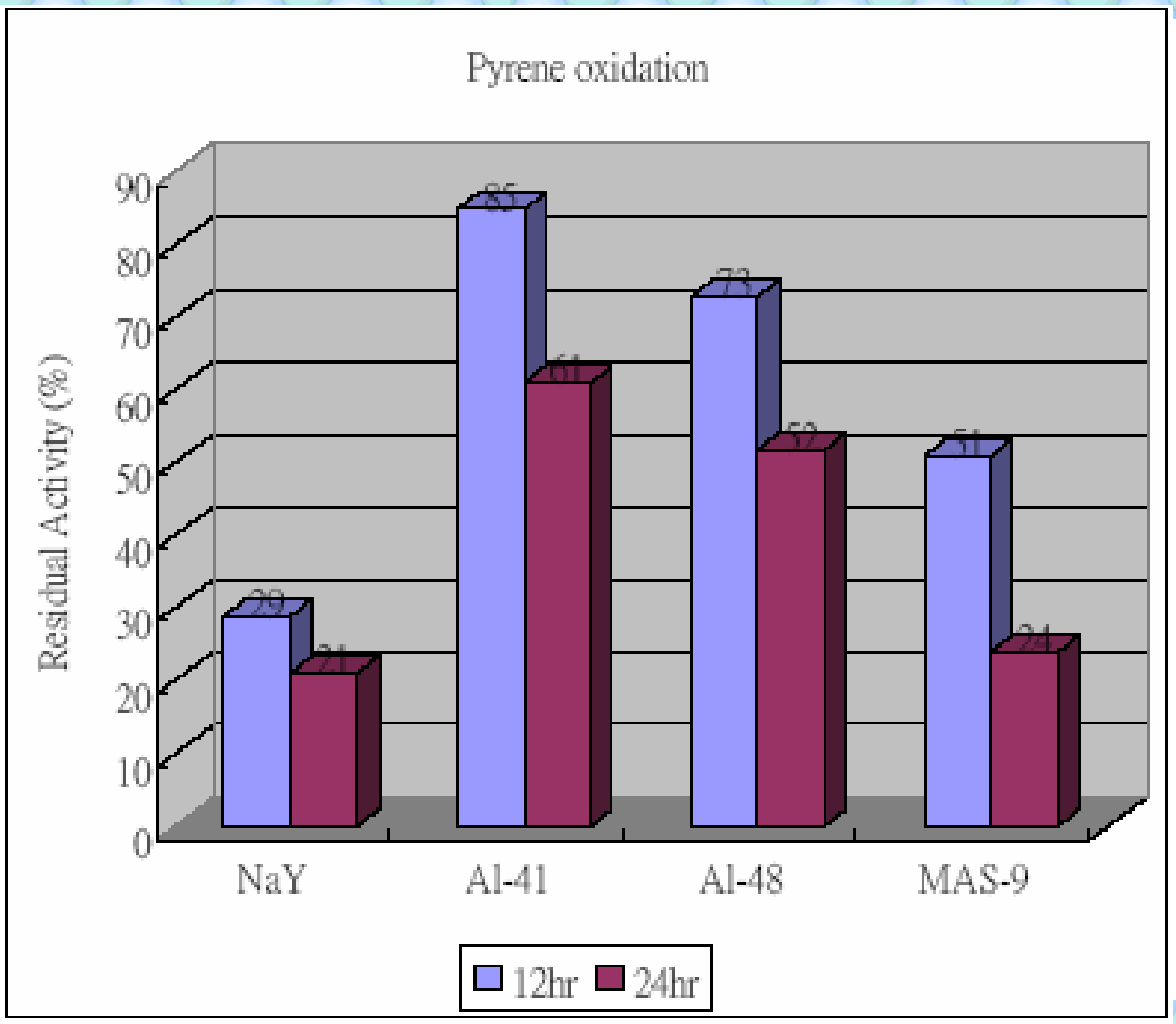




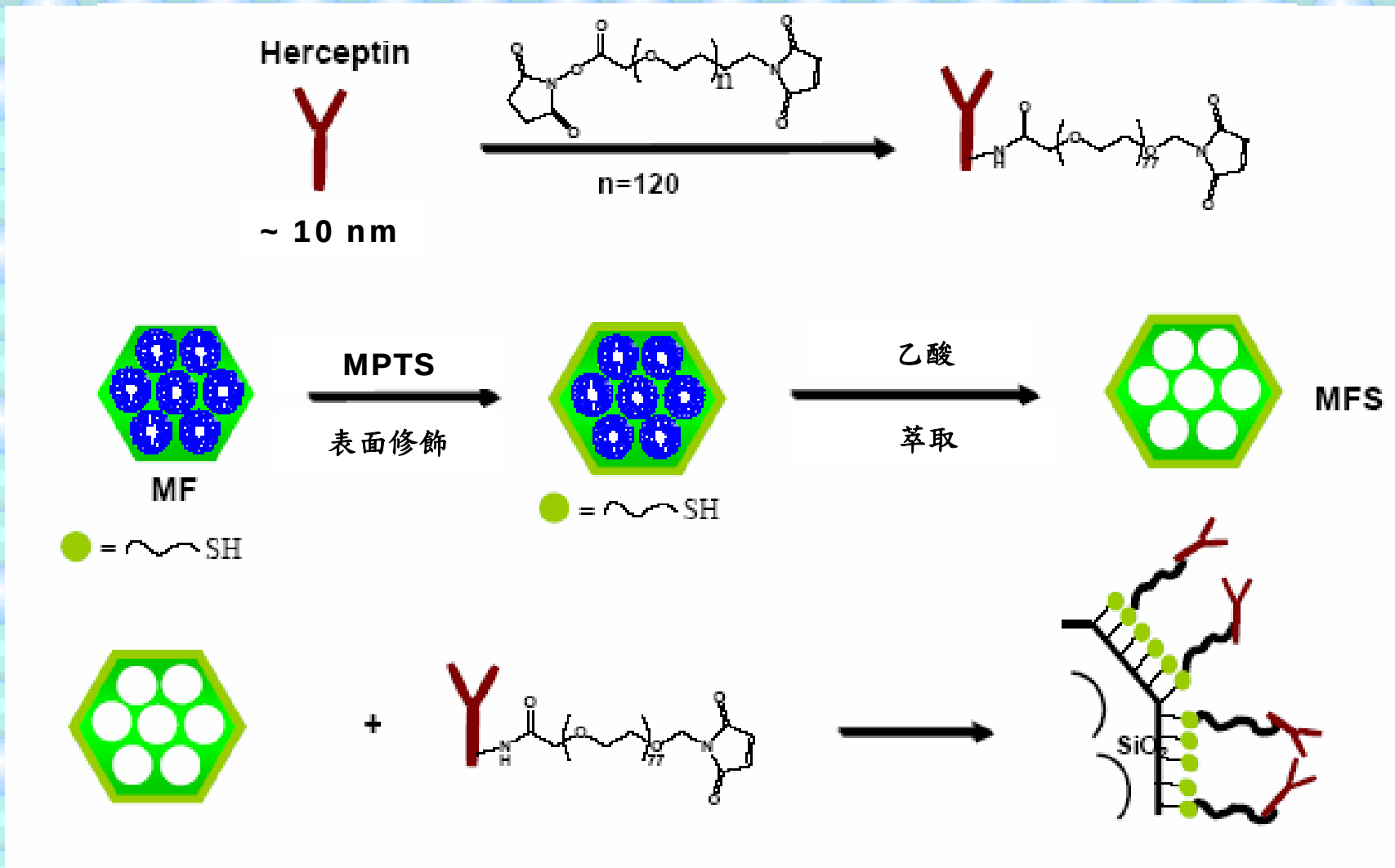
Heme group



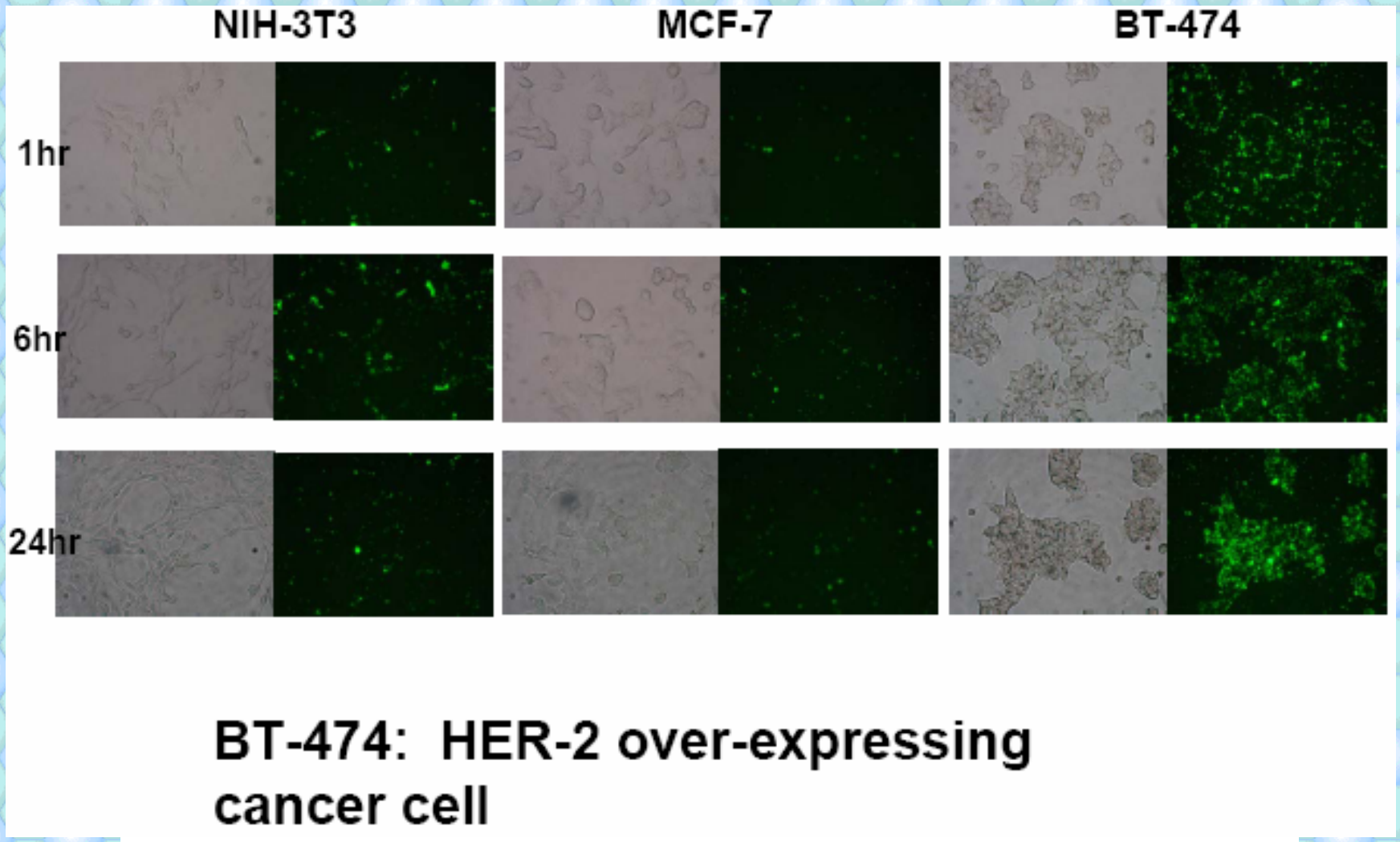
Residual activity (%) versus incubation time at 100 ˚C



F-MSN表面修飾以Herceptin



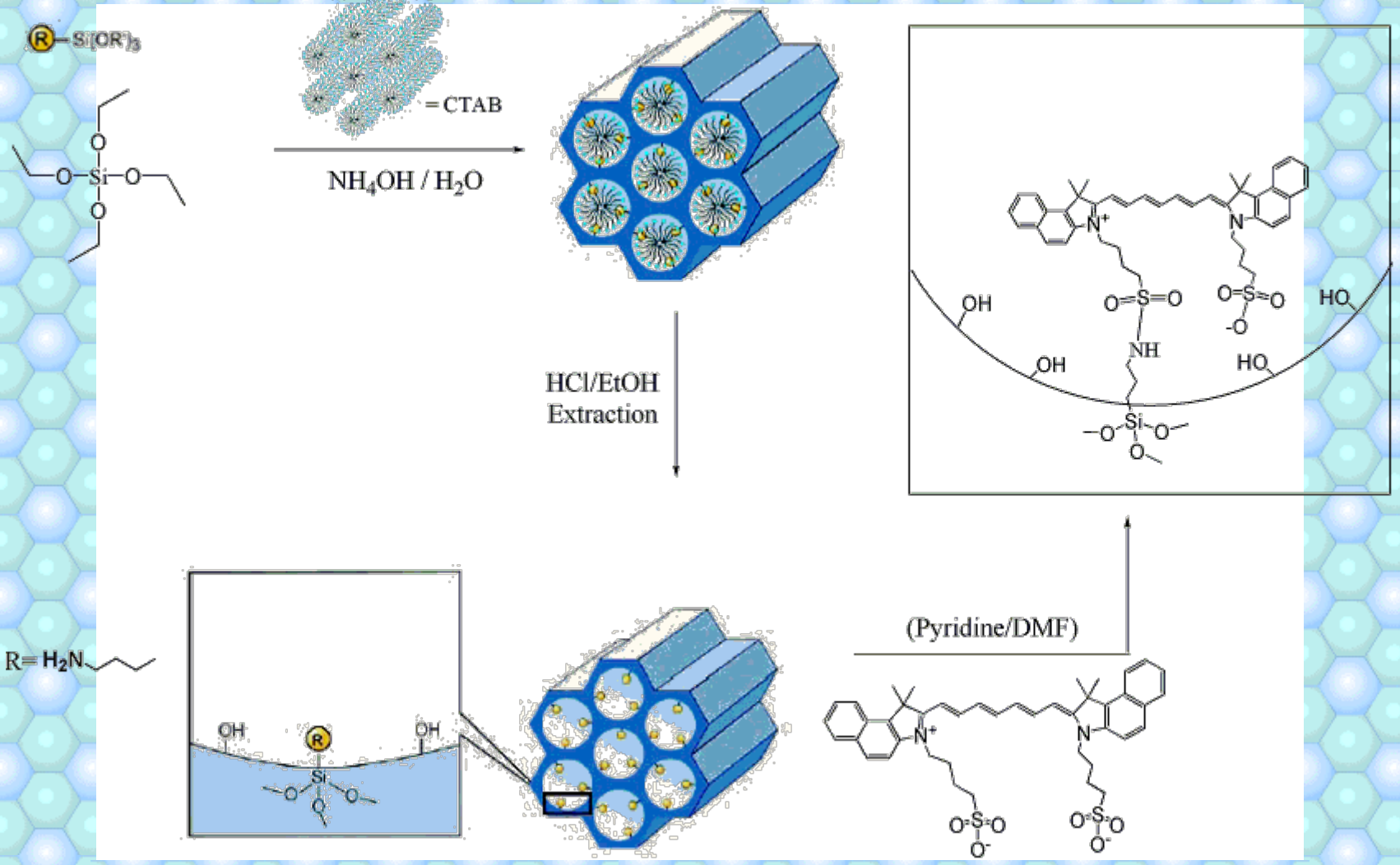
MSN-PG-Herceptin Target HER-2 Protein Over-Expressing Cancer Cell ~Different Incubation Time~



The Punch:

“藥物輸送”

“出　口”

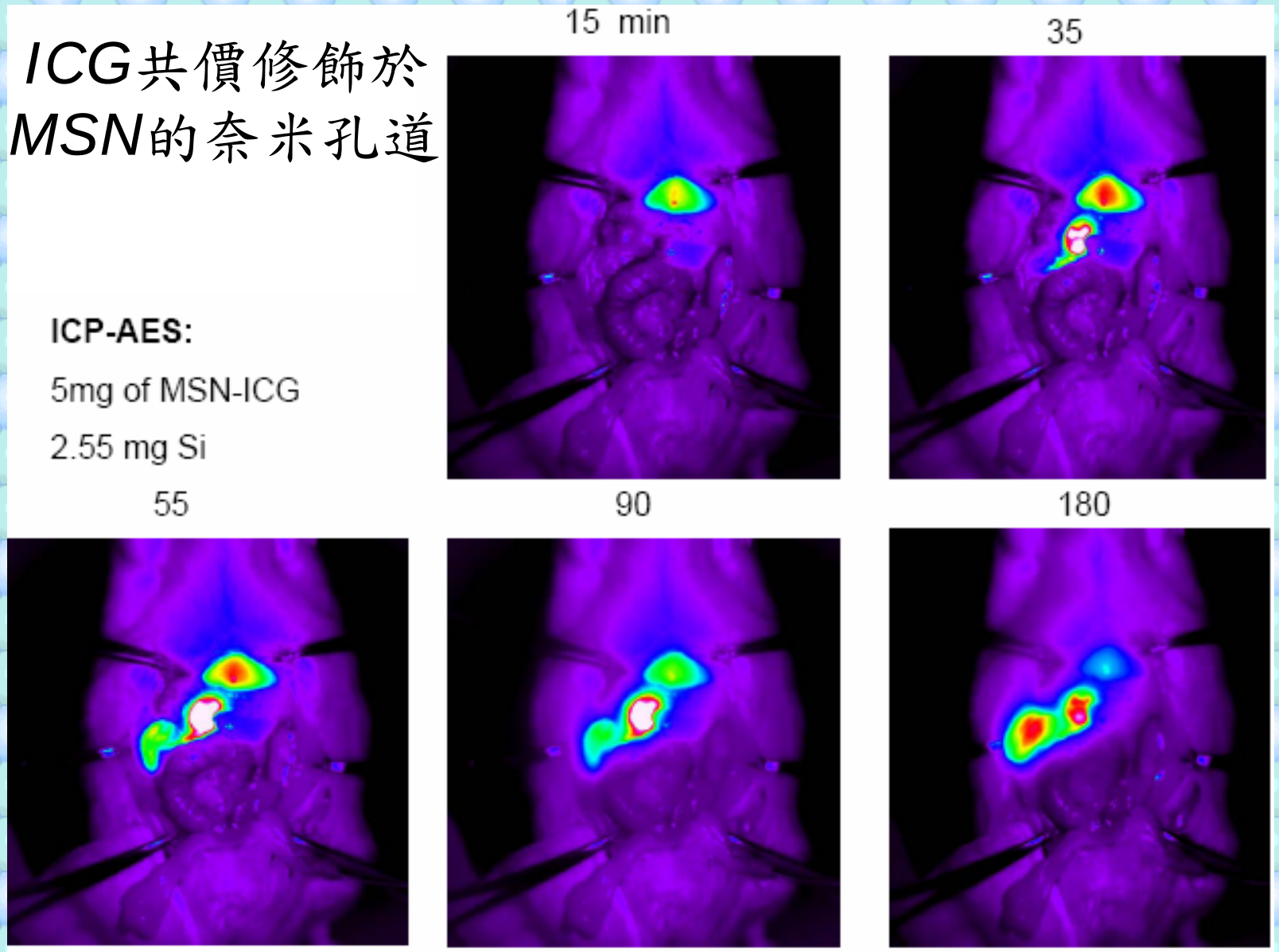

R—Si(OR')3
= CTAB
NH4OH / H2O
HCl/EtOH
Extraction
(Pyridine/DMF)
R= H2N
OH
HO
NH
ICG

*ICG*共價修飾於*MSN*的奈米孔道

ICP-AES:

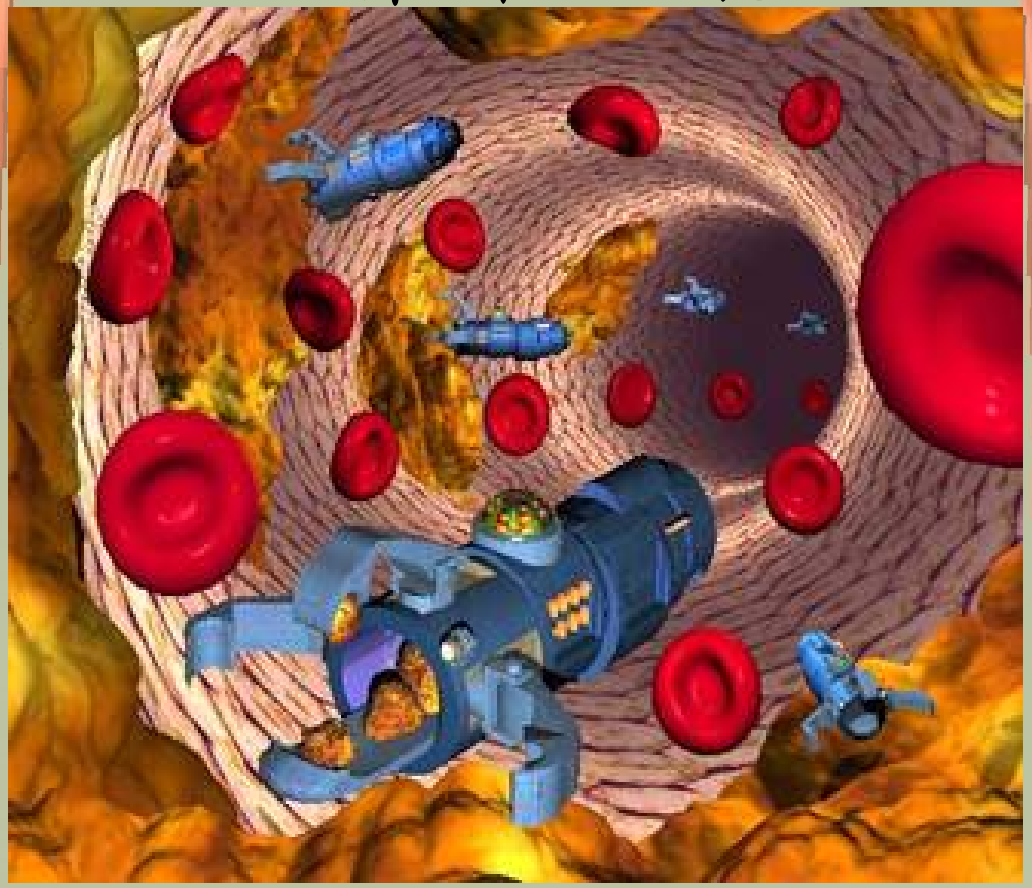
5mg of MSN-ICG

2.55 mg Si



未來夢想：

“奈米工廠”



Interdisciplinary Research

跨領域的研究

- 基礎科學
- 注意各領域現存尚未解決的問題
- 必須跳脫傳統傳統思維
- 功勞應共享
- 長期合作並非易事，除非有共享的宏觀視野


The End
Thank you for your attention

The Cast

洪燕　博士

林弘萍　教授
林天送　教授
陳永芳　教授
張　程　教授
陳耀昌　教授
黃東明　博士
劉緒宗　教授
陳振中　教授
鄭淑芬　教授
萬本儒　教授
劉尚斌　教授
朱明文　博士

蔡福裕博士
陳藹然博士
路芳　博士
趙曼倩博士
曾耀弘博士

王愛琴博士
陳曉蓉博士
黃信炅博士
鄧金培博士
林夏玉博士

蔡智斌
方雅貞
葉奕琪
羅苡嘉
劉高翔
吳思翰
林叔瑜
蘇昱澤
陳佳政

林育申
涂熊林
紀育珊
劉沂欣
李佳洪
陳壁彰
施文塵
黃志超
林孟良
閻君皖
江嘉雯
劉俊鴻
洪伸錡
王榮輝
施貝淳

國科會
教育部
中國石油公司
台灣大學
　化學系
　凝態中心

Sow-Hsin Chen(MIT)

F. Mallmace (Messina)

A. Faraone(NIST)