奈米生醫材料

演講者：鄧金培（淡江大學化學系）

99年4月27日

1. Introduction

2. Toxicity

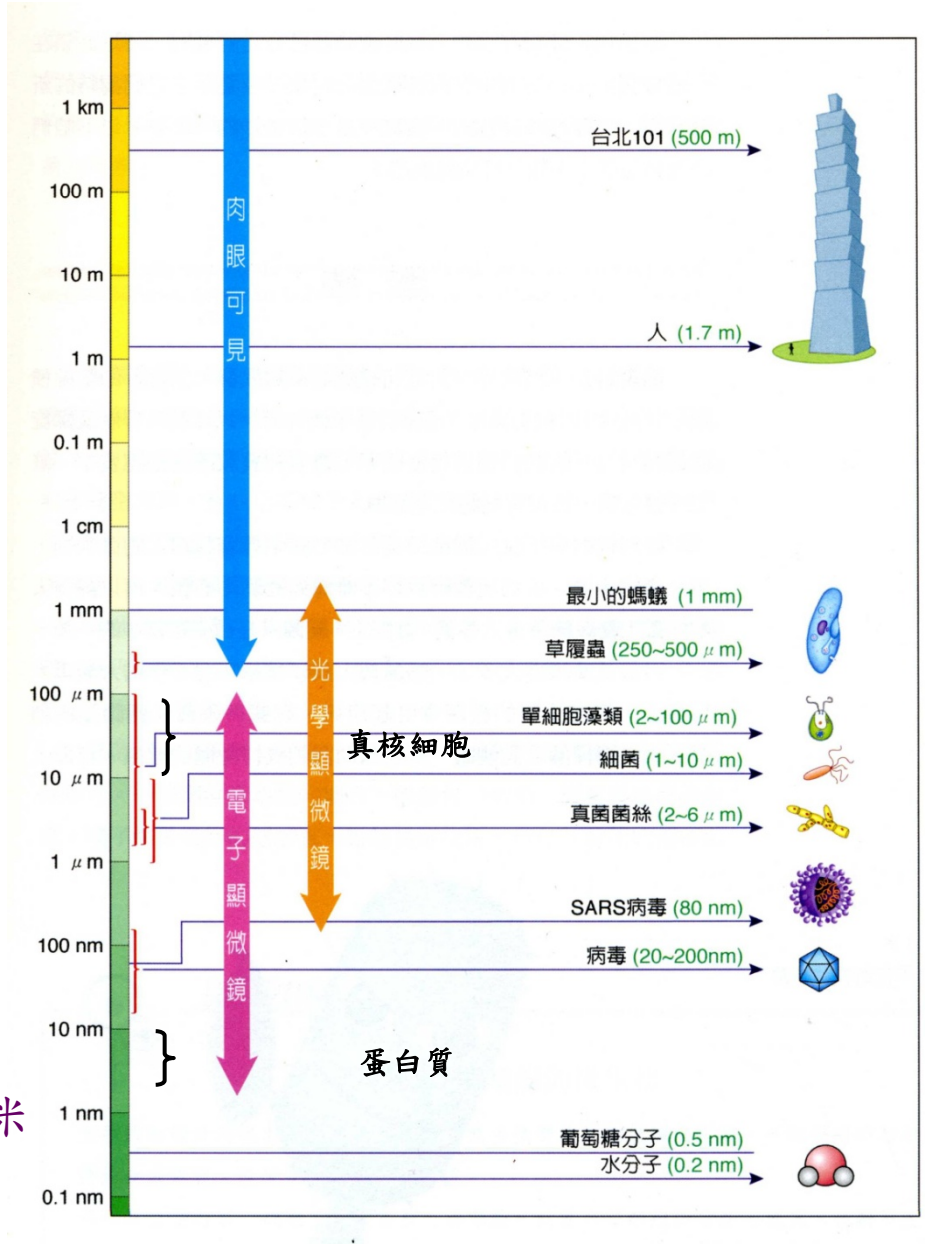
3. Sensor (detecting disease)

4. Label (on target)

奈米(nm, nano-meter)

1 奈米 = 10^{-9} (十億分之一) 公尺

1 埃 = 10^{-10} (百億分之一) 公尺
= 10^{-8} (億分之一) 公分



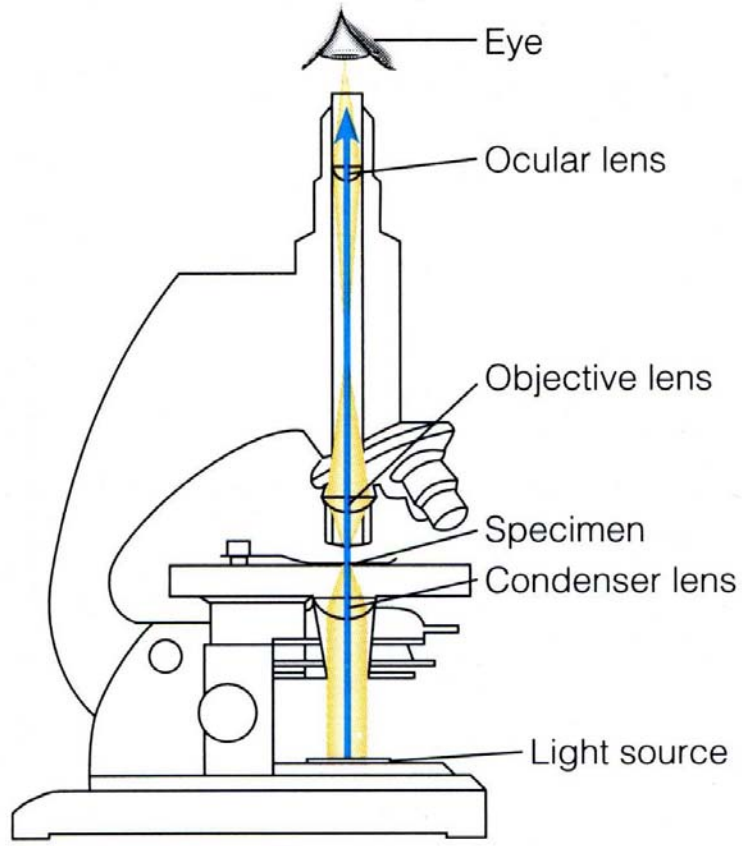
奈米尺度
(1 – 100 nm)

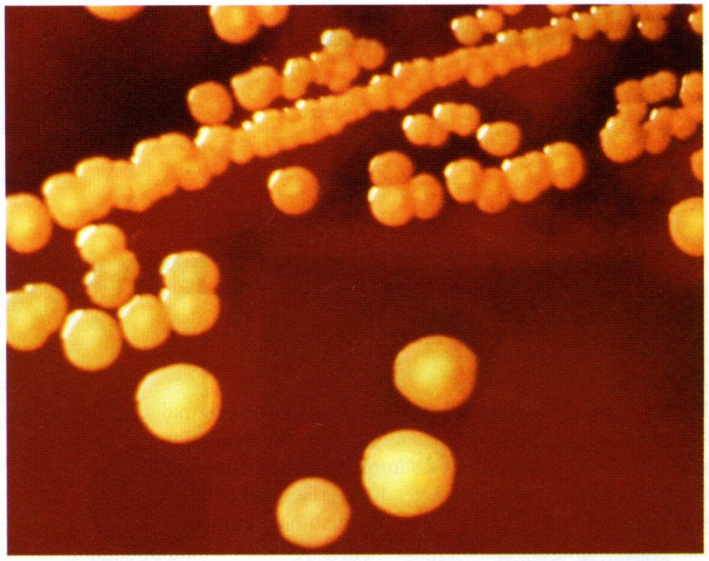
奈米

埃

觀測工具

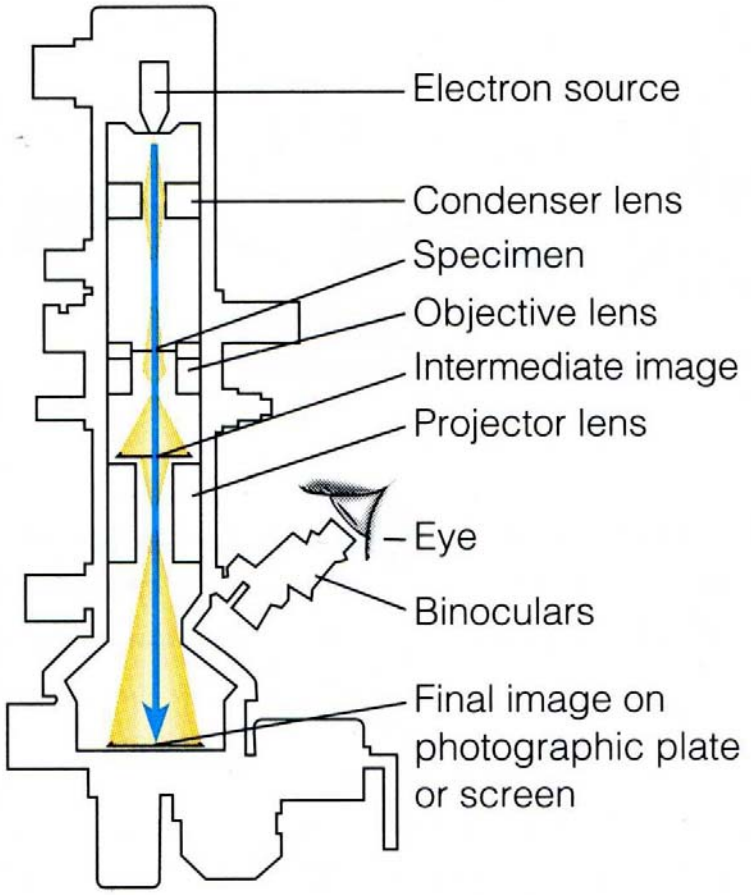
光學顯微鏡





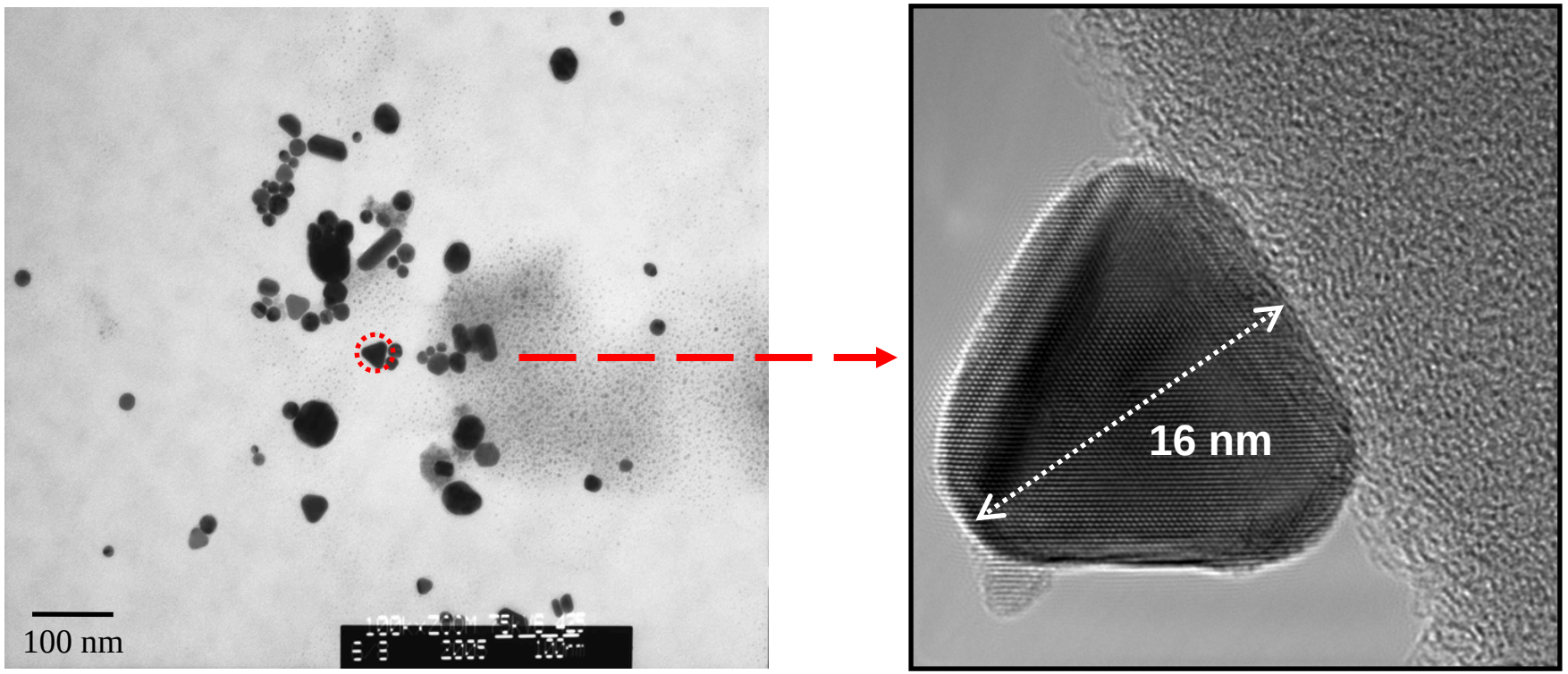
金黃色葡萄球菌 (在洋菜培養基)


TECNAI


Electron source
Condenser lens
Specimen
Objective lens
Intermediate image
Projector lens
Eye
Binoculars
Final image on
photographic plate
or screen

穿透式電子顯微鏡

金奈米顆粒在電子顯微鏡下的影像

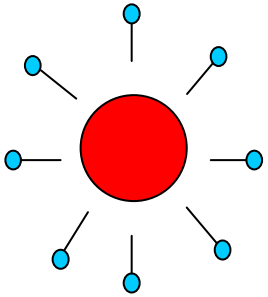


Synthesis of Au Nanoparticles in aqueous solutions

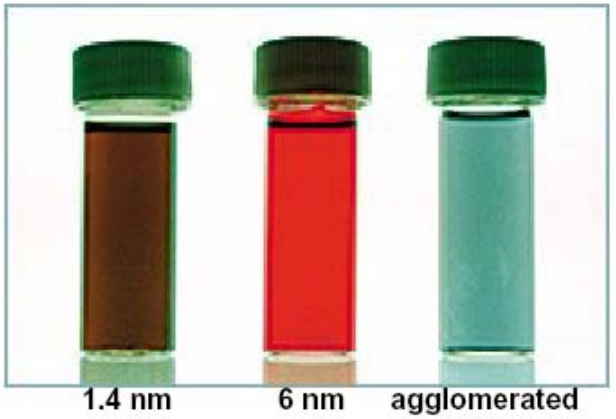
Stabilizers : polymer, thiol and surfactant

Surfactants : cationic. anionic and neutral

e.g., $CH_3(CH_2)_{15}N(CH_3)_3^+Br^-$ (CTAB)

CTAB $\xrightarrow[2.\ NaBH_4]{1.\ HAuCl_4}$ 

(By chemical reduction)



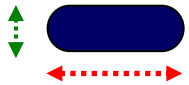
Synthesis of Au nanorods in aqueous solutions

CTAB + organic additives : Soft Rod-shape Micellar Structure

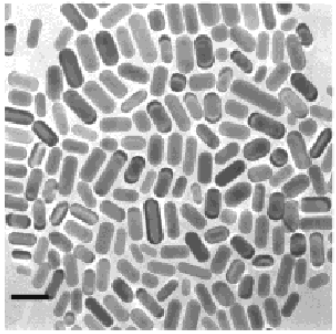
e.g., cyclohexane and acetone

CTAB/cyclohexane/acetone + $HAuCl_4$/ascorbic acid/$AgNO_3$

↓ Au NP seeds



Au Nanorod



C. J. Murphy and co-workers *Adv. Mater.* **2001**, 13, 1389

Keystones in Nanoscience

1. Size distribution

→ average size

(Electron Microscopes)

→ average physical properties

(UV-VIS, X-ray,…general instruments)

→ average chemical properties

(catalytic activity)

→ single nanoparticle detection

(special tools)

Introduction

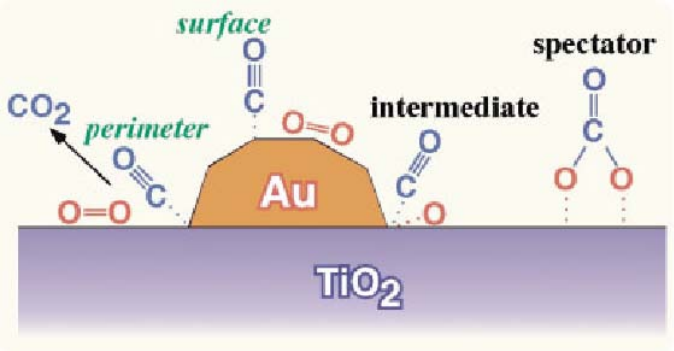
THE CHEMICAL RECORD

When Gold Is Not Noble: Catalysis by Nanoparticles (NPs)

MASATAKE HARUTA
Research Institute for Green Technology, National Institute of Advanced Industrial Science and Technology (AIST), 16-1 Onogawa, Tsukuba 305-8569, Japan

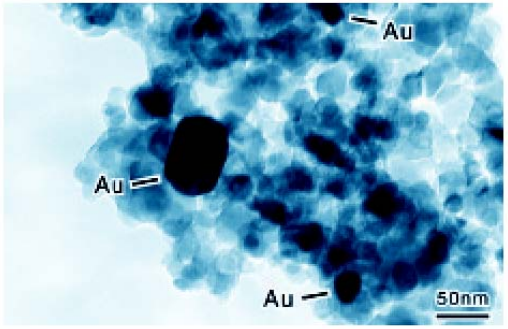
$$CO \xrightarrow[\text{Au (cat.) / support}]{O_2} CO_2$$

200 – 400 K

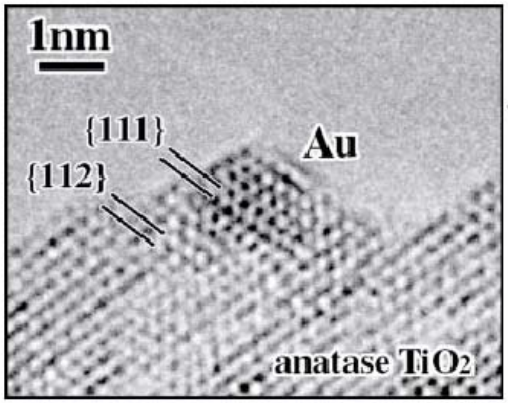


Haruta, M. et al
Chem. Record **2003**, *3*, 75

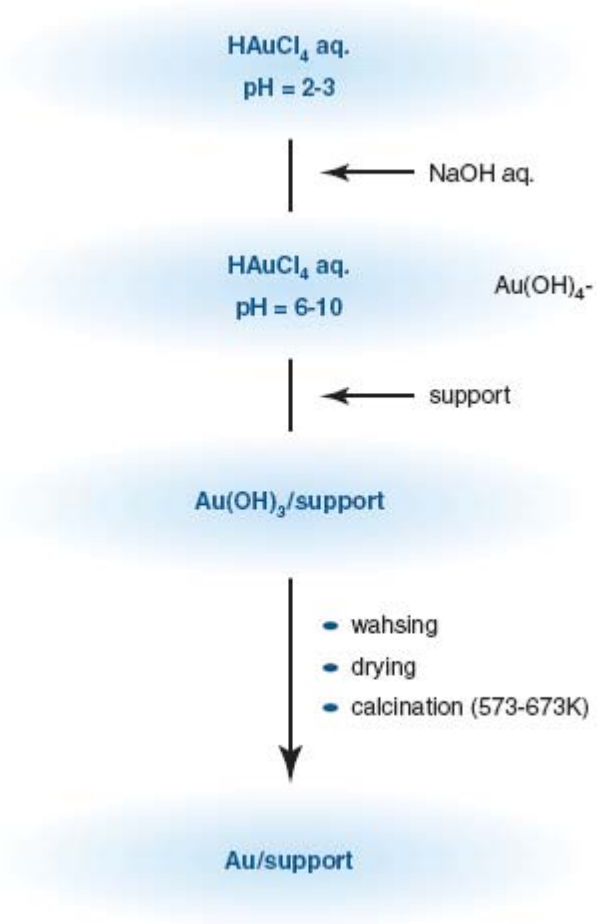
Size of Au NPs is controlled by the preparation method.



Prepared by Impregnation



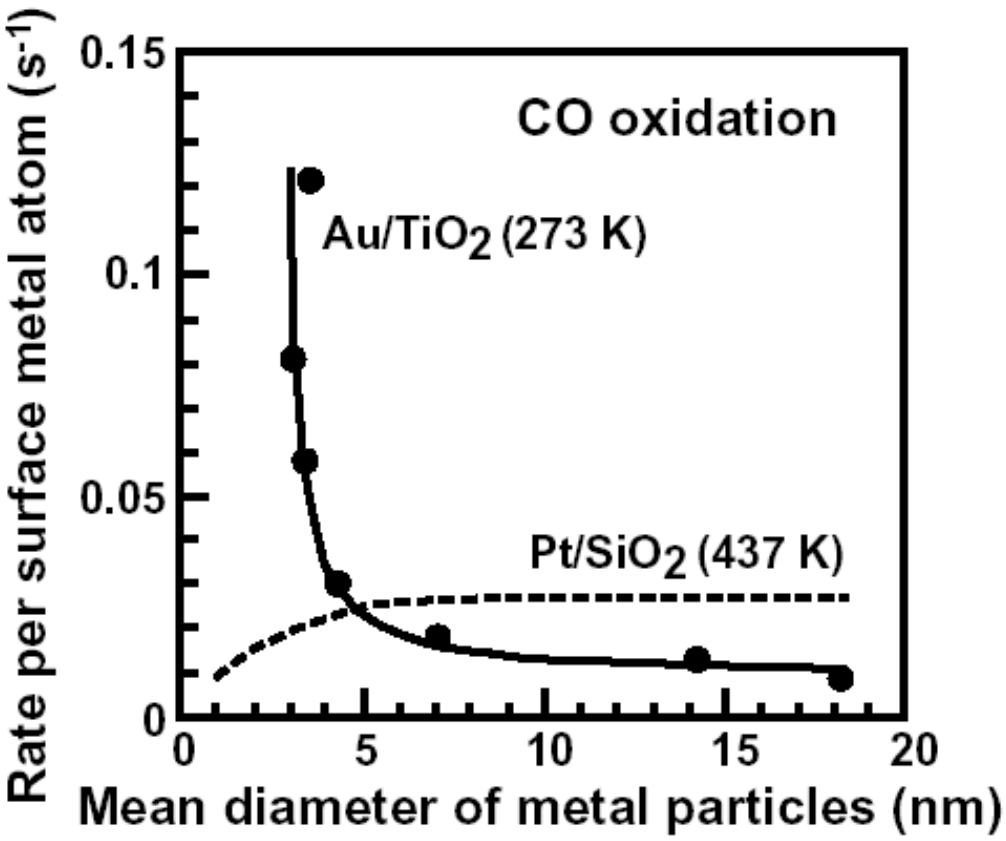
Prepared by Deposition-Precipitation



Flow chart of the procedure in the DP method.

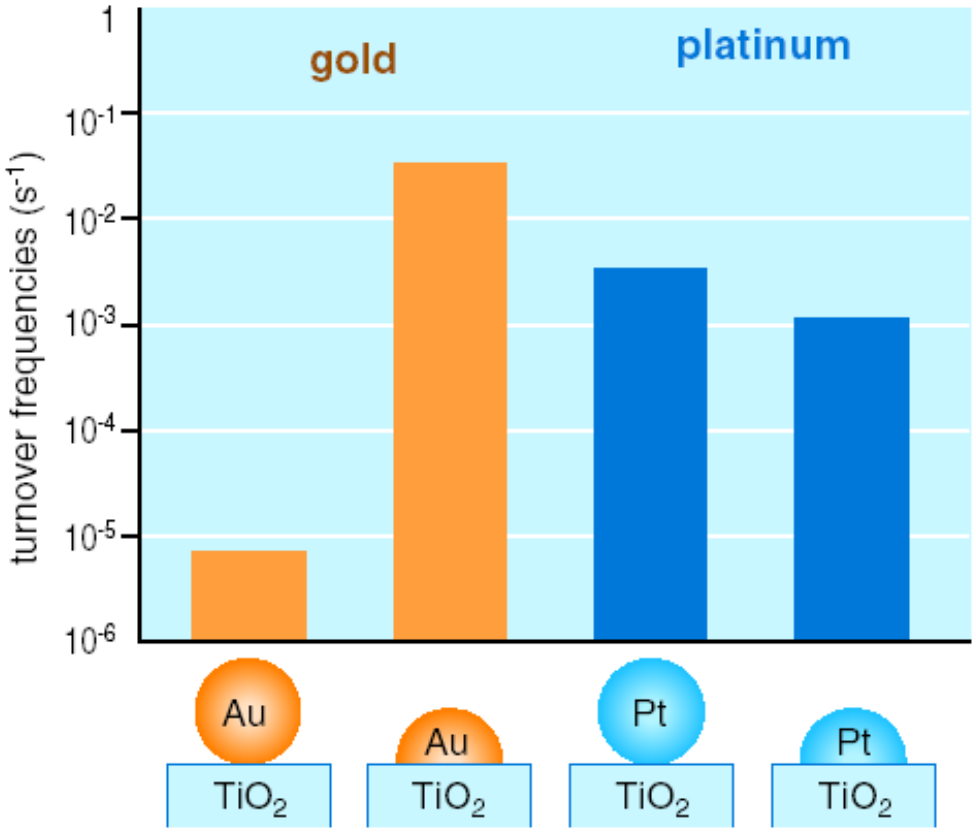
Haruta, M. et al
Chem. Record **2003**, *3*, 75

Size Effect of Au NPs on Reaction Rate



Haruta, M. et al
Chem. Record **2003**, *3*, 75

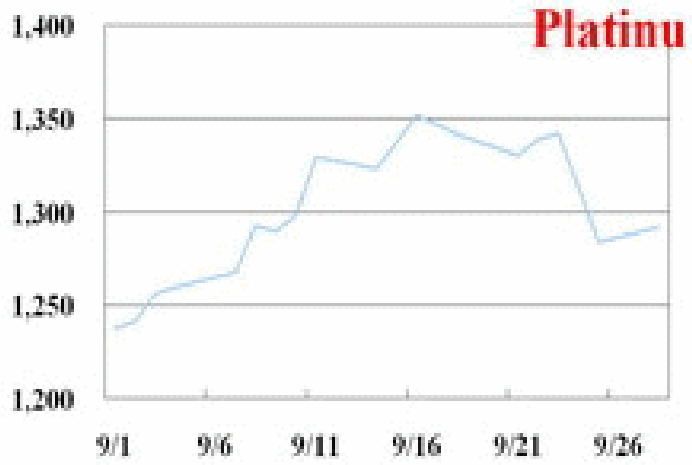
CO oxidation catalyzed by Au and Pt NPs



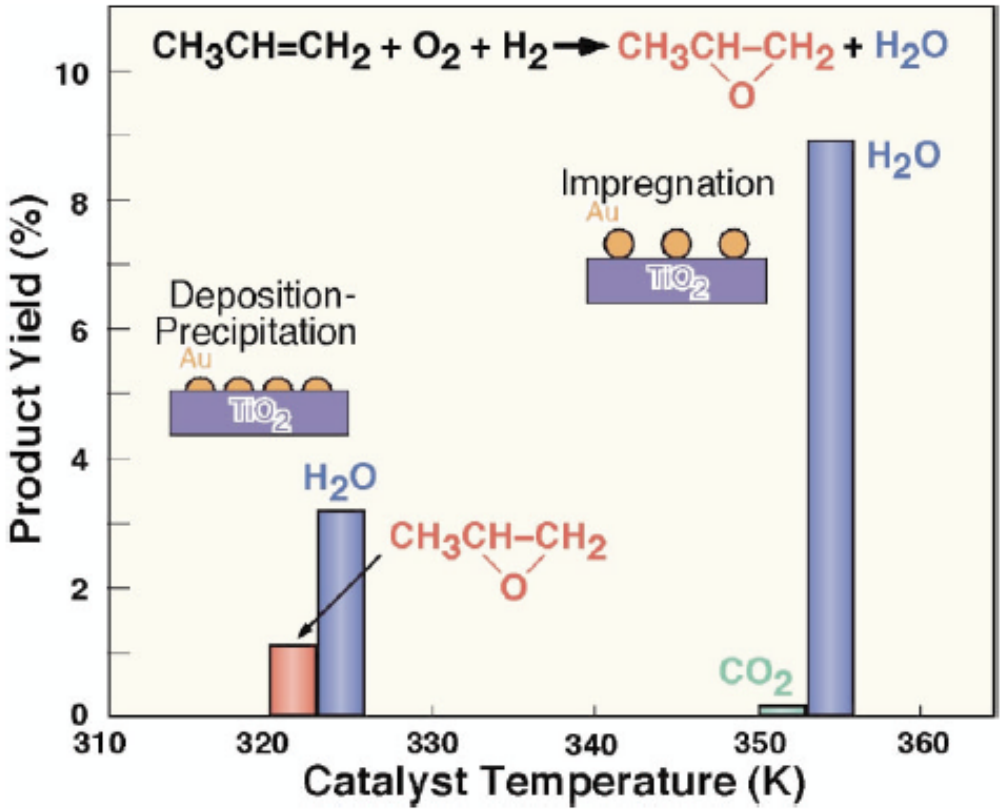
Haruta, M. et al
CATTECH **2002**, *6*, 102

2009 / 09 / 29		
METAL	PRICE	
Gold	1002.73	USD/T,oz
Silver	17.63	USD/T,oz
Platinum	1275.63	USD/T,oz
Copper	5993.34	USD/Ton

09/01 ~ 09/28 Trend Chart



Size Effect of Au NPs on Selectivity



Haruta, M. et al
Chem. Record **2003**, *3*, 75

Keystones in Nanoscience

2. Surface properties on nano-materials

- chemistry

  CO obstructs the surface and reduces the catalytic activity of nano-catalysts.

- physics

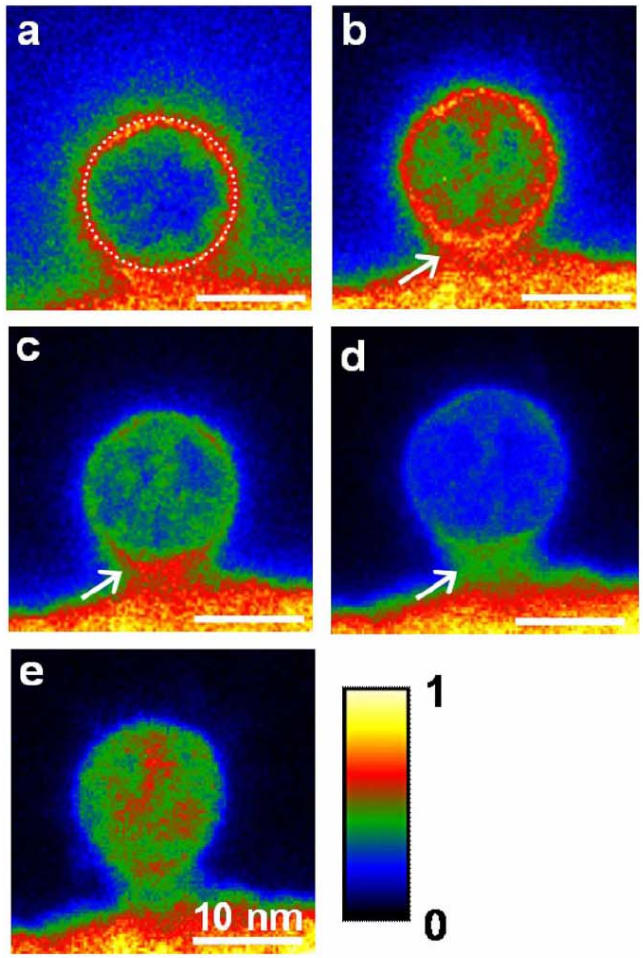


FIG. 4. (Color online) EFTEM imaging of a 13 nm Au NP. [(a)–(e)] EFTEM images acquired with an energy-selection slit of 2 eV in width at 2–4, 10–12, 14–16, 22–24, and 32–34 eV, respectively. The dotted circle in (a) indicates the projected surface of the NP. The arrows in (b)–(d) indicate the contrast enhancement due to the coupling to the amorphous carbon supporting film. The linearly normalized contrast scale is shown in the color bar.

1. Introduction

2. Toxicity

3. Sensor (detecting disease)

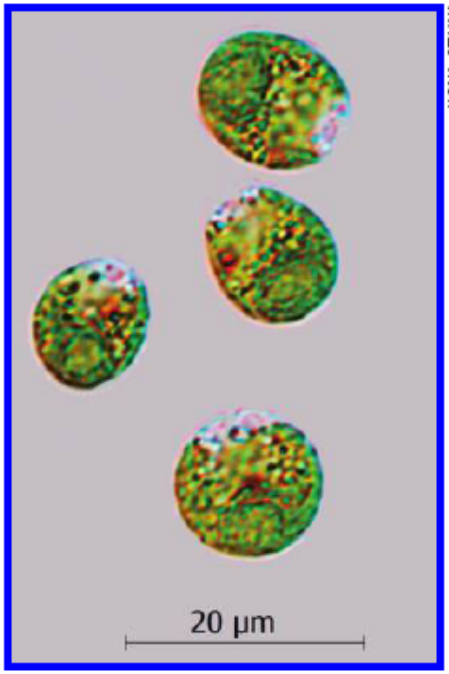
4. Label (on target)

Nanosilver toxicity: ions, nanoparticles—or both?

Nanosized silver presents an enigma. Silver nanoparticles themselves, because of their size and shape, could be toxic; on the other hand, silver nanoparticles could be toxic because they release silver ions, which are well-known for their antibacterial and other destructive behaviors. New research published in *ES&T* (DOI 10.1021/es801785m) presents evidence that points to both ions and nanoparticles as the source of nanosilver's toxicity, with nanoparticles furthering the ions' impacts.

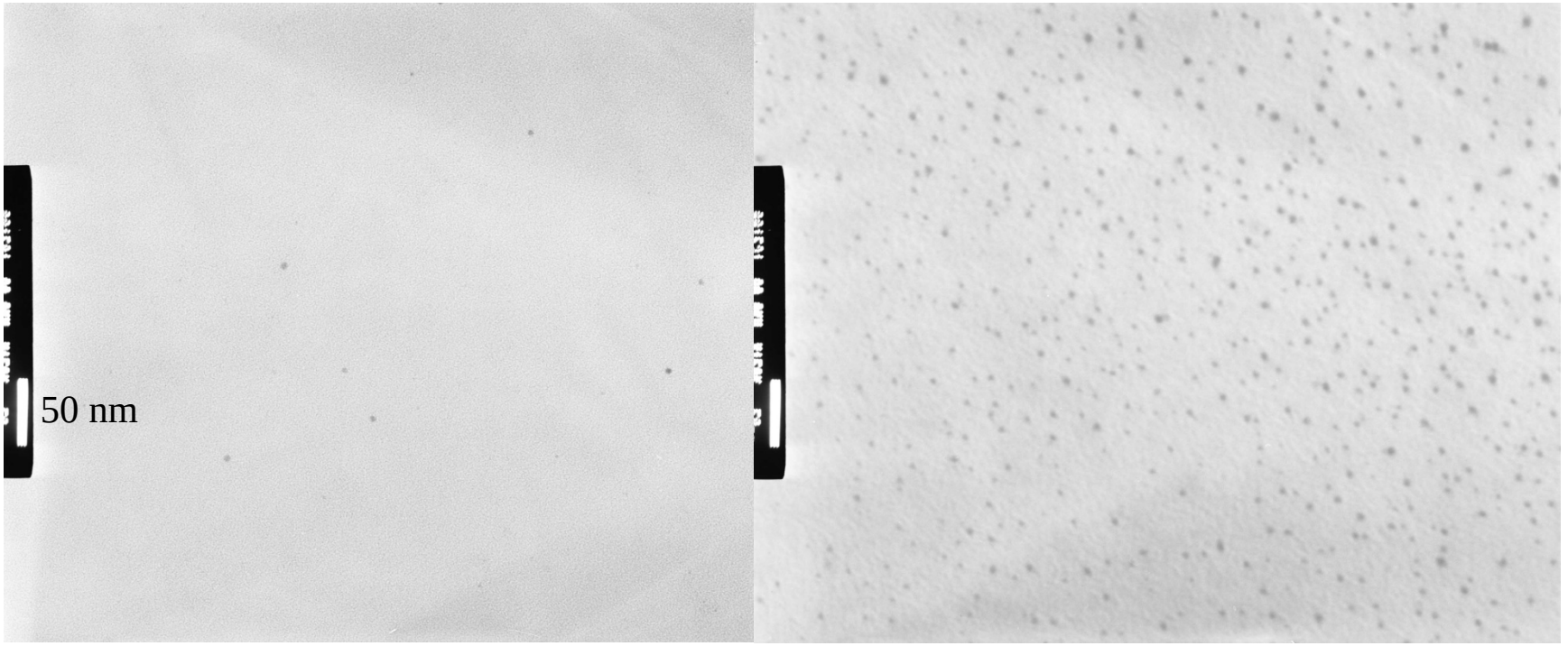
Scientists have grappled with the ion–nanoparticle question over the past few years as nanomaterials—silver and other kinds—have emerged as a topic of environmental concern. Hypothetical mechanisms of action include the direct interference of clumps or particles of nanosilver that settle on the surface of cells, disrupting cell behavior merely by making contact. Or silver particles might also act as a Trojan horse, entering a cell by bypassing its barriers to "normal"-sized silver, and then releasing silver ions that damage cell machinery.

But showing exactly how nanosilver might work in a living system has been problematic. In the new *ES&T* research, scientists hibited the algae's photosynthesis about 18 times more than nanosilver did. But after 2 hours, the nanoparticles continued to be even more toxic than the ions alone, the team reports. Adding cysteine to the algal bath removed many of the original silver

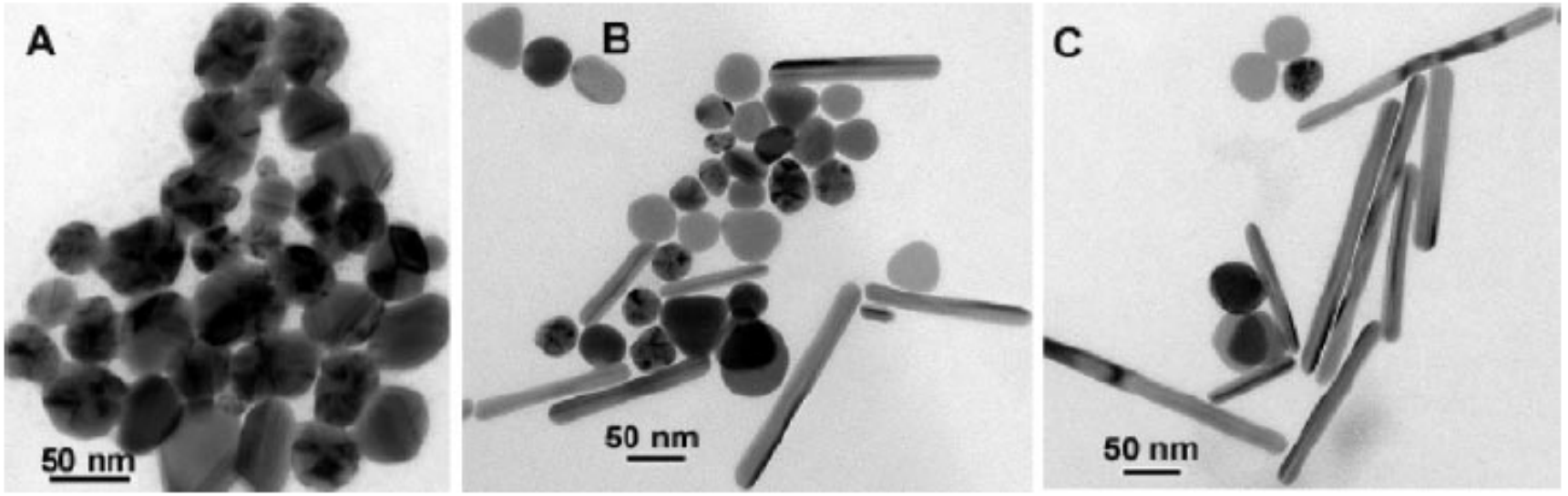


The algae *C. reinhardtii* provide a live model for interactions with nanosilver. Silver nanoparticles cut down on the plant's ability to photosynthesize through both nanoparticle and ion interactions, researchers say.

Ag Nanoparticles



Ag Nanoparticles



The study of antimicrobial activity and preservative effects of nanosilver ingredient

Abstract

In this study, we investigated the antimicrobial activity of silver nanoparticles (Ag-NPs) and platinum nanoparticles (Pt-NPs) aqueous solution, which were prepared using different stabilizer, such as sodium dodecylsulfate (SDS) and poly-(*N*-vinyl-2-pyrrolidone) (PVP), for *Staphylococcus aureus* (*S. aureus*) and *Escherichia coli* (*E.coli*) by measuring the minimum inhibitory concentration (MIC). Antimicrobial effect of Ag-NPs for *S. aureus* and *E. coli* was investigated using cup diffusion method. The growth of Gram-positive (*S. aureus*) and Gram-negative (*E. coli*) bacteria were inhibited by Ag-NPs. The MIC of Ag-NPs for *S. aureus* and *E. coli* were 5 and 10 ppm, respectively. But the Au-NPs stabilized with SDS did not show antimicrobial activity. Also, the Pt-NPs stabilized with PVP (or SDS) did not show antimicrobial activity for the test organisms.

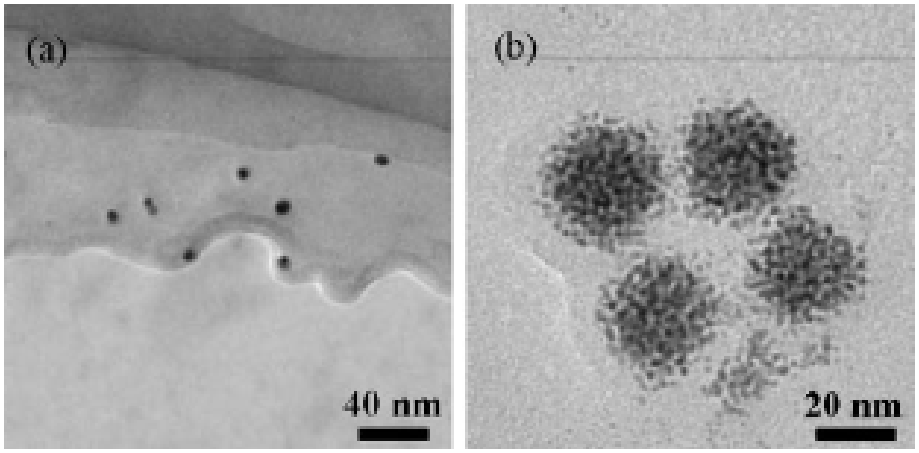


Fig. 1. TEM images obtained for (a) Ag-NPs and (b) Pt-NPs stabilized with PVP.

Antibacterial Activity

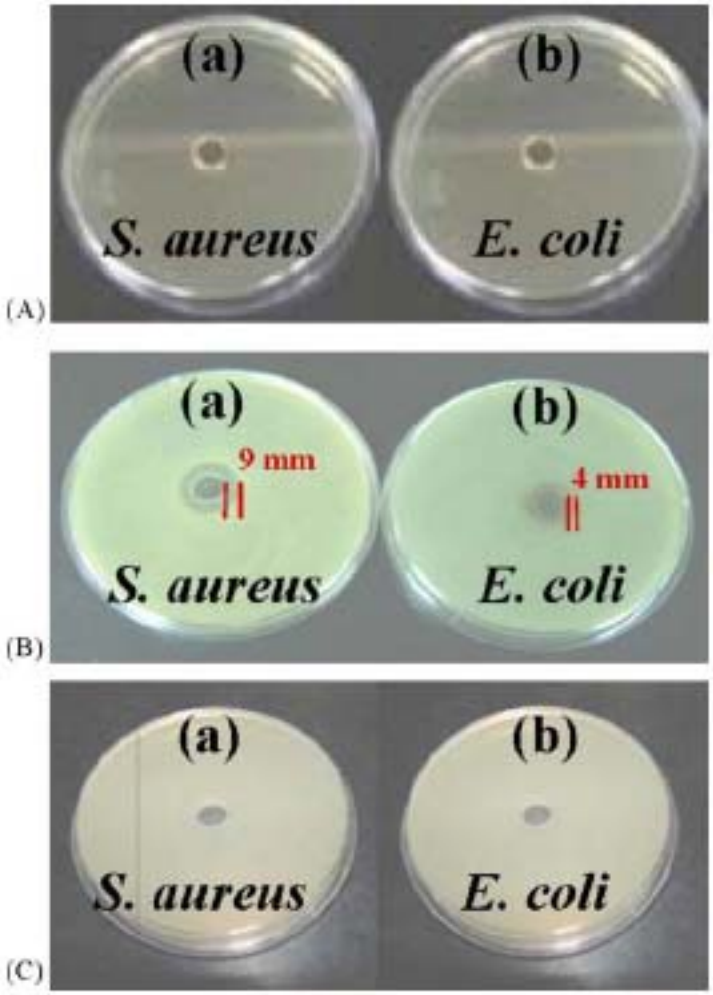


Fig. 2. Antibacterial activity of (A) Pt-NPs solution stabilized with PVP, (B) Ag-NPs solution stabilized with PVP and (C) Ag-NPs solution stabilized with SDS against *S. aureus* (KCTC 1928) (a) and *E. coli* (KCTC 1041) (b). All the concentration of Pt-NPs and Ag-NPs are 10 μL (5.4 ppm).

Dosage Test

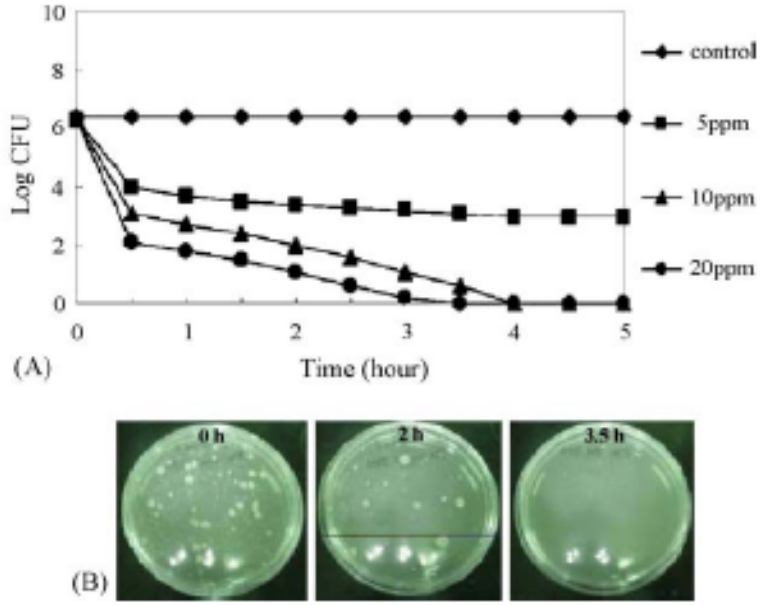


Fig. 3. (A) Growth inhibition curves of *S. aureus* in LB medium with different concentrations of Ag-NPs solution and (B) inhibition of colonies after Ag-NPs (10 ppm) treatment as the incubation time (0, 2, 3.5 h).

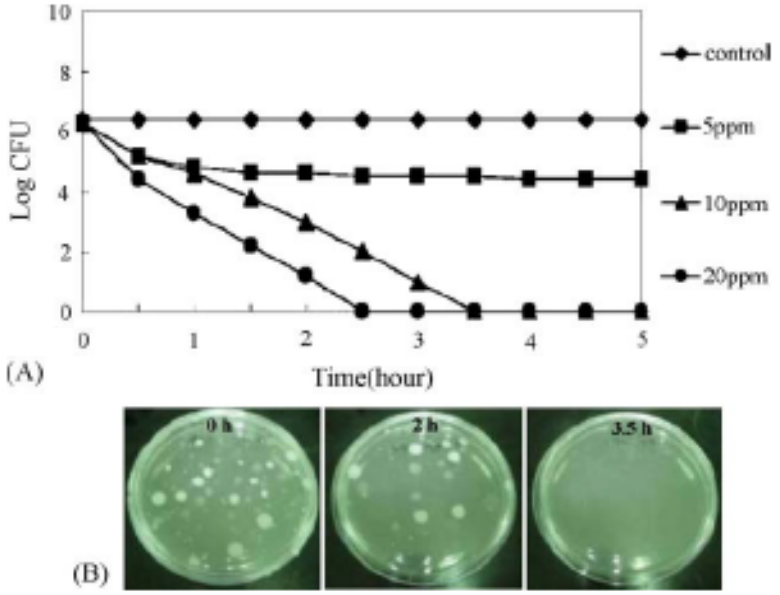


Fig. 4. (A) Growth inhibition curves of *E. coli* in LB medium with different concentrations of Ag-NPs solution and (B) inhibition of colonies after Ag-NPs (10 ppm) treatment as the incubation time (0, 2, 3.5 h).

Table 1
Growth inhibition rates of Ag-NPs against *S. aureus* and *E. coli*

Sample	Growth inhibition rate (%)	
	S. aureus (Gram-positive)	*E. coli* (Gram-negative)
Ag-NPs stabilized with PVP (10 ppm)	99.99	99.99
Ag-NPs stabilized with SDS (10 ppm)	0	0
Pt-NPs stabilized with PVP (10 ppm)	0	0
Pt-NPs stabilized with SDS (10 ppm)	0	0

Growth inhibition rate (%) = {(CFU/mL of control medium − CFU/mL of Ag-NPs or Pt-NPs solution treated medium)/(CFU/mL of control medium)}100.

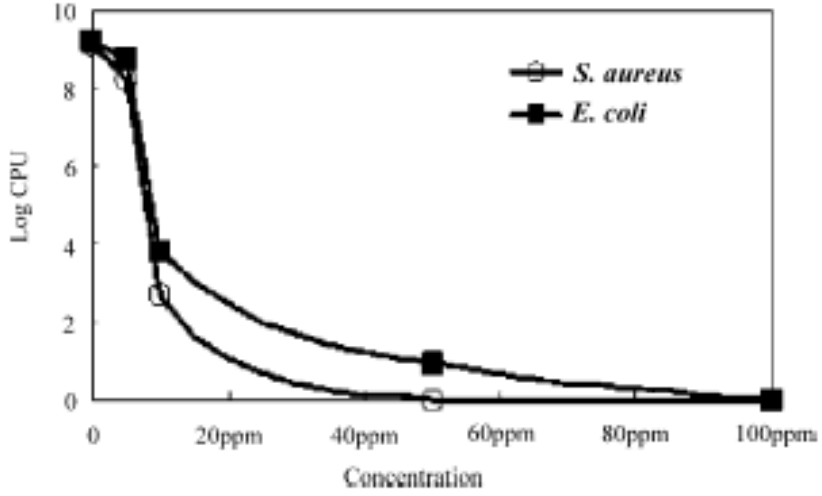


Fig. 5. Growth inhibition effect for different concentration of Ag-NPs stabilized with PVP against *S. aureus* and *E. coli*.

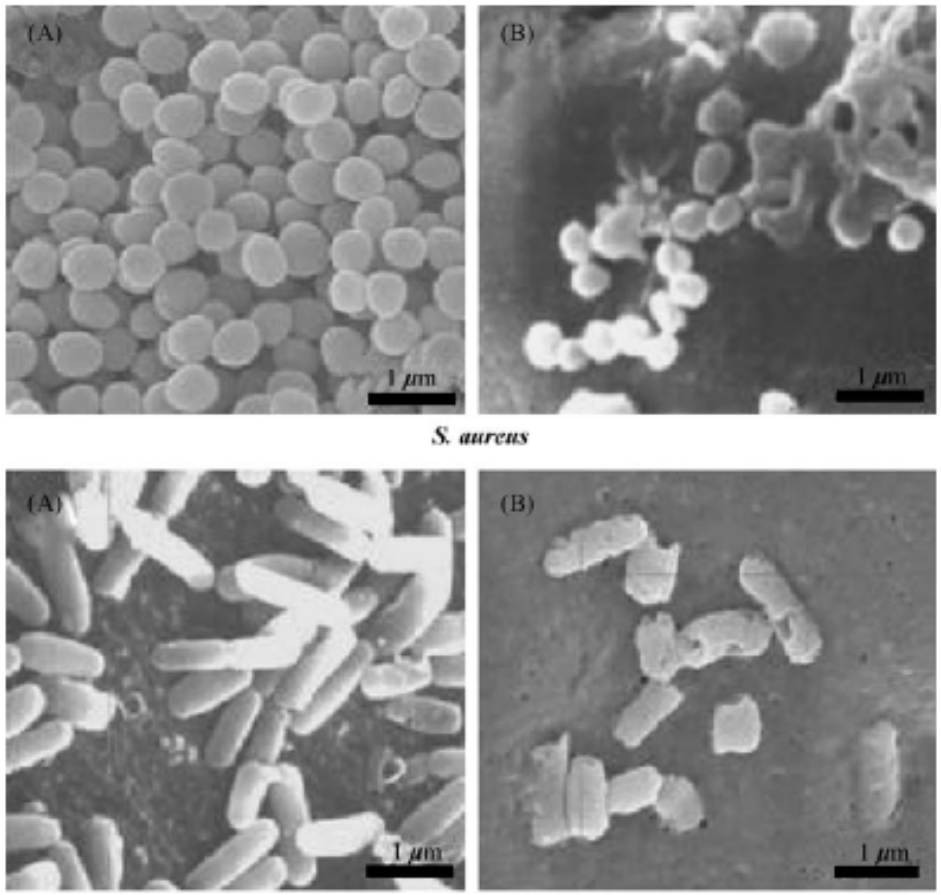
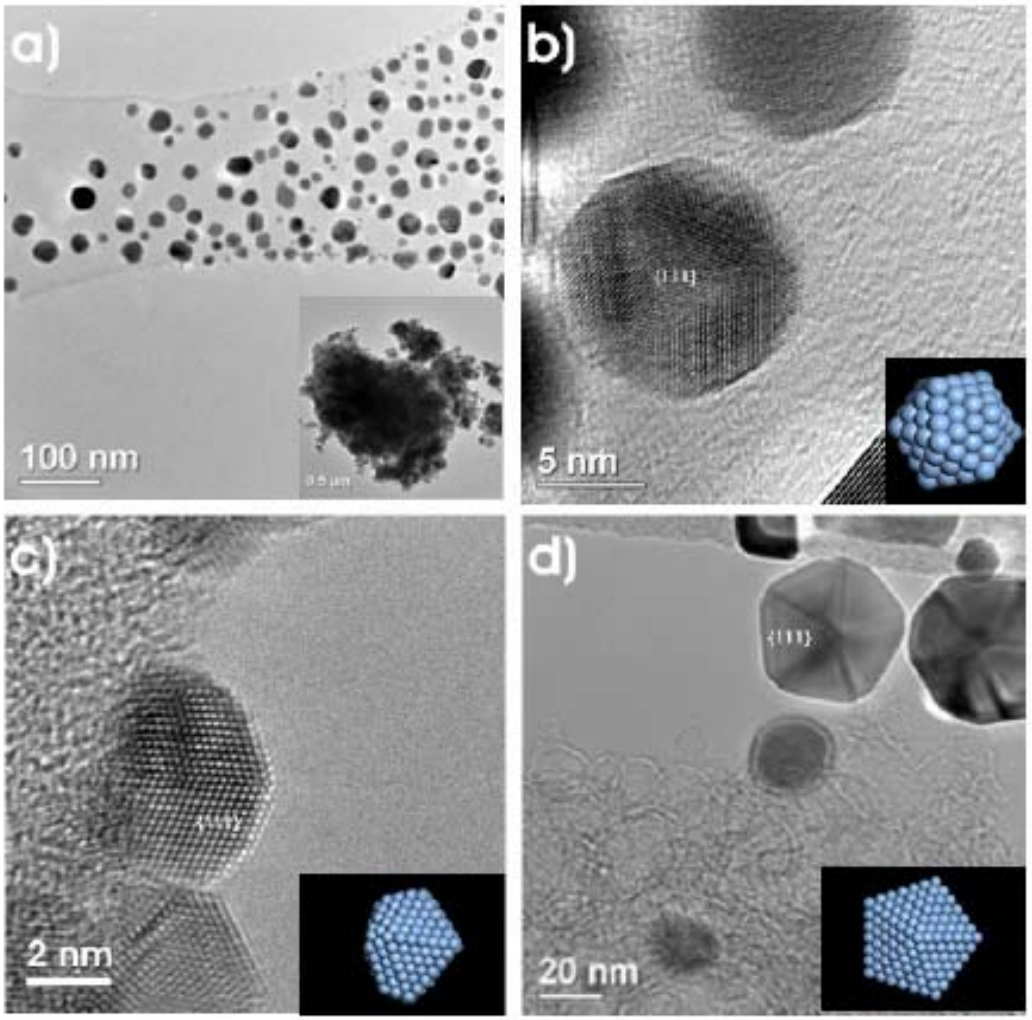
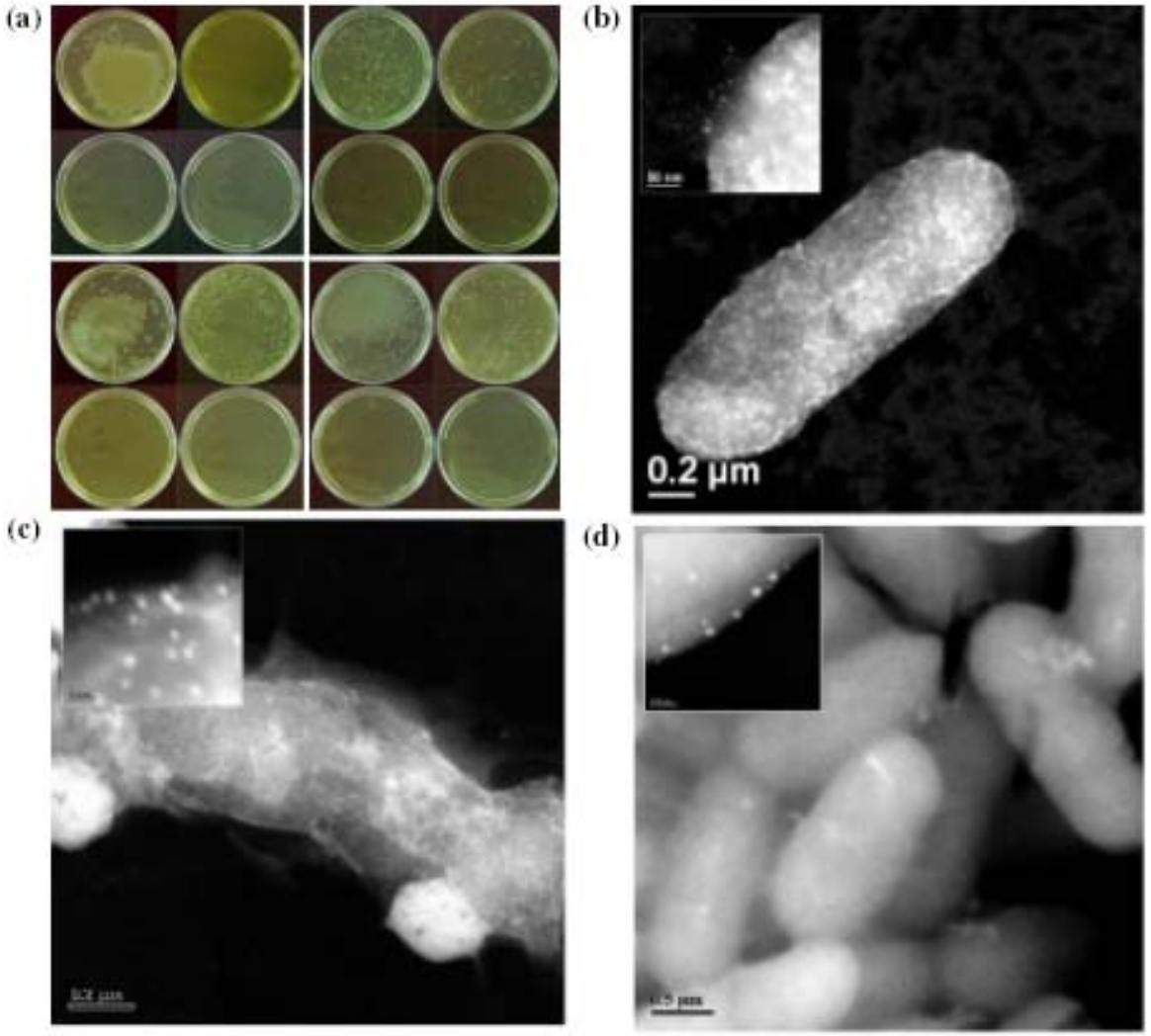


Fig. 6. Scanning electron microscopy of *S. aureus* and *E. coli*. Normal cells (A) and cells (B) grown on LB agar containing Ag-NPs solution (10 ppm).

The bactericidal effect of silver nanoparticles




(a)
(b)
0.2 µm
(c)
(d)

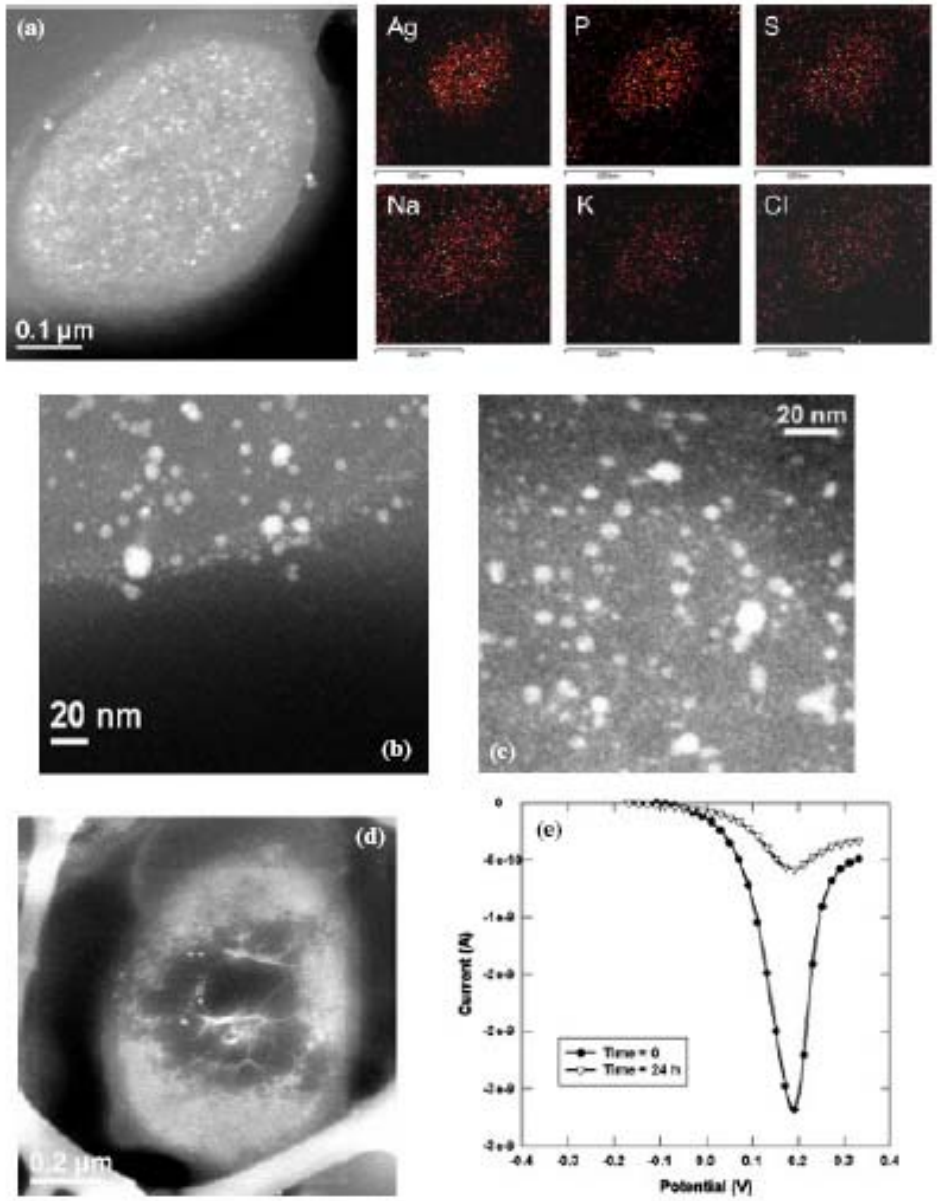
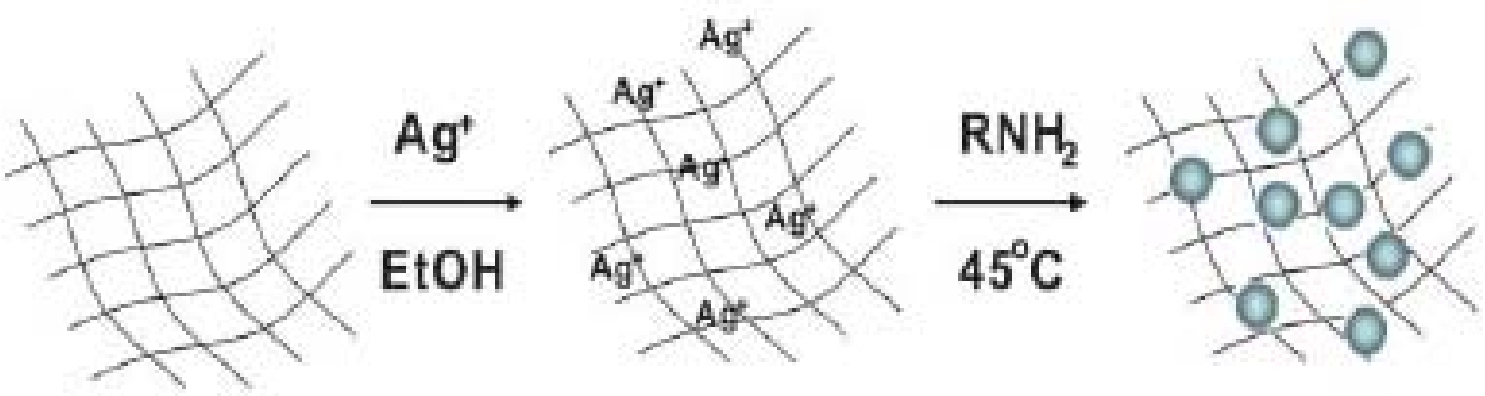


Figure 3. (a) Left: a considerable presence of silver nanoparticles is found in the membrane and the inside of an *E. coli* sample. Right: EDS elemental mapping. It can be observed that silver is well distributed through the sample. (b) Amplification of the *E. coli* membrane, where the presence of silver nanoparticles is clearly observed. (c) A close-up of the interior of an *E. coli* sample treated with silver nanoparticles. Again, the presence of silver nanoparticles is noted. (d) Image of an *E. coli* sample treated with silver nitrate, where a clear difference versus the nanoparticle treated sample is observed. As previously reported (3), a low molecular weight centre region is observed. (e) Stripping voltammetry results obtained for freshly dissolved silver nanoparticles in 0.2 M $NaNO_3$ and the curve for the same solution measured 24 h later.

A practical procedure for producing silver nanocoated fabric and its antibacterial evaluation for biomedical applications†



Scheme 1 Practical and robust deposition of silver nanoparticles on cotton fabric.

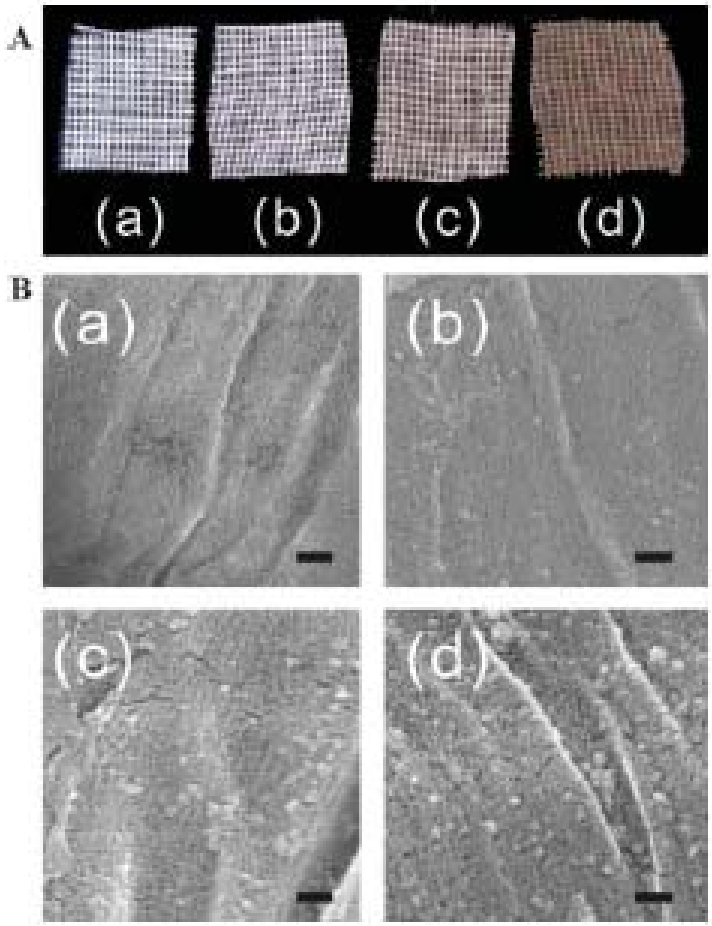


Fig. 1 Photographs of silver nanocoated cotton fabrics. A: (a) Uncoated cotton fabric, (b–d) cotton fabric coated with silver nanoparticles at various loading levels (low, medium, and high). B: FE-SEM image of each fabric sample (a–d) (scale bar = 200 nm).

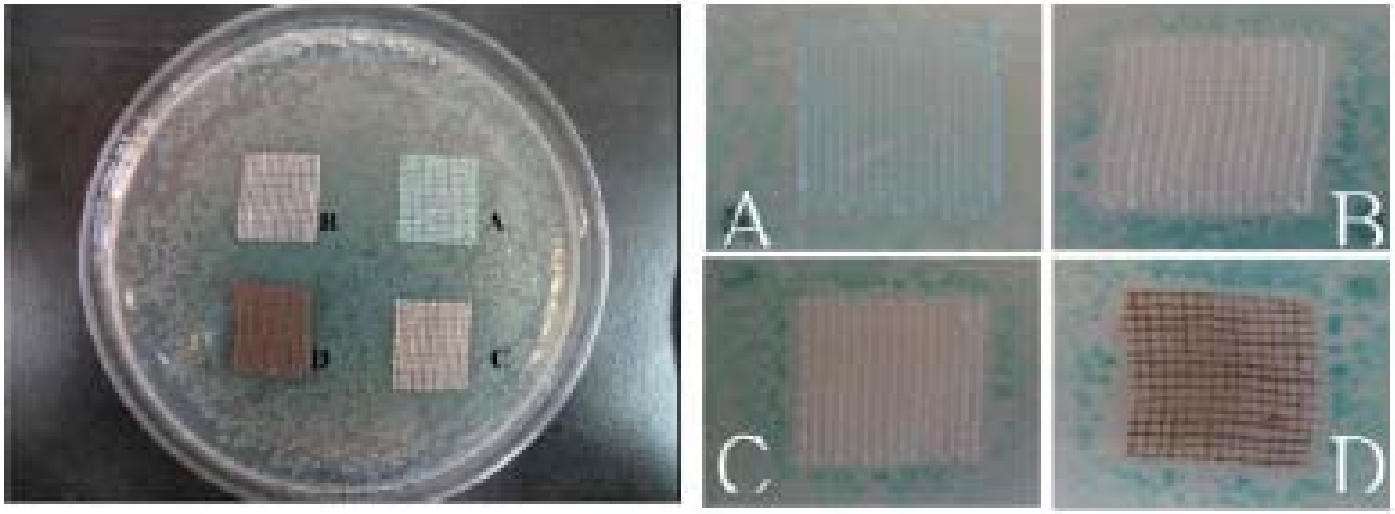


Fig. 2 Growth inhibition of *E. coli* by silver-coated cotton fabric on an agar plate with X-gal selection. A: cotton fabric. B, C and D: silver nanocoated fabric with low, medium and high loading levels, respectively.

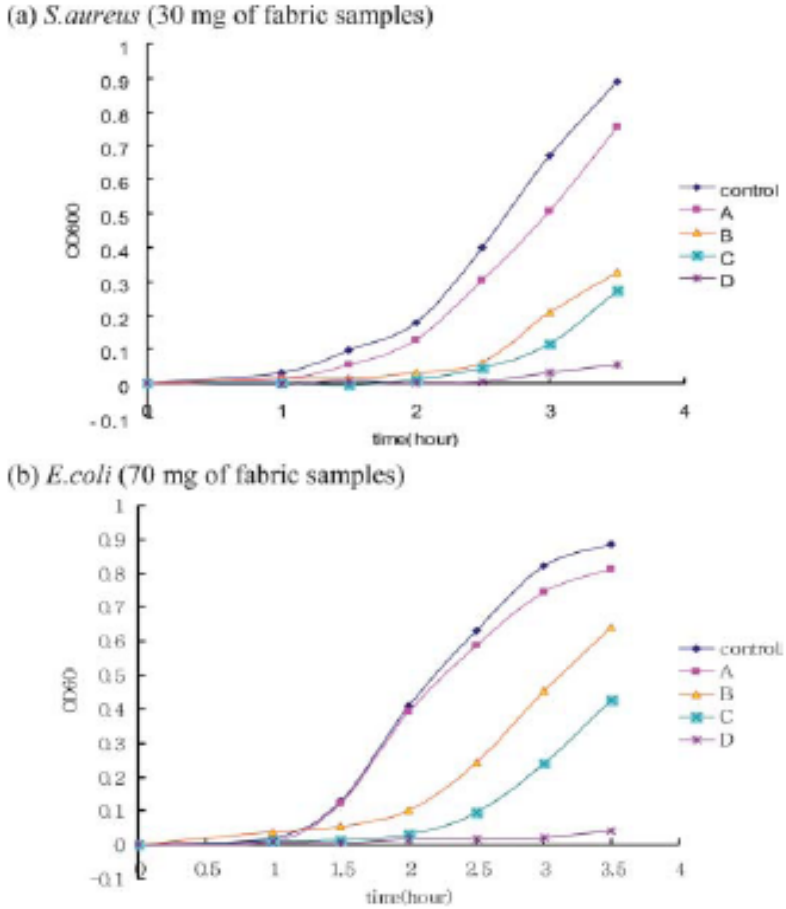


Fig. 3 Growth curve in liquid LB media: (a) *S. aureus* and (b) *E. coli*. Sample A: Non-coated cotton fabric. Samples B, C and D: 0.61, 1.4 and 5.3 mg silver per 1 g of silver nanocoated fabrics, respectively.

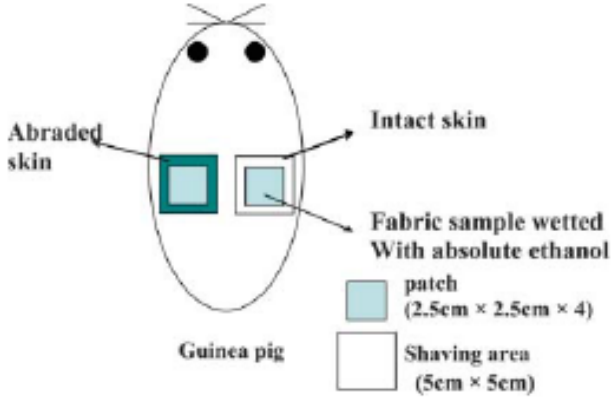
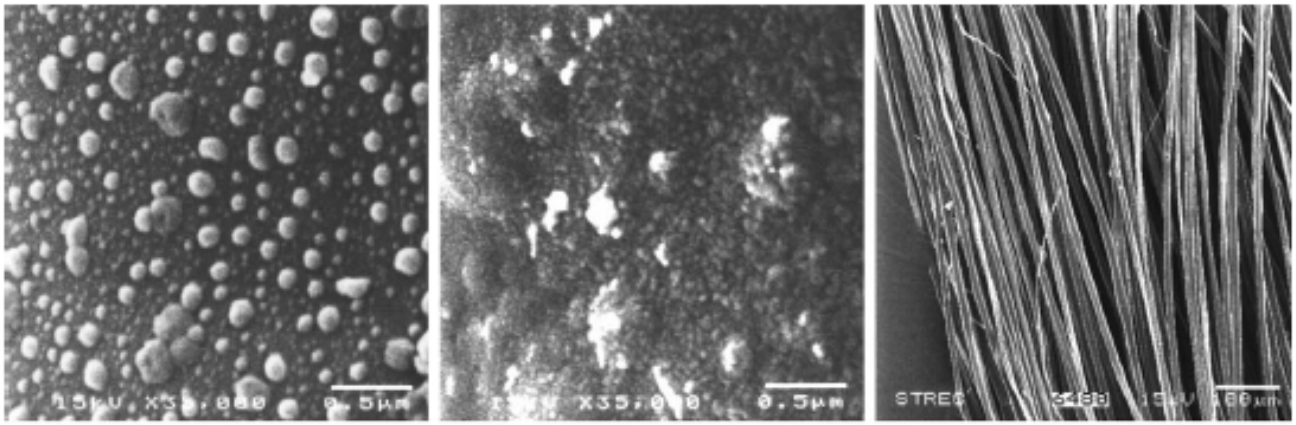


Fig. 4 Skin irritation test using guinea pigs.

Layer-by-layer deposition of antimicrobial silver nanoparticles on textile fibers



(A) (B) (C)

Fig. 3. Scanning electron microscopy of nylon (picture A) and silk (pictures B and C) fibers coated with a 20 layers PEM of PDADMAC and PMA capped silver nanoparticles.

Table 1
Antimicrobial test on silk and nylon fibers coated with 0, 10, 20 layers PEM of PDADMAC and PMA capped silver nanoparticles

Sample	Dilution factor	Average number of colonies	Equivalent colony forming unit	% Bacteria reduction
Blank silk	10^{-3}	41	4.1×10^5	–
10 Layers on silk	10^{-3}	24	2.4×10^5	41
20 Layers on silk	10^{-3}	8	8.0×10^4	80
Blank nylon	10^{-3}	45	4.5×10^5	–
10 Layers on nylon	10^{-3}	52	5.2×10^5	0
20 Layers on nylon	10^{-3}	21	2.1×10^5	53

ALEX PARUNI, PEN

This nanosilver-containing toothpaste is approved by the U.S. Food and Drug Administration, but nanosilver used in washing machines is regulated under certain conditions by EPA.

御守棉

／愛的御守信 ／ 五大御守 ／超強商品力 ／奈米銀抑菌力 ／御守小物／ 貼心叮嚀／ 得獎名單／ 大力推薦／康乃馨官網 ／

新一代衛生棉
關鍵在，抑菌。

守護妳，從抑菌開始

觀看TVCF

御守南台灣
康乃馨獻愛心

唯我時尚
抽獎活動

得獎名單

唯我時尚

五大御守

全面御守・日夜無憂

御守棉✚ 奈米核心健康護墊✚

✚健康御守

Ag

高科技奈米銀處理技術，
有效抑菌，消除異味困擾。

奈米銀可有效抑菌達**99%**

✚安心御守

獨家御守棉防護瞬吸體，
吸收更多，更加乾爽。

吸收力 100% UP

乾爽度 300% UP

✚潔淨御守

可重複黏貼封口設計，
方便存放，潔淨又衛生。

✚舒適御守

表層綿密細膩，感觸柔軟，
台灣康那香專業不織布廠
研發製造。

✚美人御守

美人專屬，雙色漾彩設計，
透氣、排濕、不悶熱。

Comfortion 御只棉 ✚御守棉

奈米銀抑菌力

奈米銀小常識 抑菌原理大剖析

新一代衛生棉 關鍵在，抑菌。

何謂全面的守護？當吸收力、透氣度、柔觸感都將成為最基本的需求時，我們可以對新一代衛生棉有何期待？康乃馨御守棉獨家研發奈米銀抑菌吸收體，萃取自天然純銀礦物質，經實驗證明，抑菌效果達99%。有了抑菌，才是全面的守護。

銀，不只是裝飾用途，還有抑菌大功效！

- 中國《本草綱目》中記載：「銀屑，安五臟、定心神、止驚悸、除邪氣、久服輕身長年 」
- 一次世界大戰：銀箔被應用於防止傷口感染。

- 中國針灸用銀針，試毒用銀簪子，都是傳統智慧利用銀具有抗菌特性的妙方。

- 古代地中海居民把銀幣放入木水桶中，阻止細菌、海藻等腐敗微生物的生長。

抑菌原理大剖析

康乃馨 Carnation

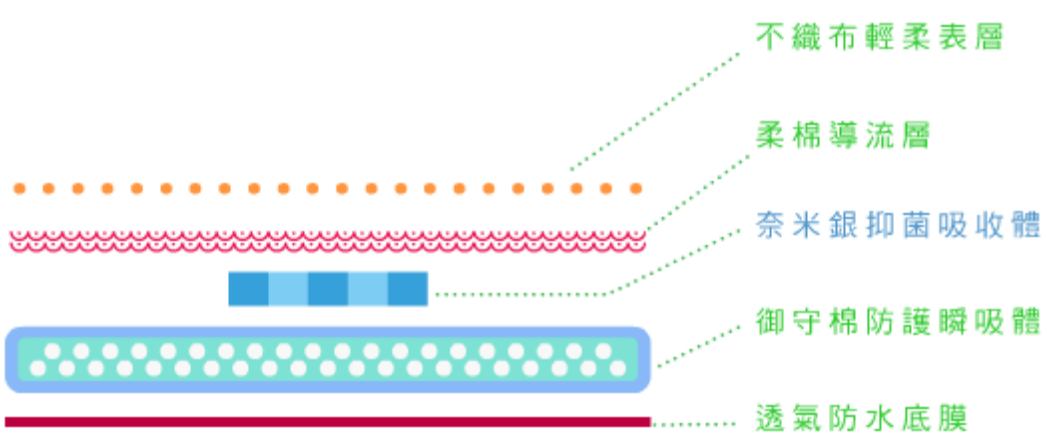
御守棉

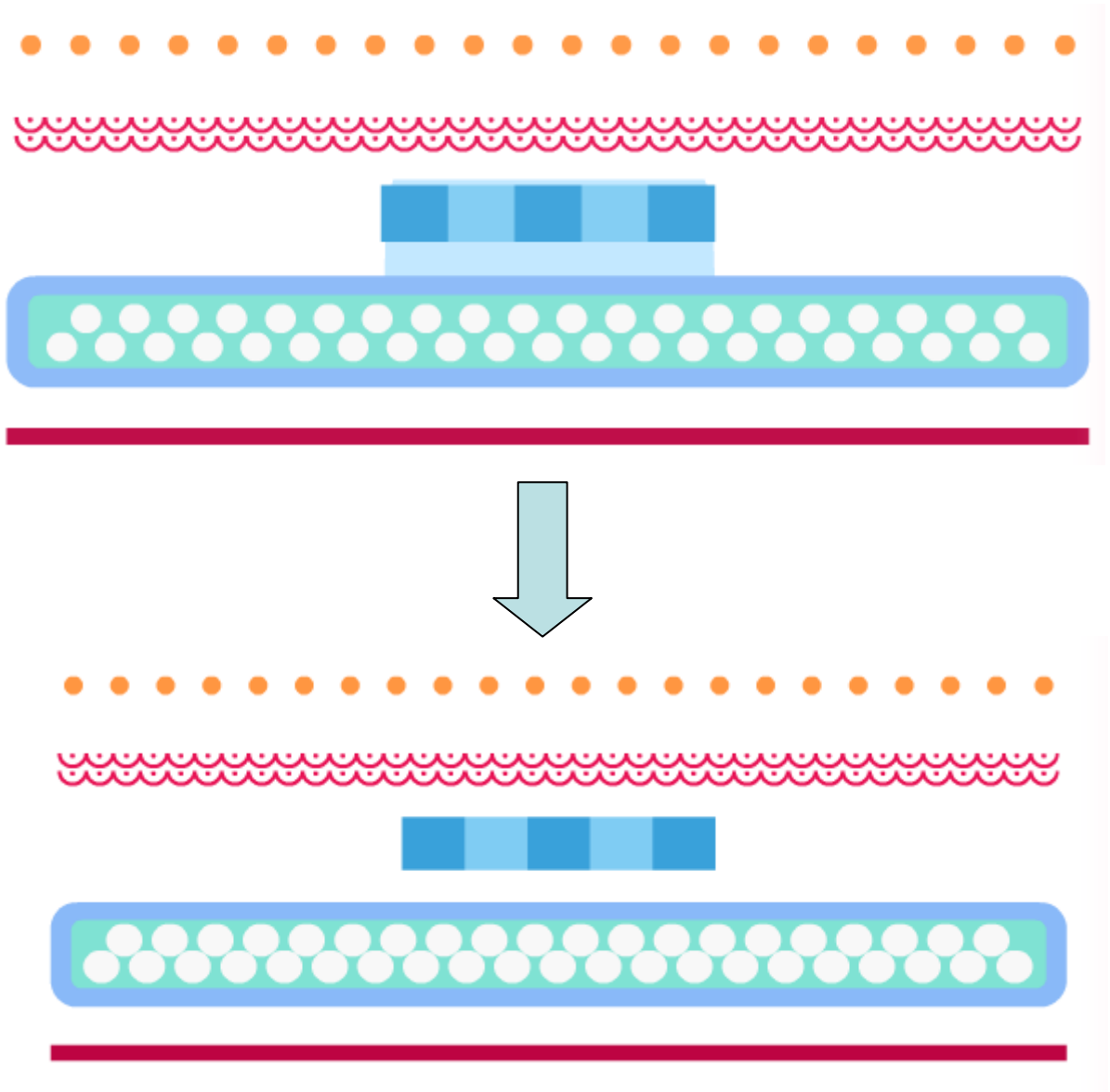
全面御守．日夜無憂

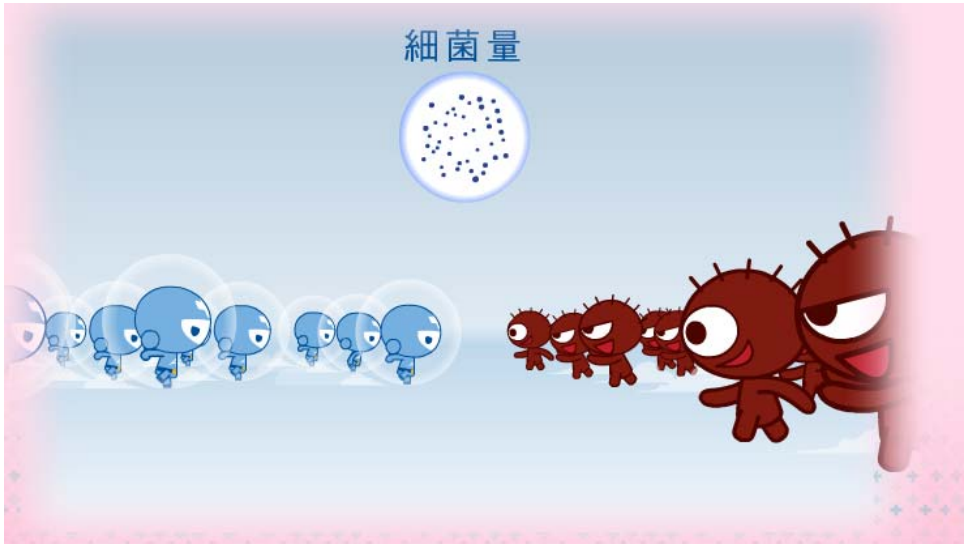
守護妳，從抑菌開始

REPLAY

想知道康乃馨御守棉獨家研發的奈米銀抑收體，
是如何達到抑菌效果99%嗎？






細菌量


細菌量


細菌量


細菌量

罕見病例

雷射美白 怎麼臉黑好幾塊？

患者十多年前類風濕性關節炎 曾接受金子療法 金顆粒經過雷射而突顯

一名患者爲了去斑接受雷射治療，上半臉卻因此黑了好幾塊，醫師追查發現，患者在十多年前曾因類風濕性關節炎接受過金子療法，這可能是國內首宗金沈著症由雷射引發而外顯的病例。

醫學大學附設醫院皮膚科主治醫師表示，這名四十三歲的女性病人，因患有類風濕性關節炎，十六、七年前曾連續兩年、每周接受金製劑注射治療，總計接受金治療量超過五克，日前因臉上的雀斑在其他醫院接受雷射治療，不料雷射後眼眶四周及鼻樑上卻出現很多藍黑色的斑塊，先後經亞歷山大雷射及紋雅各雷射治療，情況卻越來越嚴重。

經過皮膚切片檢查發現，在電子顯微鏡下可明顯看到真皮層有長期累積的金顆粒。到目前爲止，國內文獻上還沒有這樣的病例報告，國外也只有兩個病例。

醫院免疫風濕科主任指出，過去醫學上發現，金化合物製成的金製劑可壓制免疫反應，因此可治療類風濕性關節炎等免疫疾病，是當時治療的主流；但因金子療法可能導致過敏、腎炎引起蛋白尿等副作用，必須每個月驗血驗尿追蹤，如今醫學發達，還有其他更好的治療藥物，如氯化奎寧、磺胺製劑、抗癌藥ＭＴＸ等，因此近十年來，金子療法已幾乎不再使用。

表示，這名患者皮膚中的金沈積經過雷射，在皮膚內發生物理變化，使顏色突顯出來，在光學原理下，金元素經表皮及真皮層的透光，皮膚外表會呈現出藍黑色，而不是一般想像中的金光閃閃。他參考國外文獻上唯一治療成功的病例，以長波紅寶石雷射治療，目前患者右半臉的藍黑色已逐漸變淡，仍持續治療中。

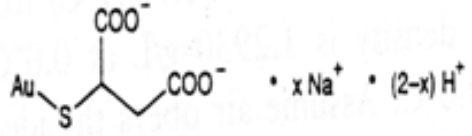
他強調，並非接受過金子療法的患者都可能沈積在體內，與使用的量有關，而由於日曬亦可能引起金沈著症顯現出來，所以患者一定要注意防曬，接受雷射治療前，亦要先接受小區域測試。至於目前很流行的食物加金箔的吃法，說，沒有文獻報告會因此產生金沈積在體內，但如果每周吃、連續吃兩年，就很難說了。

Safety of Self-Injection of Gold and Methotrexate

ANNE BARBARA ARTHUR, ALICE V. KLINKHOFF, and ALVENA TEUFEL

ABSTRACT. ***Objective.*** We review our experience with safety, efficacy, and practicality of self-administration of gold and methotrexate (MTX) in 40 patients.

Methods. Between 1992 and 1995, 40 patients with rheumatoid arthritis (RA) and psoriatic arthritis (PsA) followed in the drug monitoring clinics of the Mary Pack Arthritis Centre were taught to self-administer parenteral gold or MTX. Self-injection education was recommended to patients who were stable and improved taking parenteral gold or MTX, and who had not experienced serious side effects. Charts were reviewed to extract and analyze prospectively collected data regarding safety, efficacy, and compliance.



White to yellowish-white powder, metallic taste. Very sol in water. Practically insol in alcohol, ether. Aq solns are colorless to pale yellow. pH of a 5% aq soln: 5.8-6.5.

THERAP CAT: Antirheumatic.

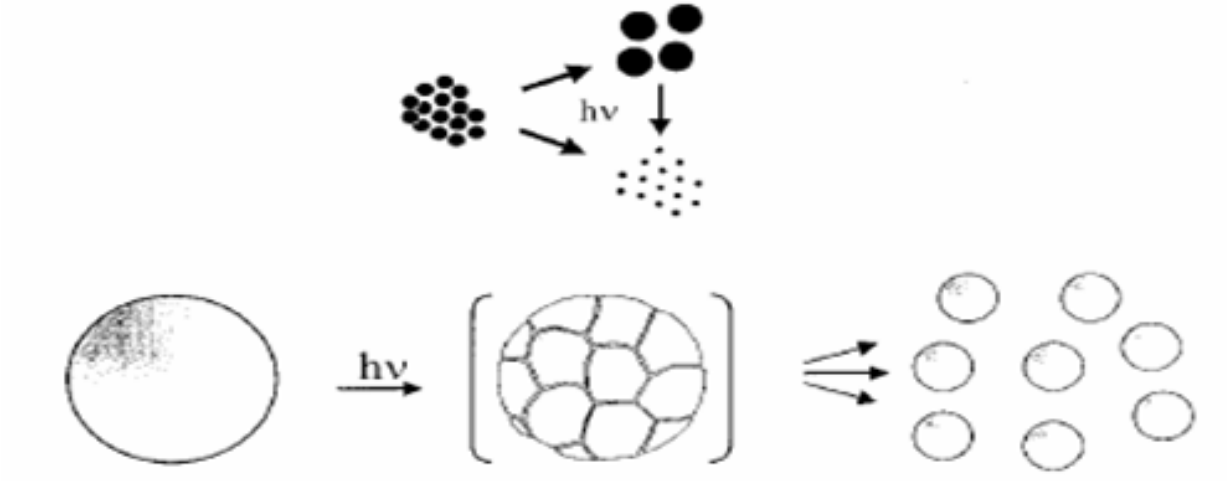
Q-Switched Laser-Induced Chrysiasis Treated With Long-Pulsed Laser

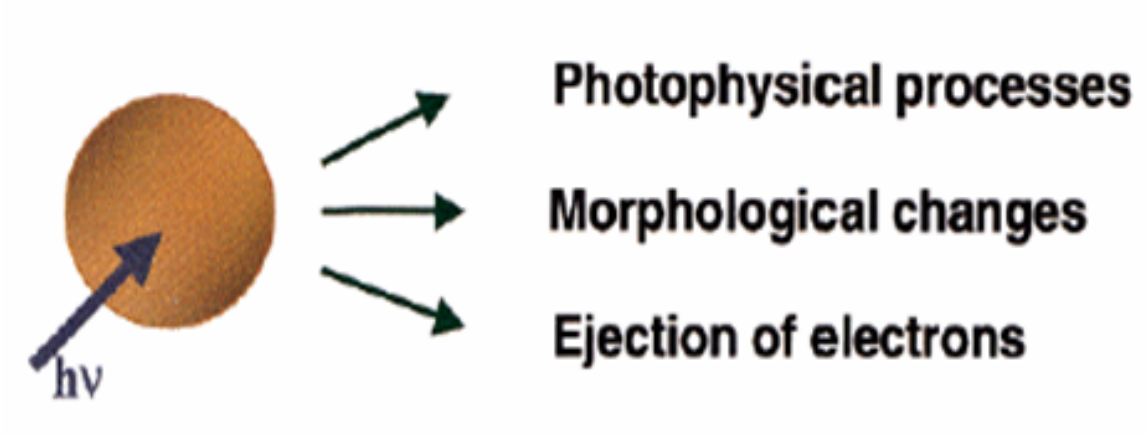
Patricia Lee Yun, MD; Kenneth A. Arndt, MD; R. Rox Anderson, MD; Wellman Laboratories of Photomedicine, Massachusetts General Hospital, Boston (Drs Yun and Anderson), Skin Care Physicians of Chestnut Hill, Chestnut Hill, Mass (Dr Arndt)

Response of Normal-Appearing Skin in a Patient With Chrysiasis to Lasers With Different Irradiance

Laser	Pulse Width, s	Irradiance, W/cm^2	Fluence, J/cm^2	Skin Response
Q-switched alexandrite (first treatment)	5×10^{-8}	7×10^{7}	3.5	Blue macules
Q-switched ruby	3×10^{-8}	3×10^{7}	2.0	Blue macules
Pulsed dye	3×10^{-7}	5×10^{6}	1.5	Blue macules
Normal mode ruby	3×10^{-3}	1.7×10^{4}	Up to 50	Erythema, no darkening

SCHEME 4: Photoinduced Fusion and Fragmentation of Metal Nanoparticles





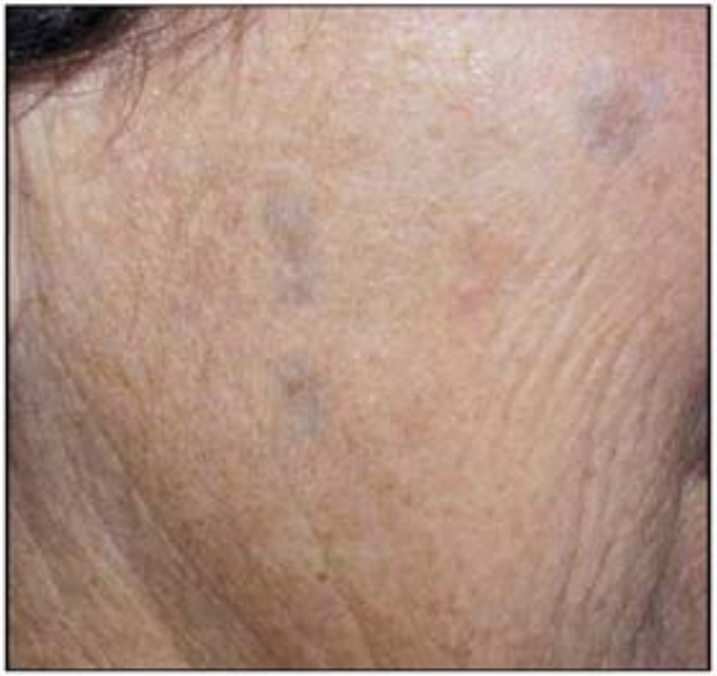
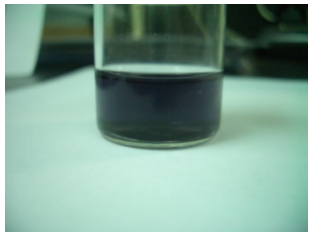


Figure 1. Blue macules of chrysiasis approximately 1 year after Q-switched alexandrite laser treatment for lentigines.



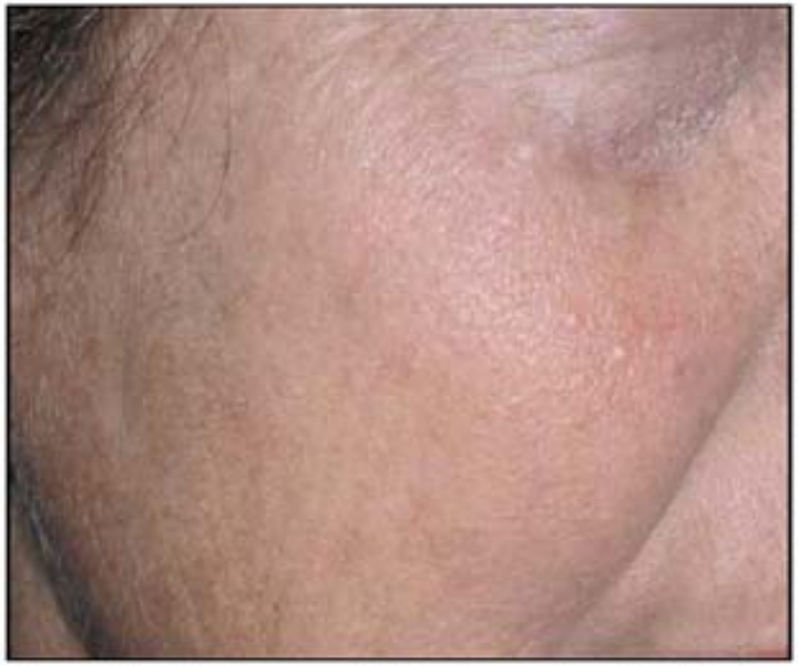


Figure 3. Substantial improvement of chrysiasis macules on the cheek after 2 treatments with a long-pulsed ruby laser (compare with Figure 1).

1. Introduction

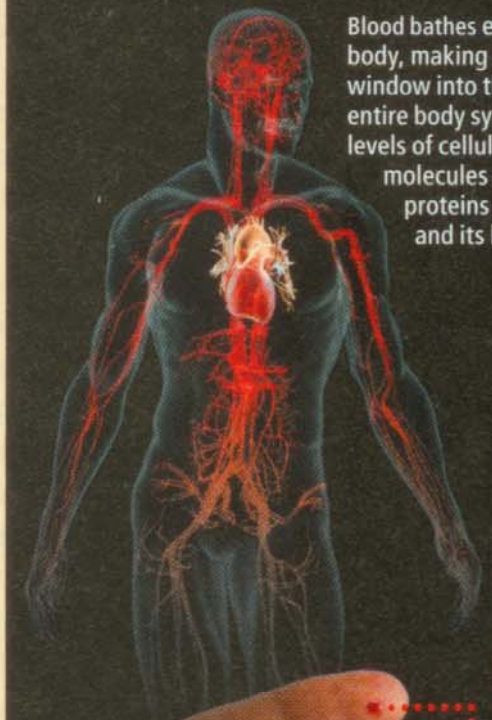
2. Toxicity

3. Sensor (detecting disease)

4. Label (on target)

PENNIES PER PROTEIN

Information is the most valuable commodity in a systems approach to medicine, so diagnostic tests will have to easily and accurately measure large numbers of biological molecules for a few cents or less per measurement. Extreme miniaturization allowed the authors and their colleagues to produce a prototype chip that can measure concentrations of a panel of cancer-associated proteins in a droplet of blood in 10 minutes, at a cost of five to 10 cents per protein.



Blood bathes every organ in the body, making it an excellent window into the state of the entire body system. Abnormal levels of cellular signaling molecules or organ-specific proteins can flag a problem and its location.

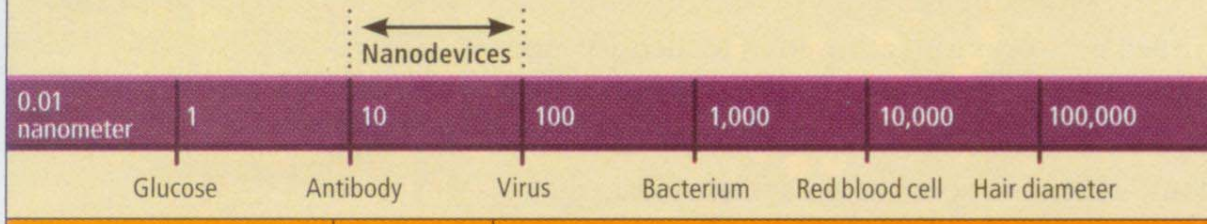
Sample barcode containing 12 strips for detecting proteins associated with inflammation and prostate function. Results of a test of blood from a prostate cancer patient show high concentrations of prostate-specific antigen (*center*) and interferon-gamma (*right*).

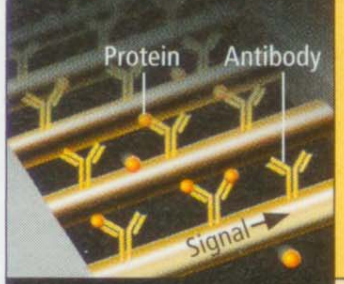
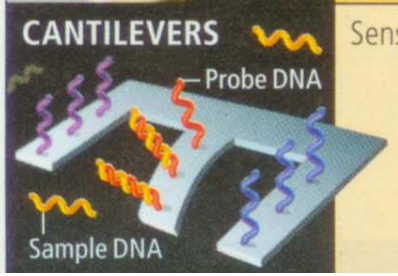
Microfluidic channels within a four-centimeter-wide chip can take up a droplet of whole blood and separate plasma from cells. The plasma and proteins suspended within it flow down the narrower channels.

Proteins flow across an array of antibody-studded bars. Each bar contains antibodies that will bind only to a specific protein. After the plasma has been sampled, fluorescent tags washed across the "barcode" array attach only to protein-bound antibodies.

NANOTECH IN MEDICINE

At the scale of one nanometer—one billionth of a meter—materials and devices can interact with cells and biological molecules in unique ways. The nanoscale technologies already used in research or therapies are generally between 10 nanometers, the size of an antibody protein, and 100 nanometers, the size of a virus. These devices and particles are being applied as sensors to detect molecules such as proteins or DNA, as imaging enhancers, and as a means to target specific tissues and deliver therapeutic agents.



NANOTECHNOLOGY	USE	HOW IT WORKS
NANOWIRES 	Sensing	Conductive wire, 10 to 20 nanometers thick, is strung across a channel through which a sample will pass. To detect proteins or DNA, probes made of complementary antibodies or DNA are attached to each wire. When a protein meets its matching antibody, it binds to the probe and changes the conductive properties of the wire, allowing the event to be detected electronically.
CANTILEVERS 	Sensing	Molecular probes, such as single-stranded DNA, can also be attached to beams just a few nanometers thick. When exposed to a DNA sample, complementary strands bind to the probes on the cantilever, causing the beams to bend slightly. That response can be detected visually or by a change in the beams' electrical conductivity.

金奈米顆粒在醫療檢測的應用

★ 自己可以在家驗孕嗎？

利用驗尿的方式，可以早在受孕第八天就可測出有否懷孕，但有兩點要注意：

1 驗孕片精確度要夠，所以若第八天檢驗沒有懷孕反應，過兩天還要再驗一次，因為真正那一天排卵未必確定。

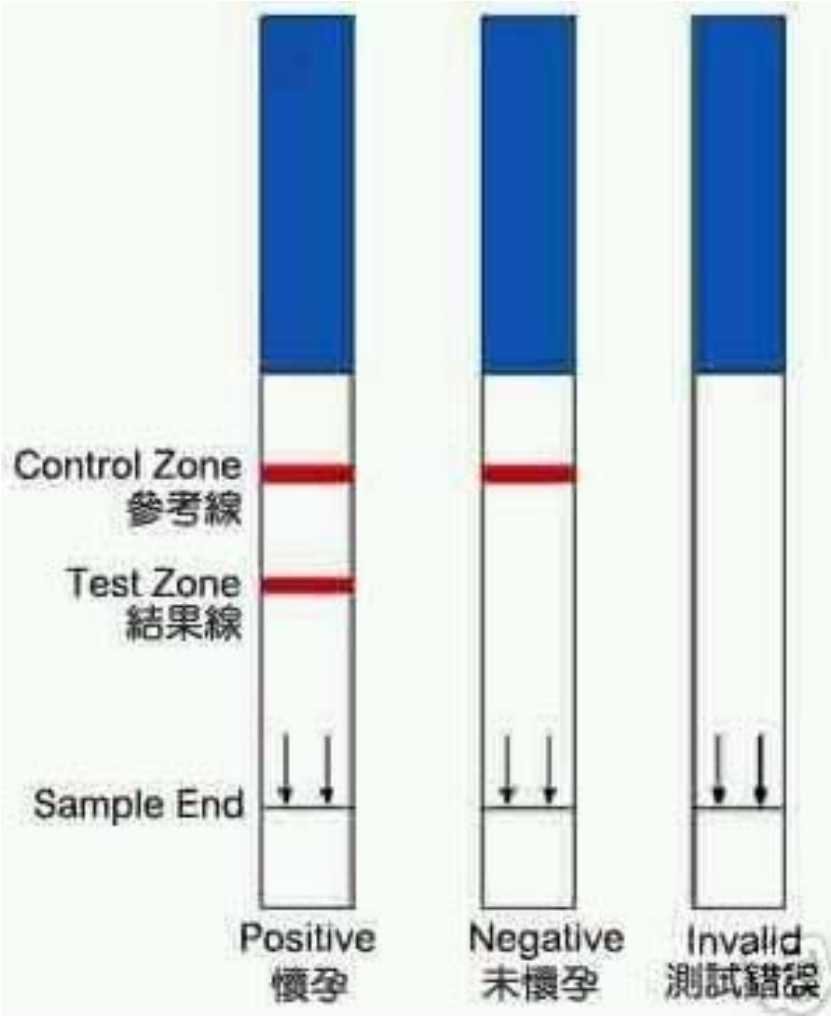
2 最好是檢驗早上起床後第一泡尿，敏感度最高。

★ 懷孕測試劑　測試原理

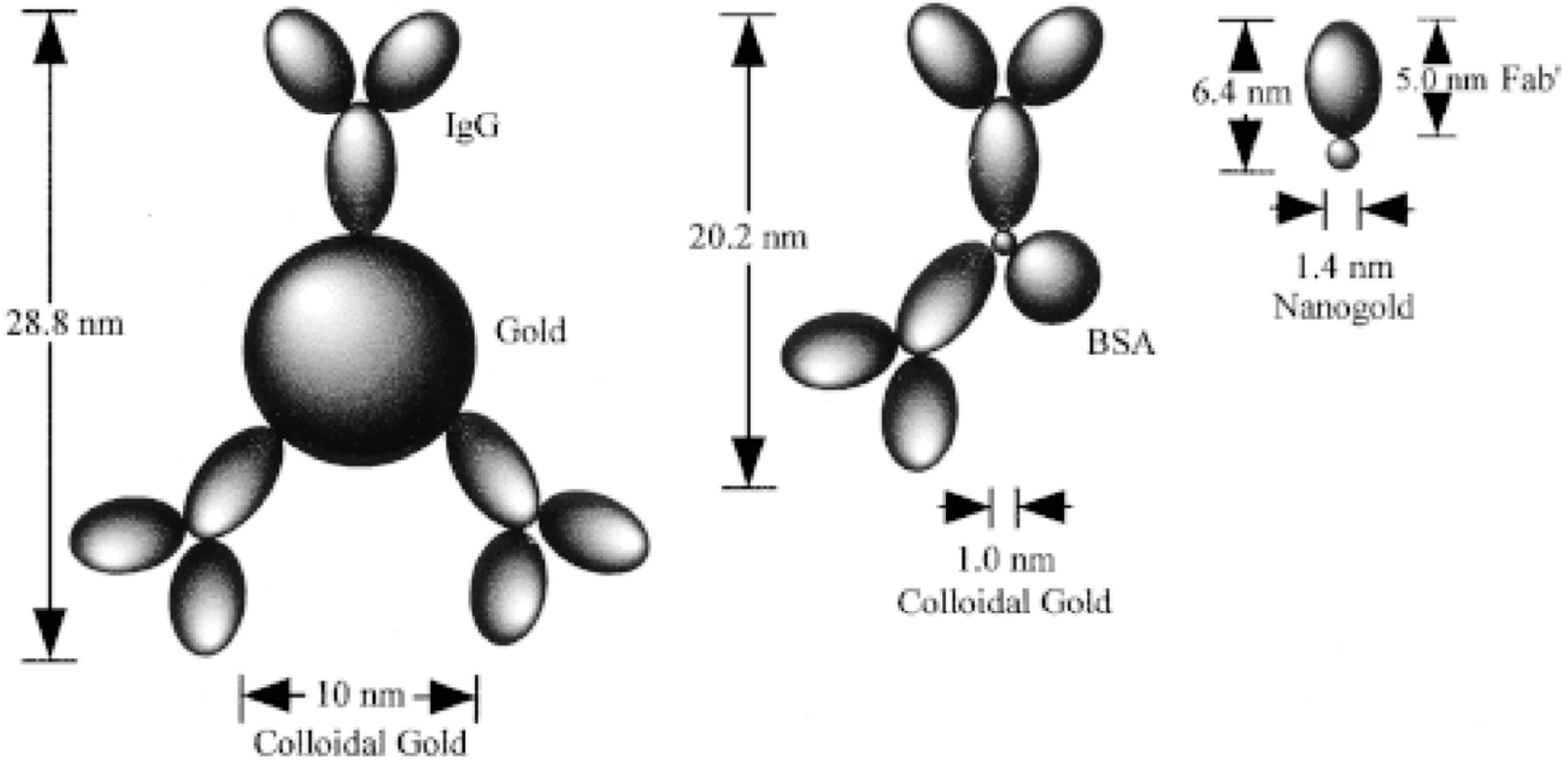
在性行為發生以後，受精卵完成結合，就慢慢在輸卵管內移動，六、七日後，抵達子宮內，就像種子植入在土壤內一樣，受精卵埋進子宮內膜，母體的血液提共營養，最早期的胎盤細胞開始繁殖，同時分泌胎盤荷爾蒙，這種胎盤荷爾蒙進入母體血液，再經母體腎臟從尿液中排出，當濃度到達一定高度，驗孕劑就會有陽性反應。

所以，在受精卵結合後，最快要等六、七日，才可以在血液中測知胎盤荷爾蒙的濃度，再過六、七天，尿中的濃度就才足夠使一般驗孕劑產生反應。因此，粗略的計算下，約在性行為後十四天左右，可以自尿液中檢驗出是否有懷孕。

HCG (human chorionic gonadotropin)

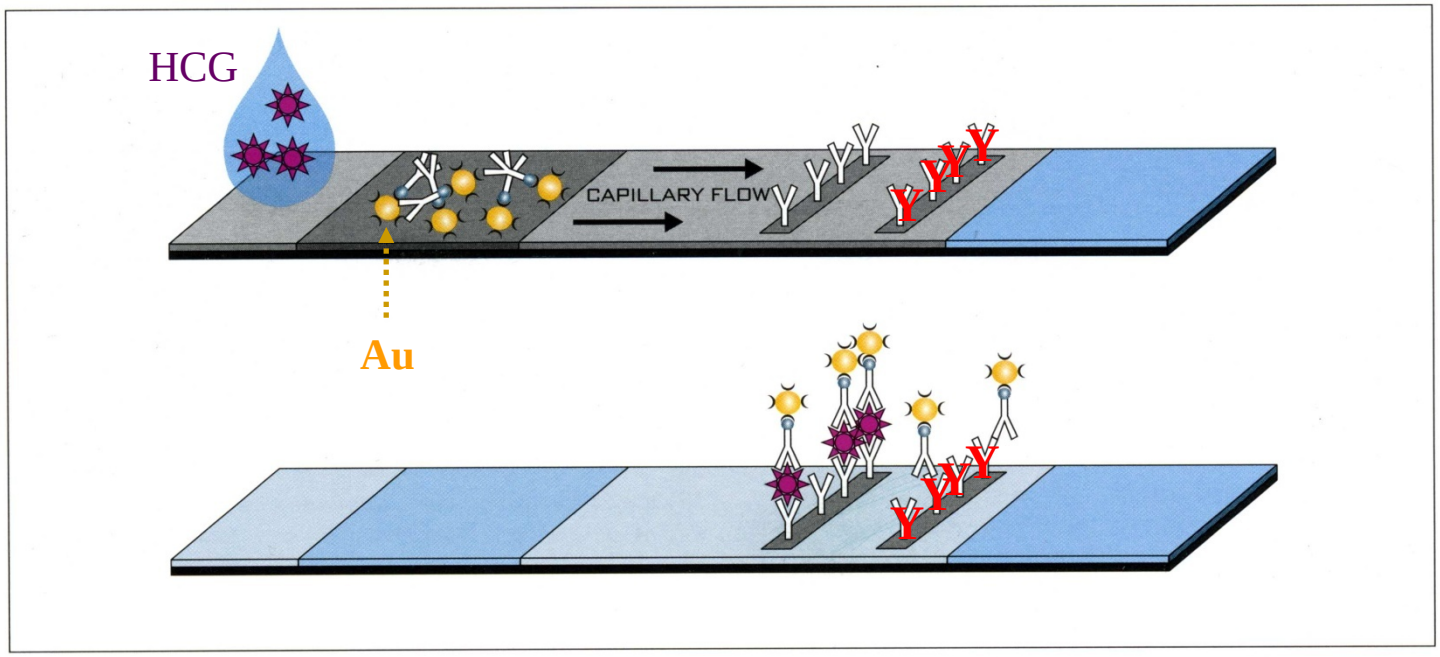

Control Zone
參考線
Test Zone
結果線
Sample End
Positive
懷孕
Negative
未懷孕
Invalid
測試錯誤

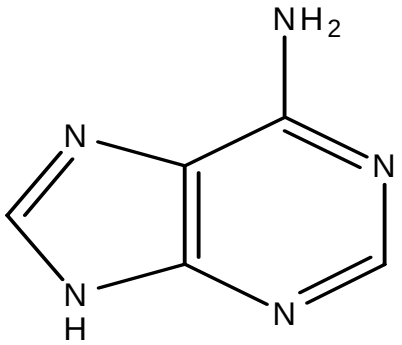

For in-vitro diagnostic use only
DIAGNOSTIC TEST
Cassette Format
Store at room temperature (4°C-30°C)
Test band
Control band
S
T
C
Negative
Positive
Invalid
Dispense five drops of sample into the sample well


IgG
28.8 nm
Gold
10 nm
Colloidal Gold
20.2 nm
BSA
1.0 nm
Colloidal Gold
6.4 nm
5.0 nm Fab'
1.4 nm
Nanogold

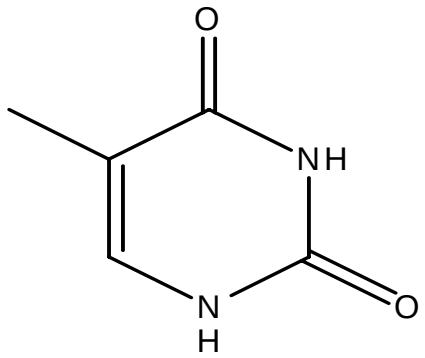
Development of a Qdot™ Lateral Flow Assay

A Simple Multiplexing Strip Test

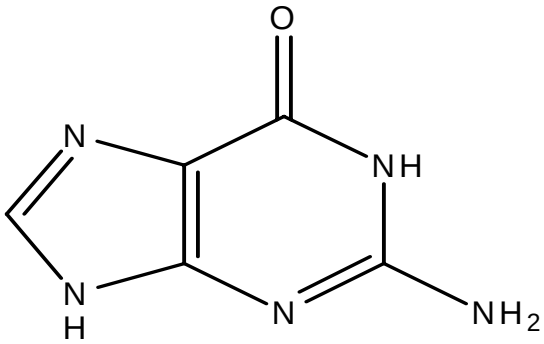




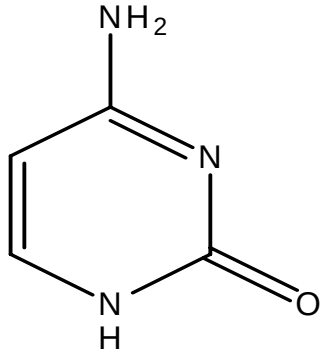
Adenine (A)



Thymine (T)

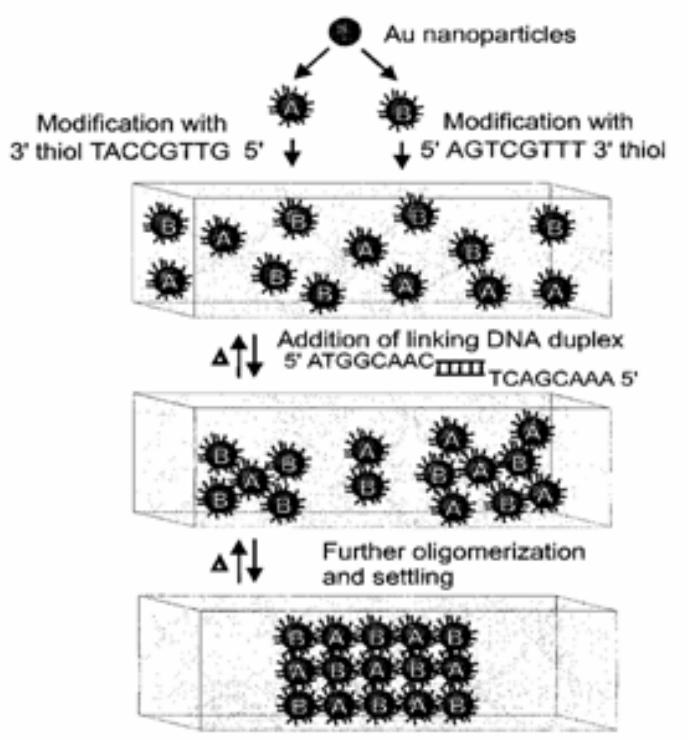


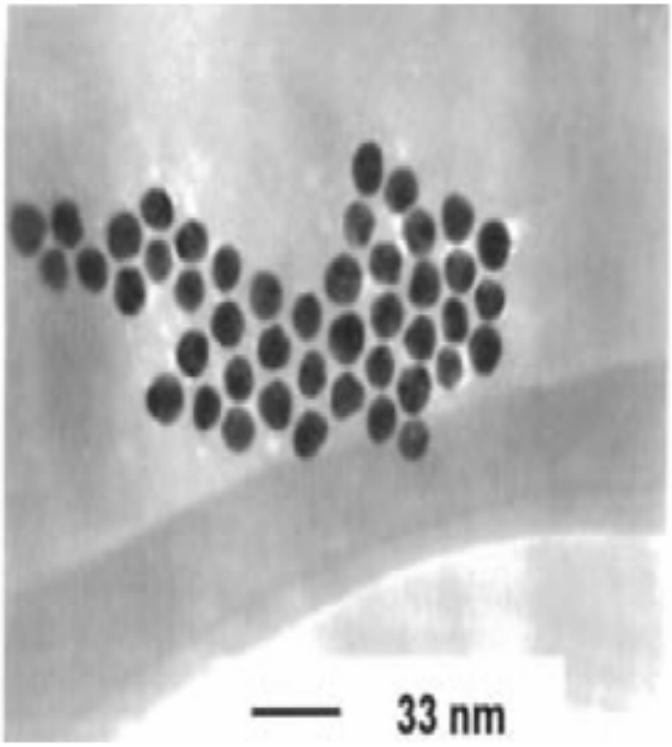
Guanine(G)



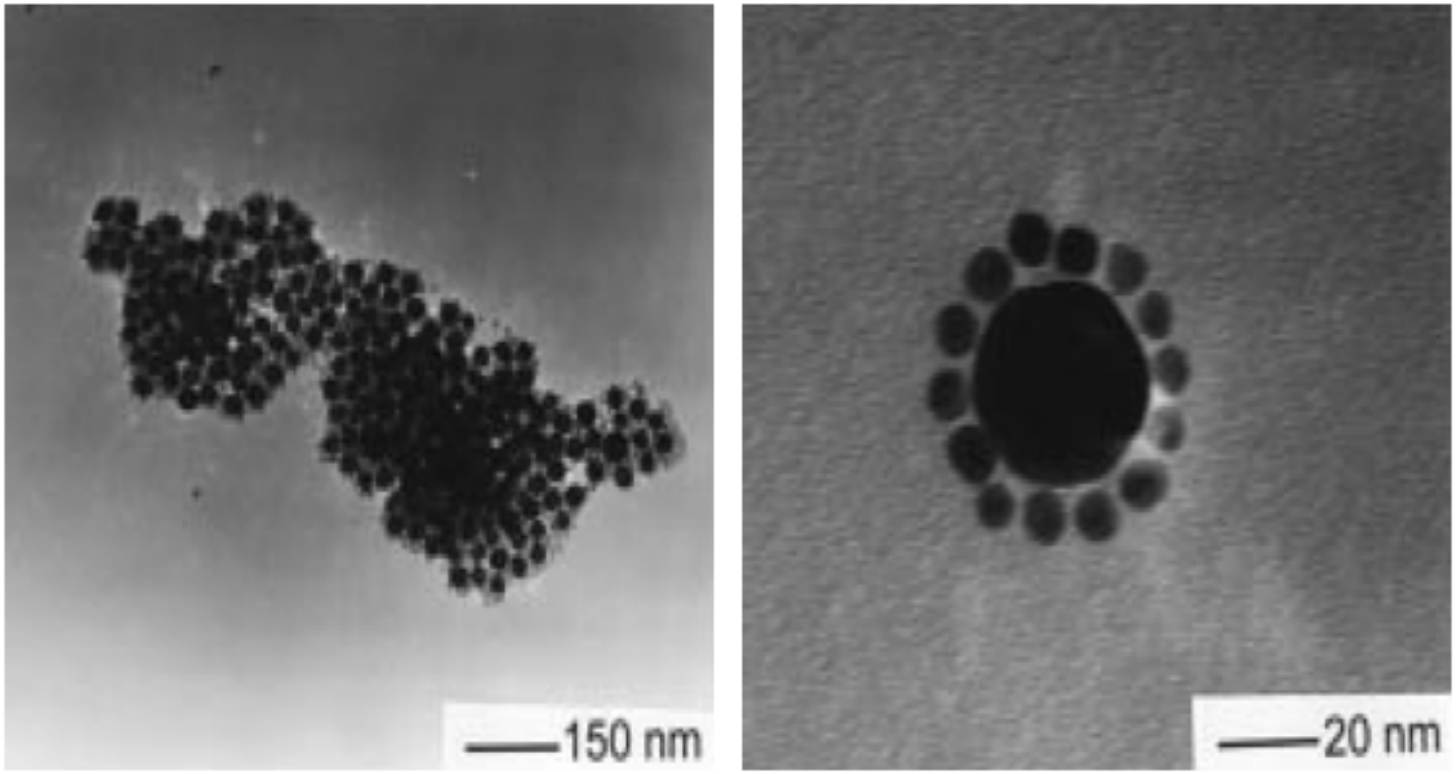
Cytosine (C)

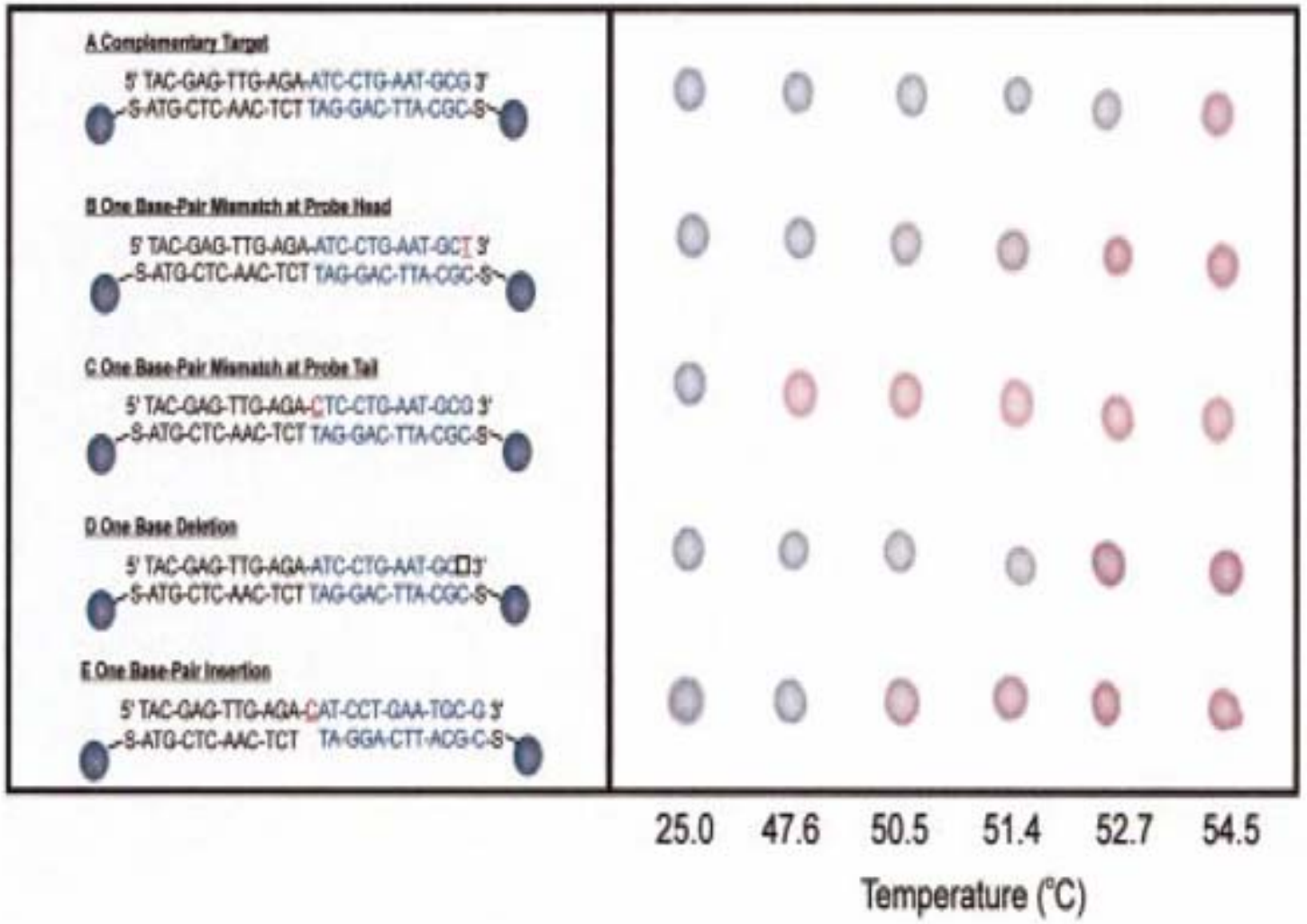
Oligonucleotide functionalized Au nanoparticle





Satellite structure of nanoparticle




A Complementary Target
5' TAC-GAG-TTG-AGA-ATC-CTG-AAT-GCG 3'
S-ATG-CTC-AAC-TCT TAG-GAC-TTA-CGC-S
B One Base-Pair Mismatch at Probe Head
5' TAC-GAG-TTG-AGA-ATC-CTG-AAT-GCT 3'
S-ATG-CTC-AAC-TCT TAG-GAC-TTA-CGC-S
C One Base-Pair Mismatch at Probe Tail
5' TAC-GAG-TTG-AGA-CTC-CTG-AAT-GCG 3'
S-ATG-CTC-AAC-TCT TAG-GAC-TTA-CGC-S
D One Base Deletion
5' TAC-GAG-TTG-AGA-ATC-CTG-AAT-GC 3'
S-ATG-CTC-AAC-TCT TAG-GAC-TTA-CGC-S
E One Base-Pair Insertion
5' TAC-GAG-TTG-AGA-CAT-CCT-GAA-TGC-G 3'
S-ATG-CTC-AAC-TCT TA-GGA-CTT-ACG-C-S
25.0
47.6
50.5
51.4
52.7
54.5
Temperature (°C)

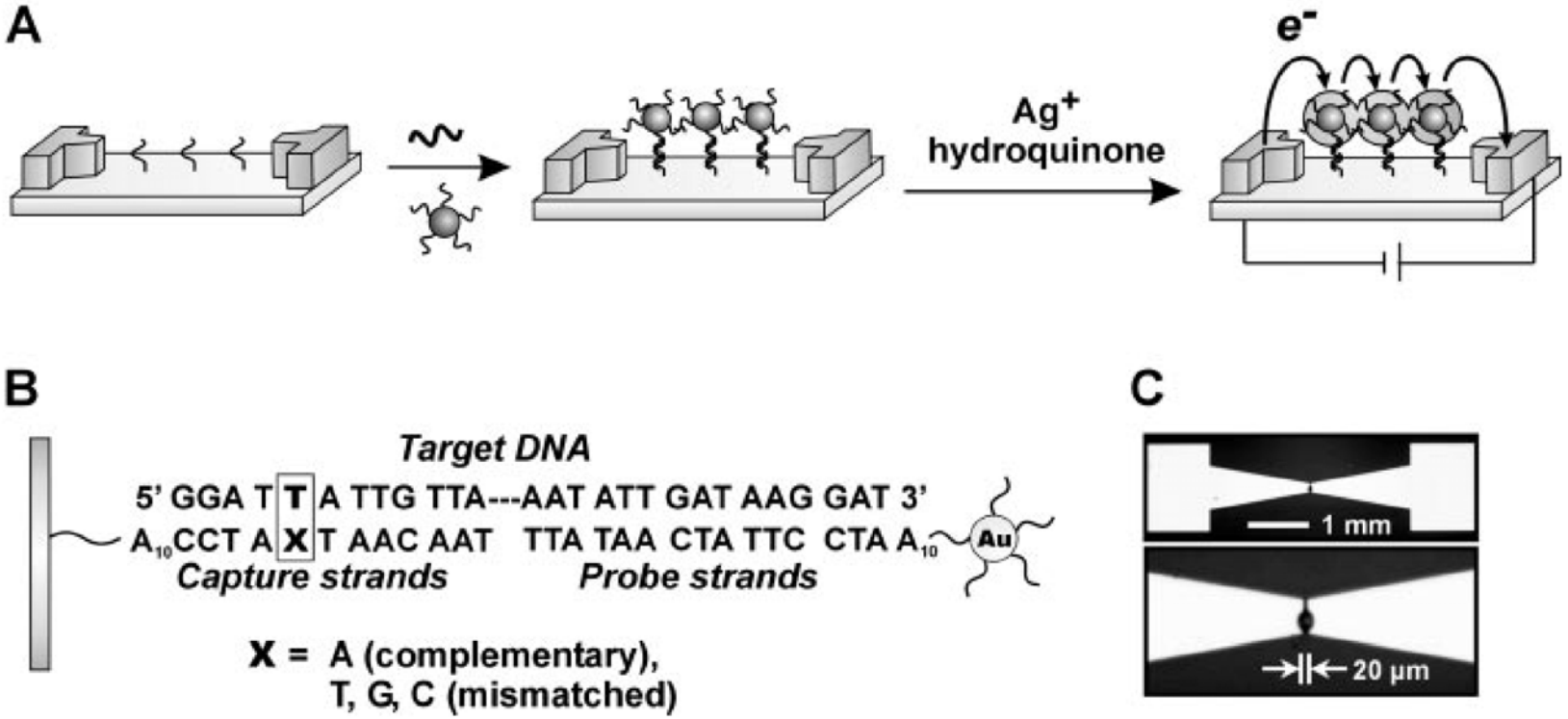
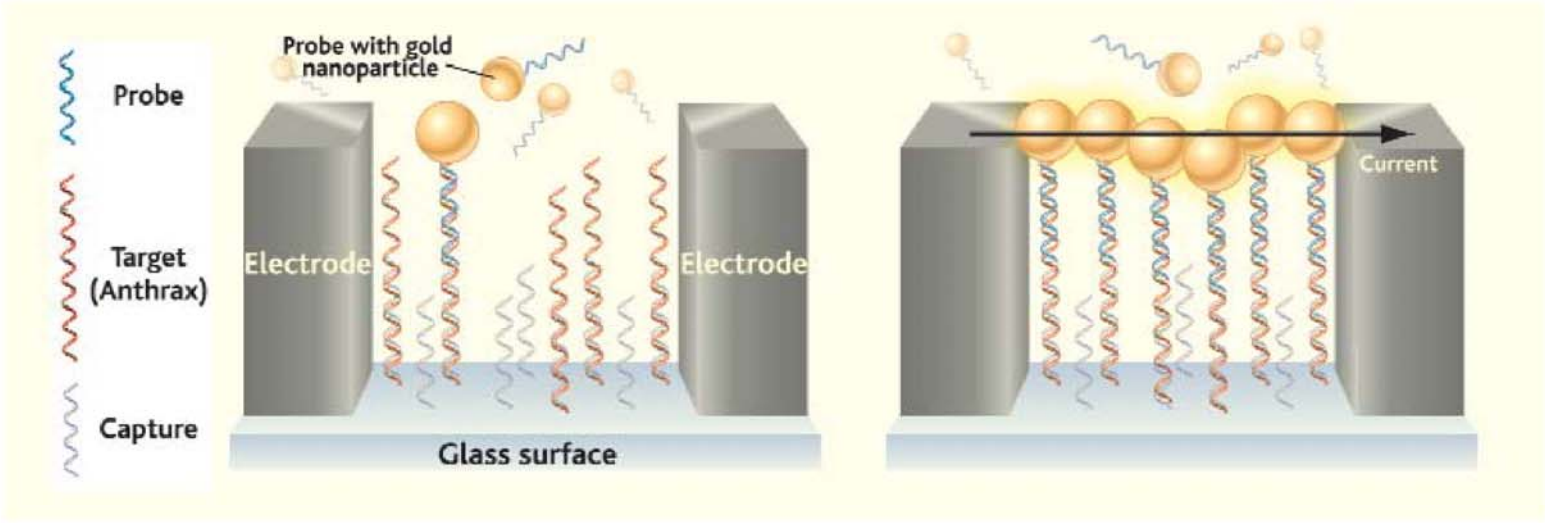
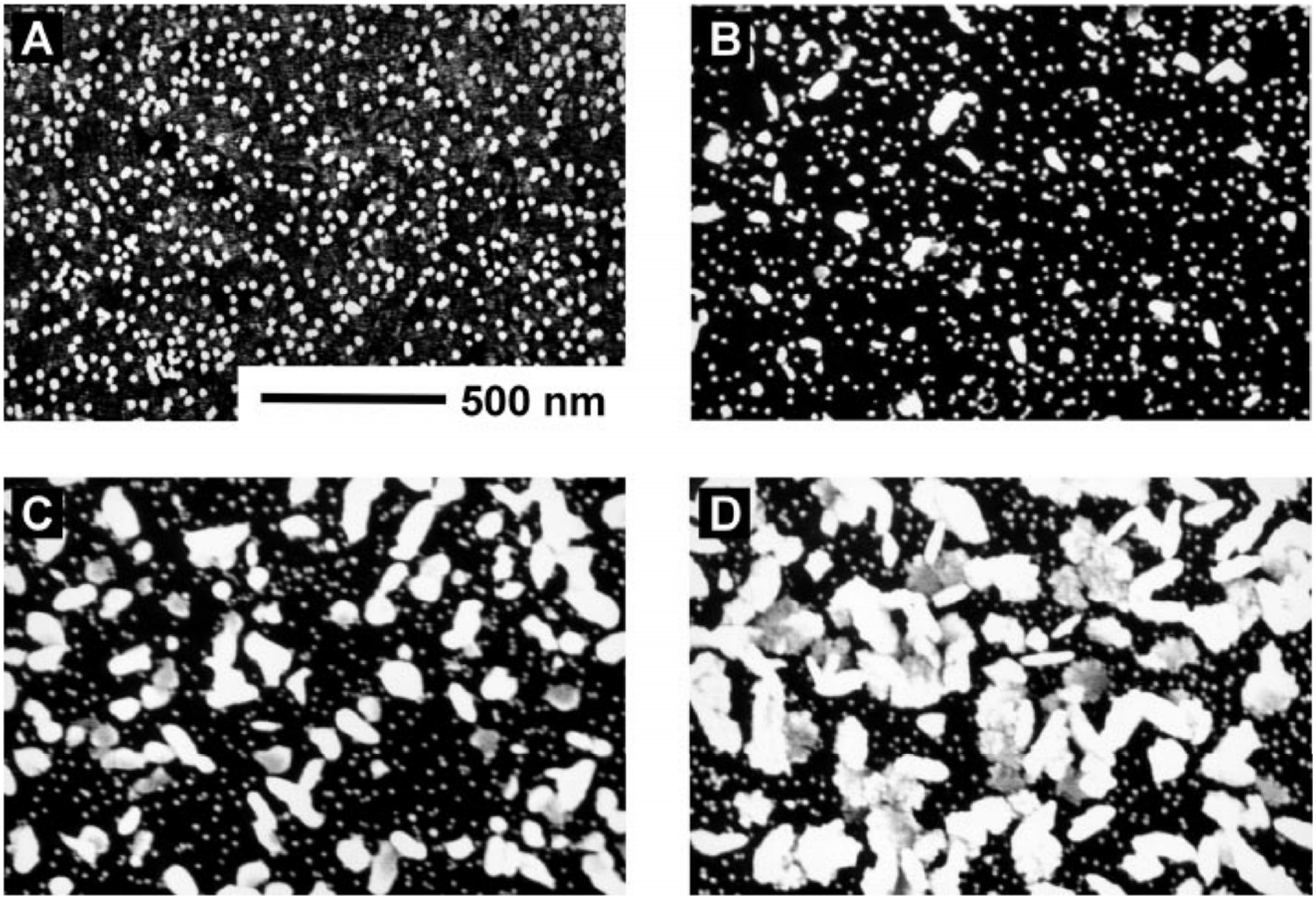
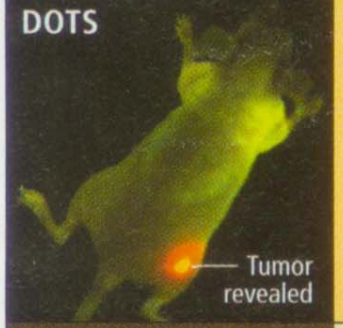
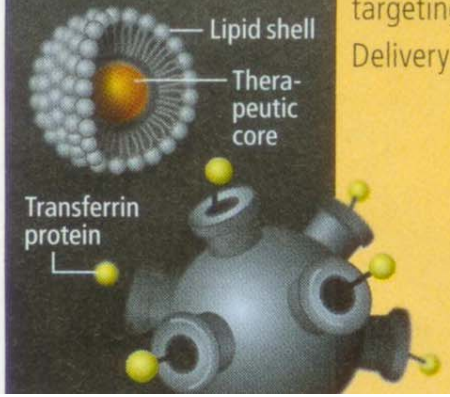


Fig. 1. (**A**) Scheme showing concept behind electrical detection of DNA. (**B**) Sequences of capture, target, and probe DNA strands. (**C**) Optical microscope images of the electrodes used in a typical detection experiment. The spot in the electrode gap in the high-magnification image is food dye spotted by a robotic arrayer (GMS 417 Microarrayer, Genetic Microsystems, Woburn, MA).



Golden gate. New technique detects target DNA (here, anthrax) by using it to link fixed "capture strands" with "probe strands" attached to current-carrying gold nanoparticles.


A
500 nm
B
C
D

QUANTUM DOTS 	Imaging	Nanocrystals made of inorganic elements such as cadmium or mercury encased in latex or metal respond to light by emitting fluorescence at different wavelengths and intensities depending on their composition. Antibodies attached to the crystals can cause the dots to bind to a select tissue, such as a tumor, which can then be more easily seen with conventional imaging devices.
NANOSHELLS 	Tissue targeting, Imaging	Solid silica nanospheres, sometimes encased in a thin layer of gold, will travel through the bloodstream without entering most healthy tissues, but they tend to accumulate in tumor tissue. Therapeutic molecules can be attached to the spheres, or once a large number of the nanoshells accumulate in a tumor, heat delivered to the tumor will be absorbed by the spheres, killing the tissue. Depending on their composition, nanoshells can also absorb or scatter light, enhancing tumor images made with certain forms of spectroscopy.
NANOPARTICLES 	Tissue targeting, Delivery	Particles composed of a variety of materials can be constructed to contain therapeutic molecules in their core and to release them at a desirable time and location. Such delivery vehicles include simple lipid shells that passively leak through tumor blood vessel walls, then slowly release a traditional chemotherapy drug into the tissue. Newer nanoparticles are more complexly designed, including exterior elements such as antibodies to target tumor-specific proteins, and materials that minimize the particles' interaction with healthy tissues.

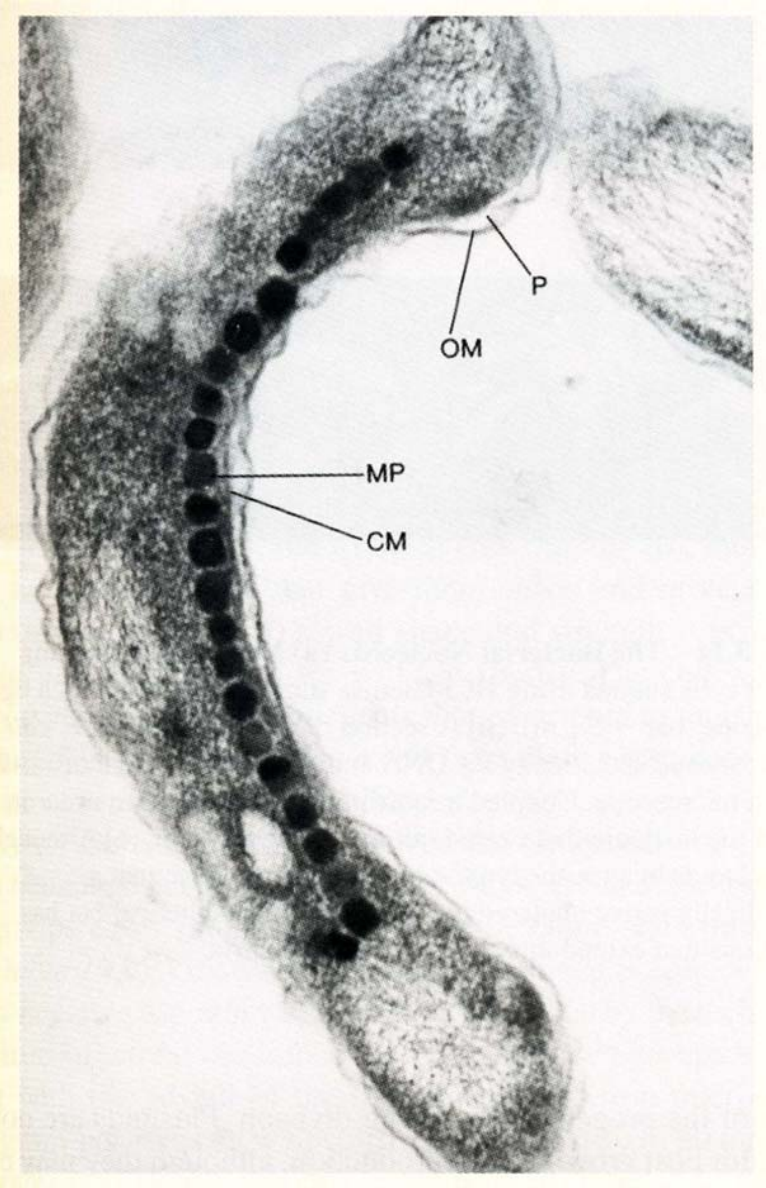
1. Introduction

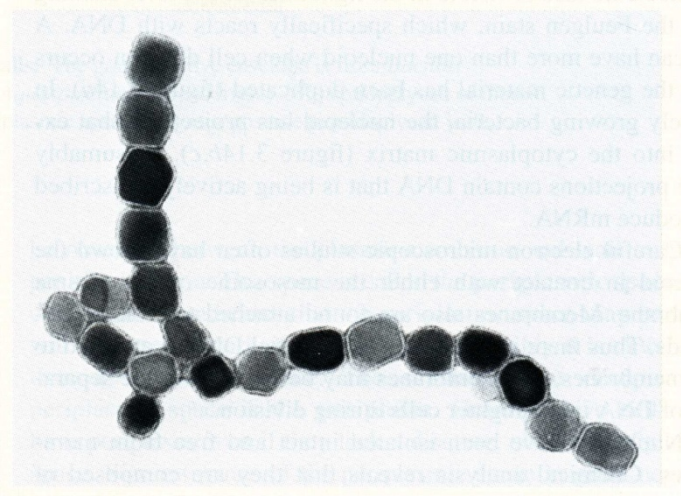
2. Toxicity

3. Sensor (detecting disease)

4. Label (on target)

Living Magnets





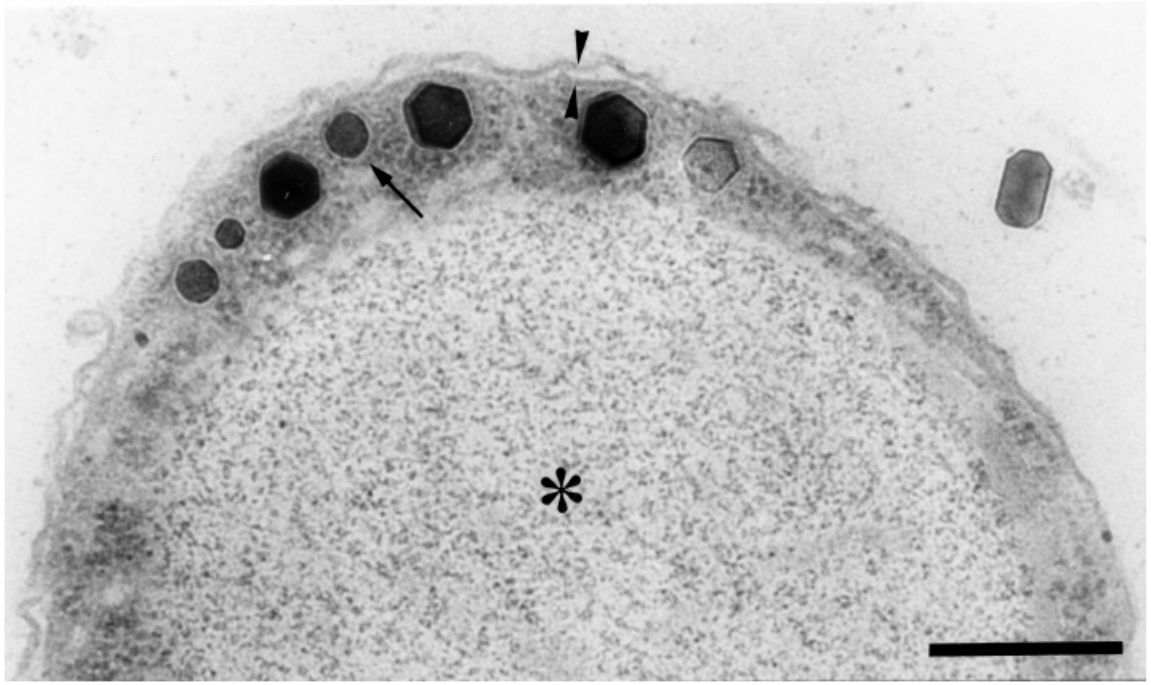
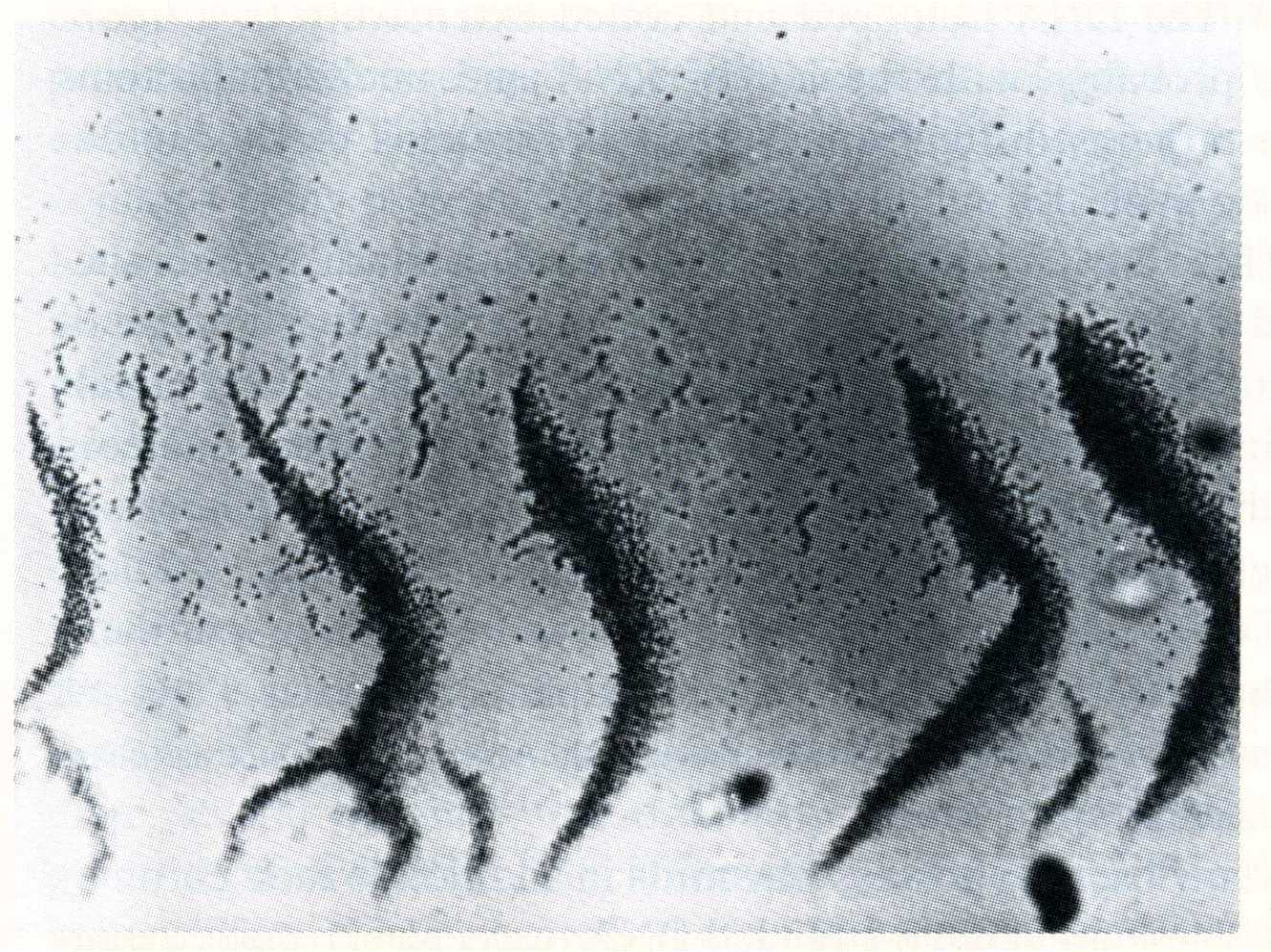


FIG. 1. Ultra-thin section of an uncultured magnetotactic coccus from microcosm observed by transmission electron microscopy. Note the magnetosomes enveloped by an organic membrane (arrow), the gram-negative cell envelope (arrowheads) and one large phosphorus-containing granule (asterisk). Bar = 250 nm.



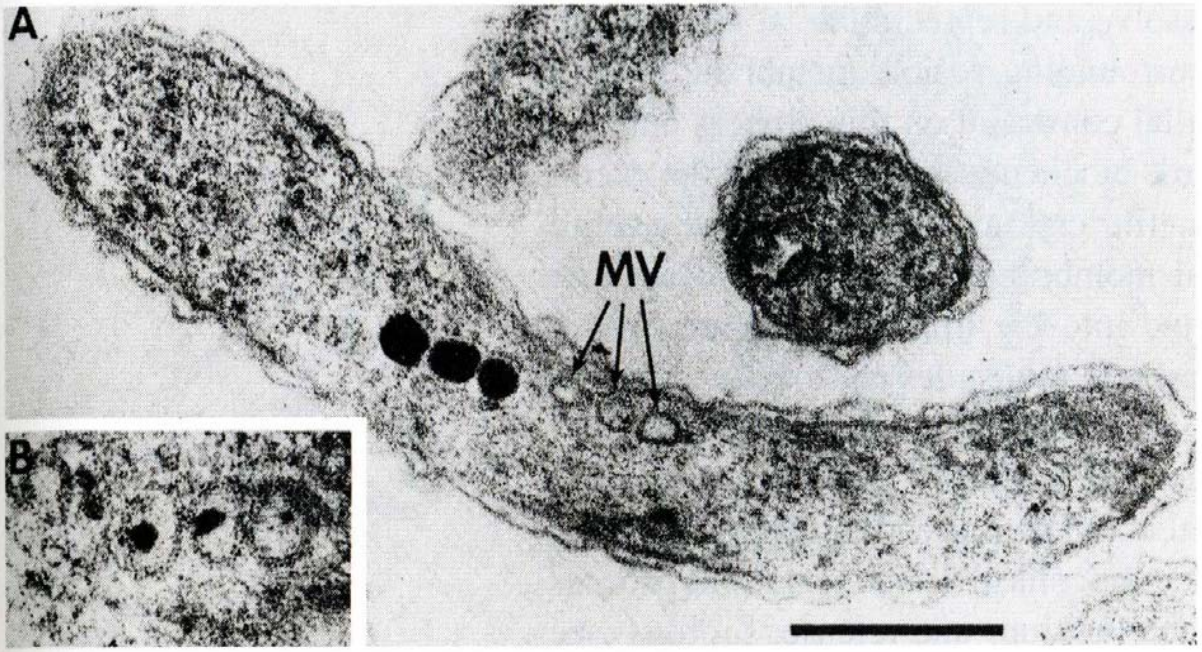


Fig. 5.5 Section through a magnetotactic bacterial cell showing: (A) three mature magnetite crystals and three empty magnetosome vesicles (MV); (B) vesicles containing immature magnetite particles. Scale bar, 250 nm.

IOP PUBLISHING NANOTECHNOLOGY

Nanotechnology **18** (2007) 285604 (7pp) doi:10.1088/0957-4484/18/28/285604

Preparation and antibacterial activity of Fe_3O_4@Ag nanoparticles

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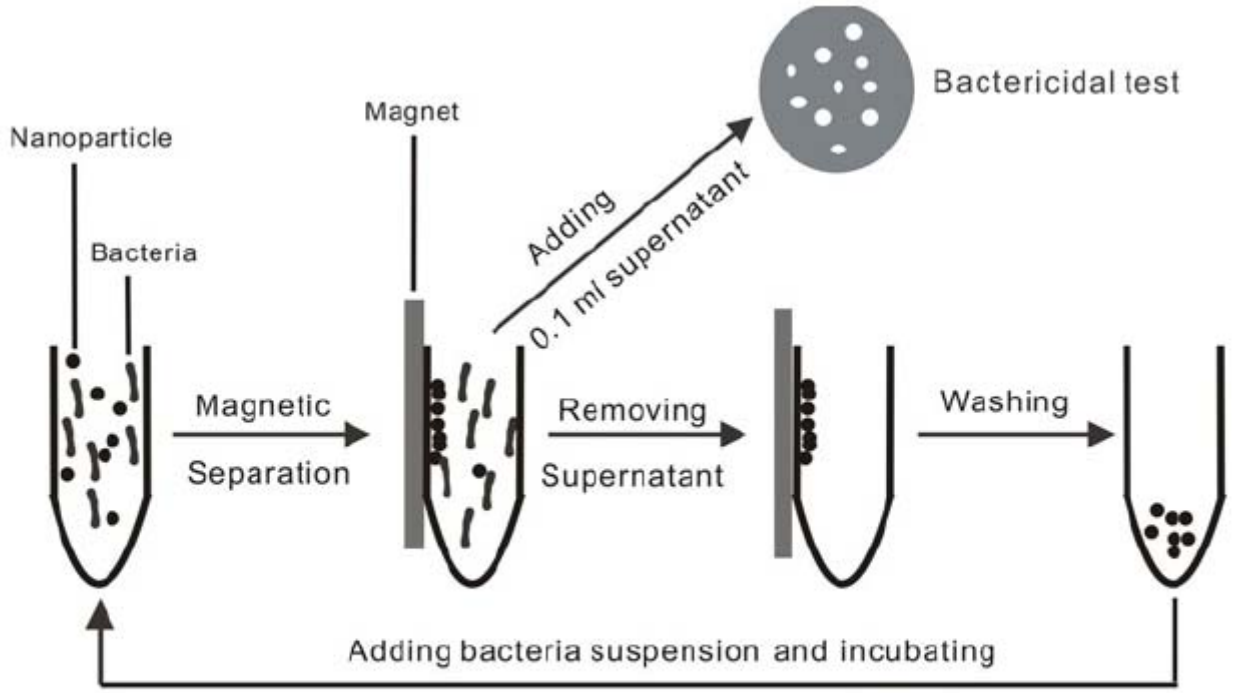


Figure 1. Schematic illustration of the antibacterial rate for recycled Fe_3O_4@Ag nanoparticles for different recycling times.

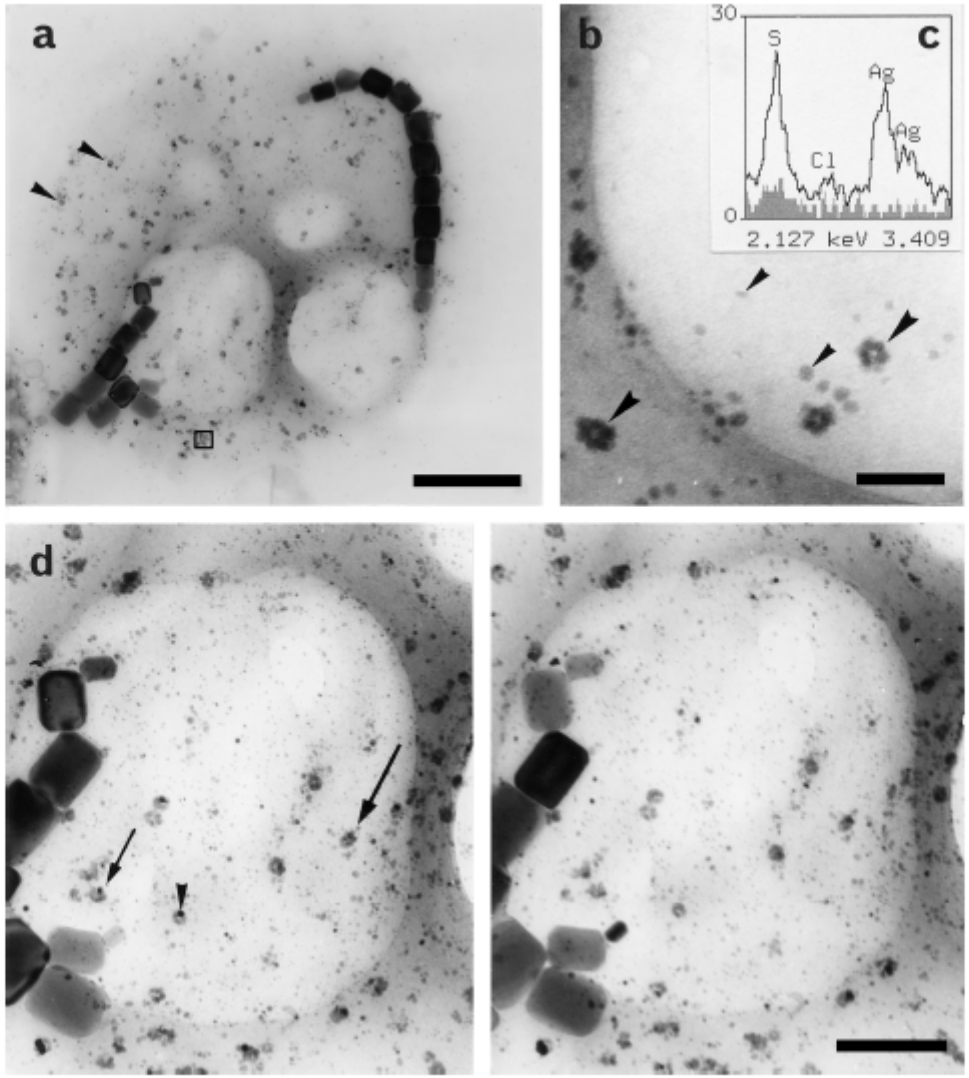
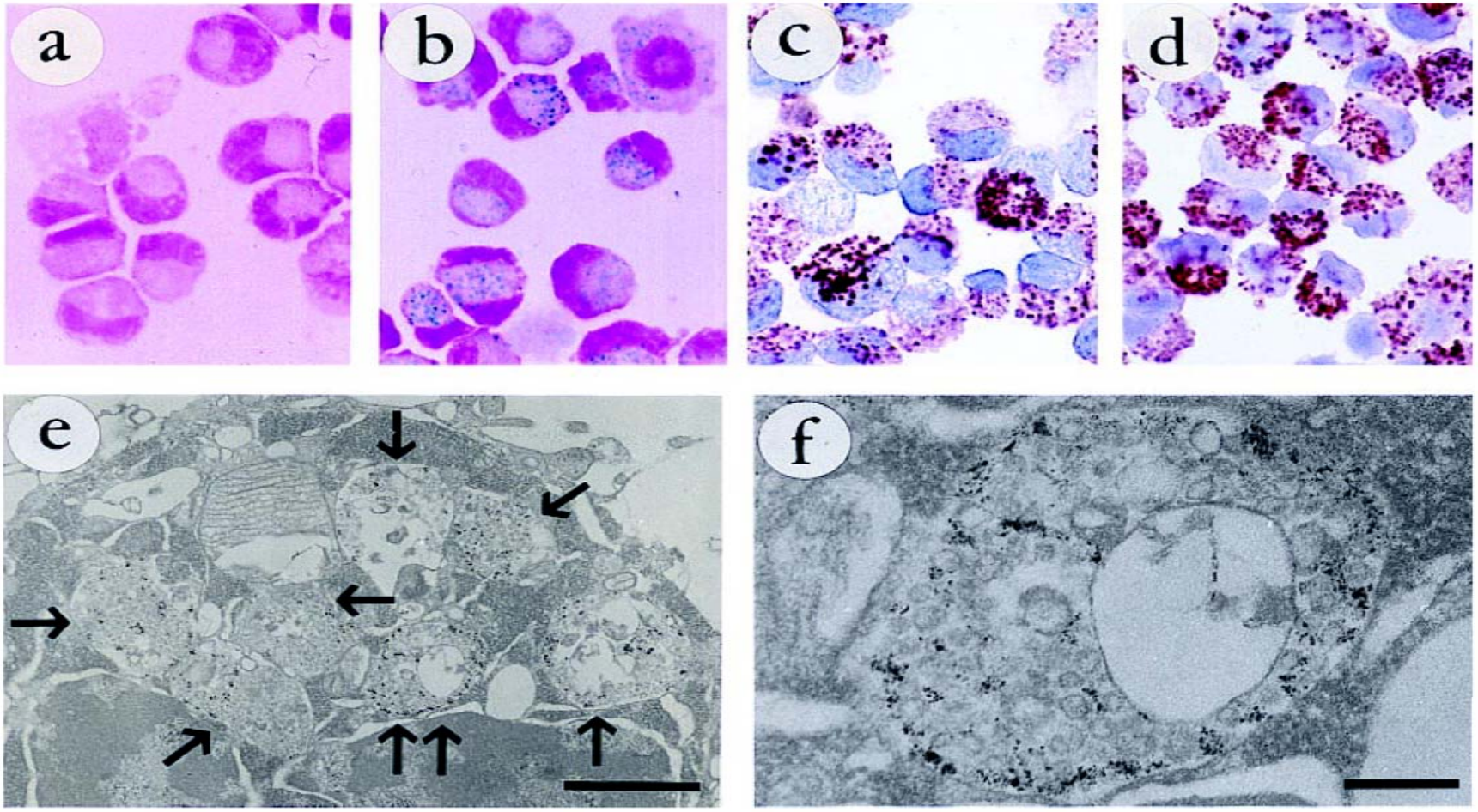
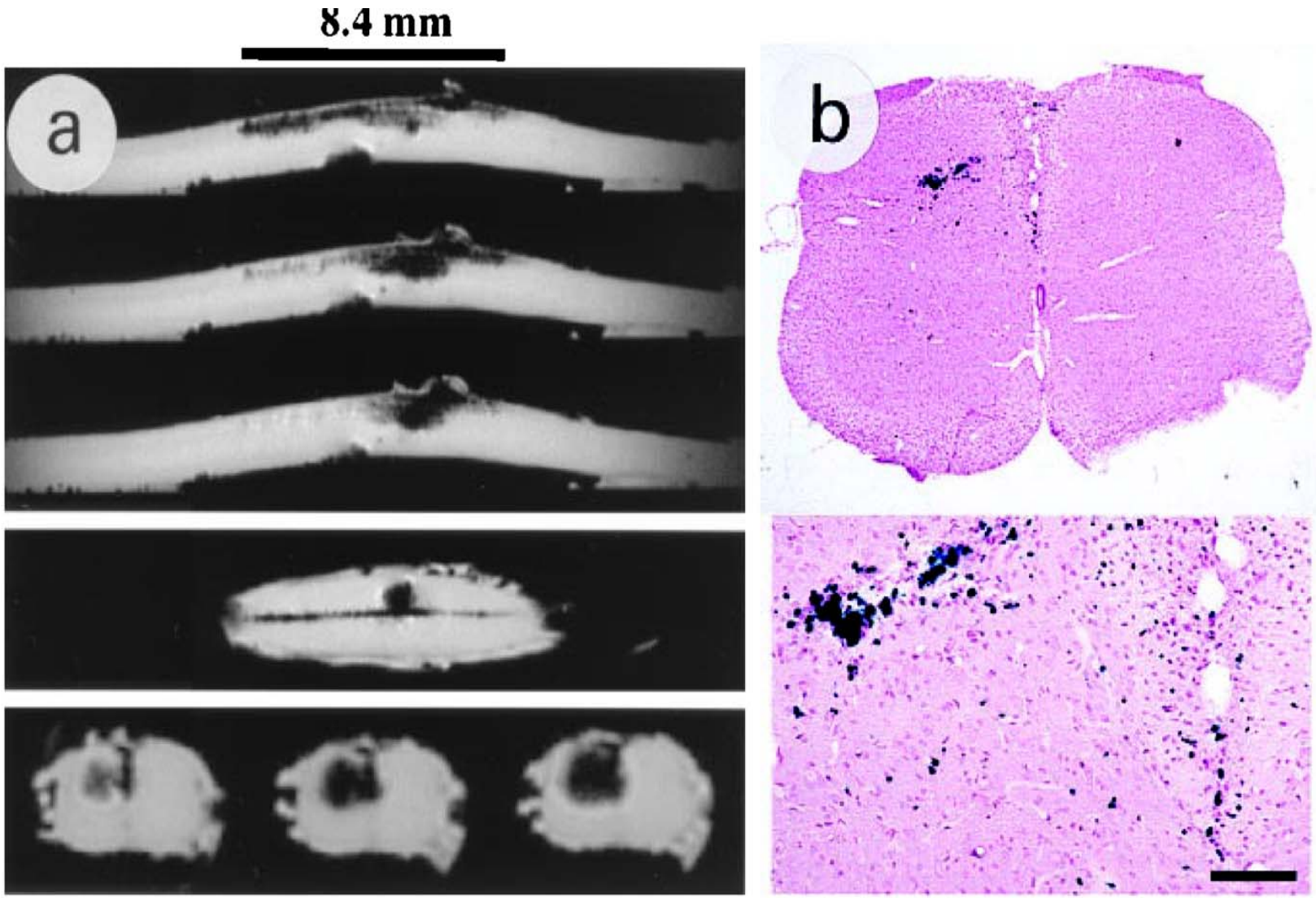
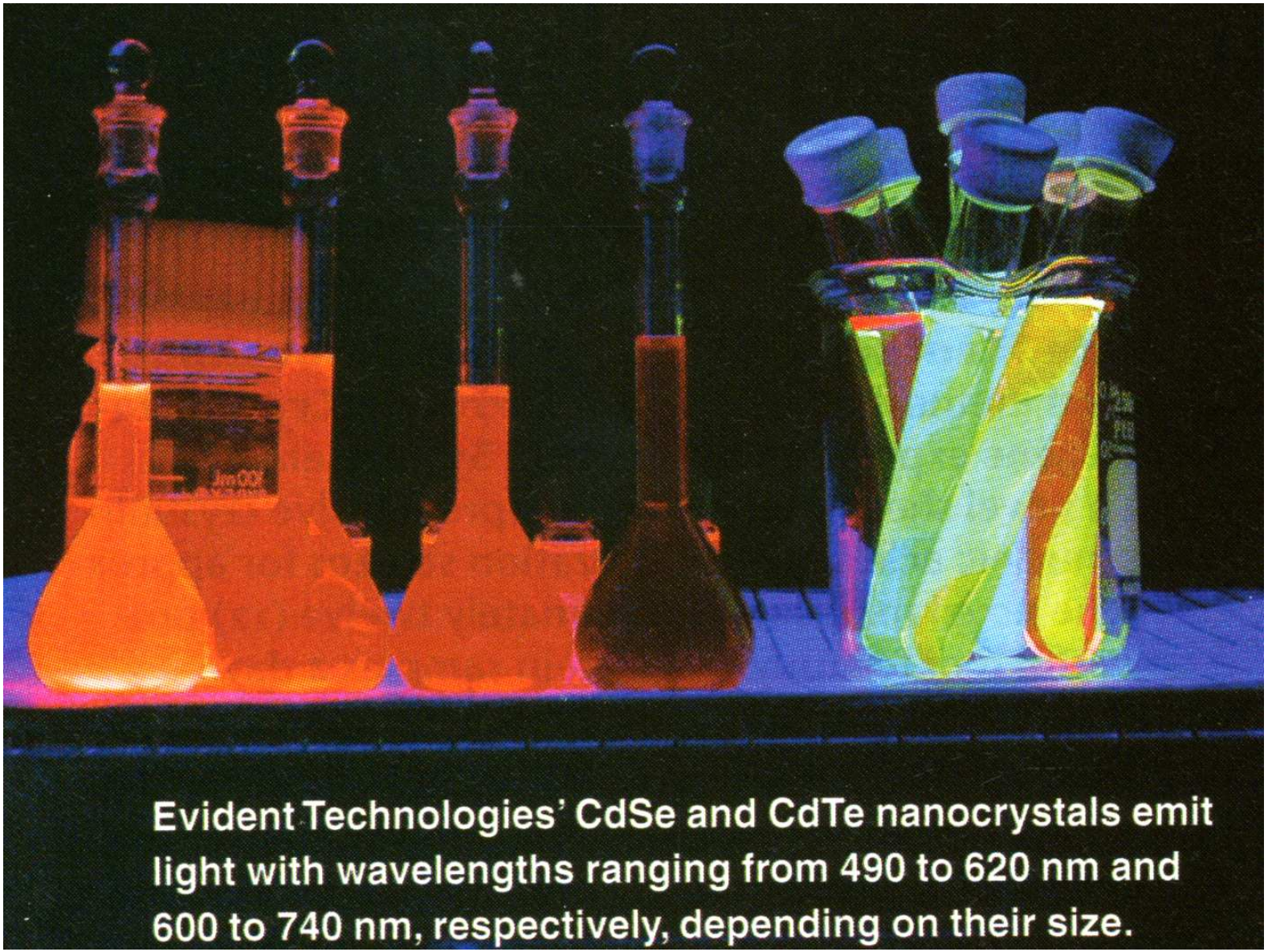


FIG. 6. Transmission electron micrographs and spectra of morphotype 1 bacteria exposed to AgCl for 24 h. (a) Whole magnetotactic bacterium showing numerous electron-dense deposits (arrowheads). The square shows the site where the EDX spectrum shown in (c) was taken. Bar = 0.5 μm. (b) Larger magnification showing

Magnetic nanoparticle in magnetic resonance tracking of cell migatrion




8.4 mm
a
b



Evident Technologies' CdSe and CdTe nanocrystals emit light with wavelengths ranging from 490 to 620 nm and 600 to 740 nm, respectively, depending on their size.

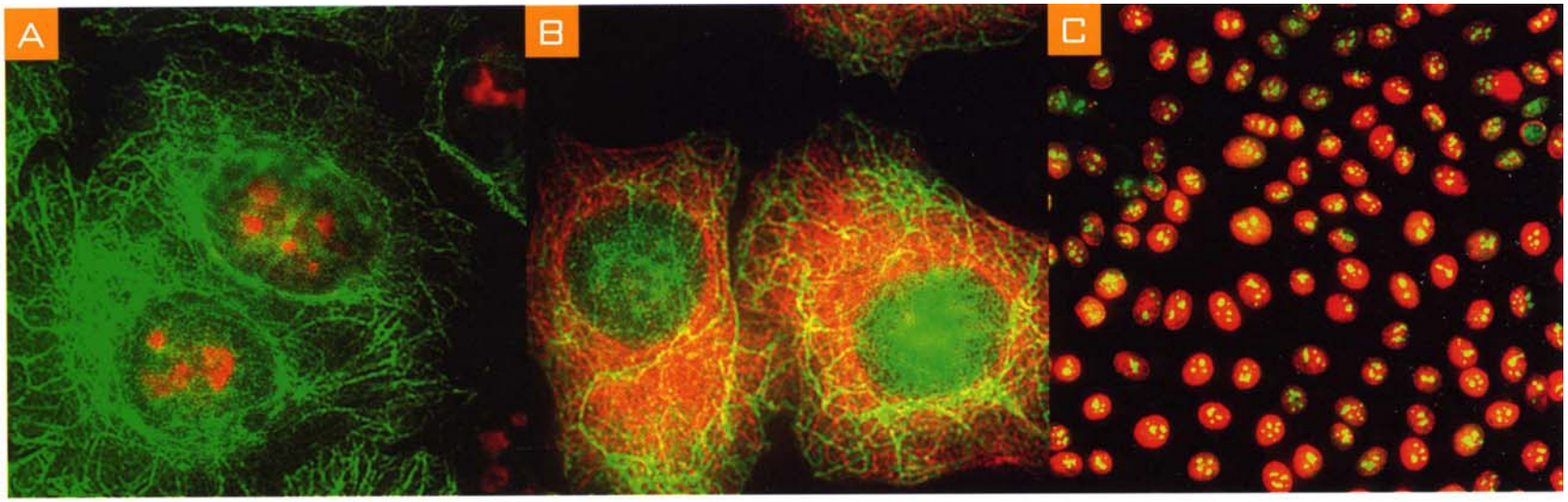
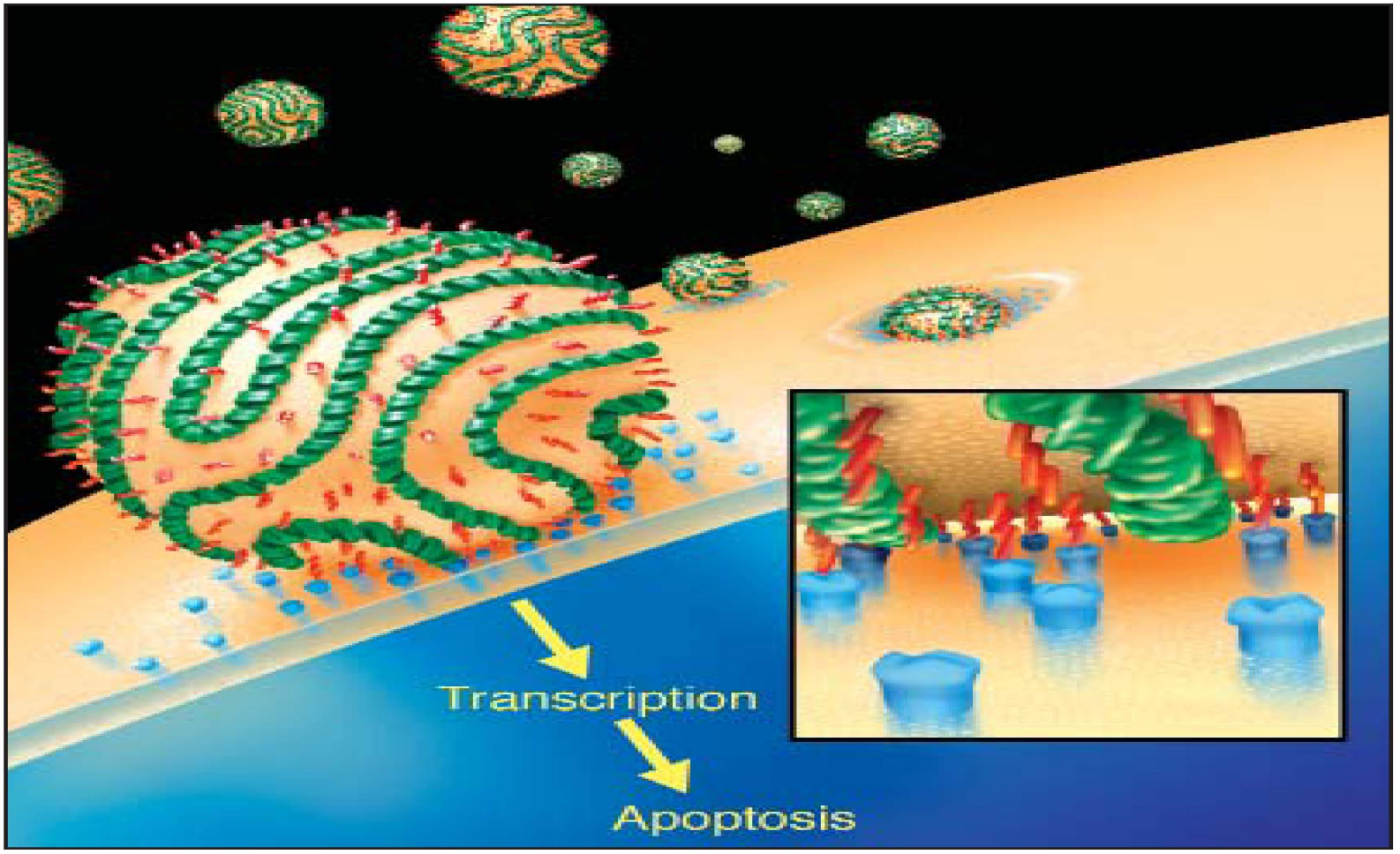


FIGURE 1. DOUBLE LABELING WITH QDOT SECONDARY ANTIBODY CONJUGATES. Two cellular targets in fixed human epithelial cells were detected simultaneously with different combinations of Qdot Secondary Antibody Conjugates after the cells were incubated with the appropriate primary antibodies. A: Cytokeratin (green, Qdot 565 anti-Mouse Conjugate) and Ki-67 (red, Qdot 655 anti-Rabbit Conjugate). B: Cytokeratin (green, Qdot 565 anti-Mouse Conjugate) and microtubules (red, Qdot 655 anti-Rat Conjugate). C: Ki-67 (green, Qdot 565 anti-Rabbit Conjugate) and nucleosomes (red, Qdot 655 anti-Mouse Conjugate). Magnification: 100X in A and B, 20X in C.



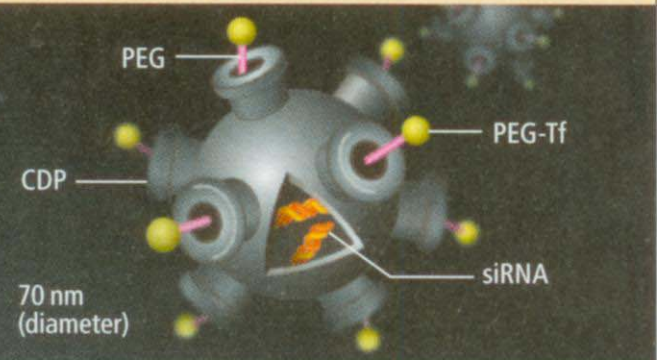
Bull's-eye. Nanoparticles packed with targeting molecules (red) anchor to integrins (blue) on the outside of a tumor blood vessel cell before shuttling mutant DNA (green) inside.

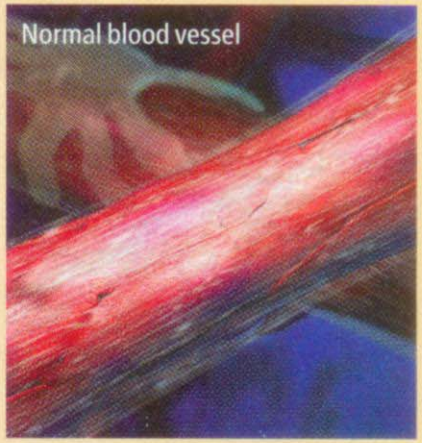
DESIGNED TO DELIVER

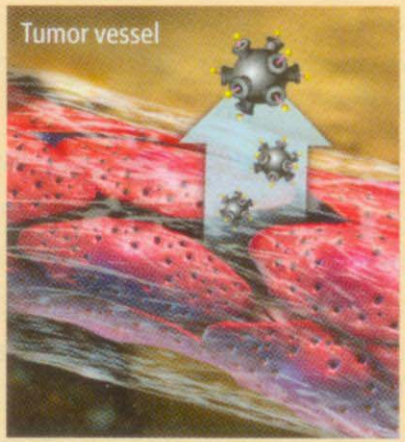
An experimental nanoparticle therapeutic called CALAA-01 illustrates some of the advantages such agents can offer. In addition to having a natural tendency to accumulate in tumors, nanoparticles can be designed to home to one or more receptors commonly found on cancer cells. The particles' mode of cell entry also allows them to evade cellular pumps that eject some drugs.

CUSTOMIZED STRUCTURE

The particle is built with biocompatible materials: a cyclodextrin-containing polymer (CDP) with polyethylene glycol (PEG) stalks to which transferrin proteins (Tf) are attached. Inside, as many as 2,000 siRNA molecules—the therapeutic agents—are stored.

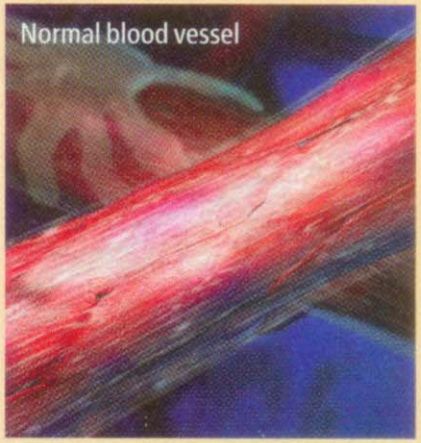


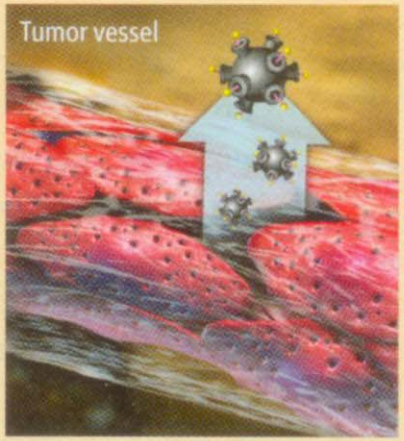




PASSIVE TUMOR TARGETING

When the particles enter a patient's bloodstream, they circulate freely but cannot penetrate most blood vessel walls. Tumor vessels are abnormally leaky, with large pores that allow nanoparticles to pass through and accumulate in the tumor tissue.



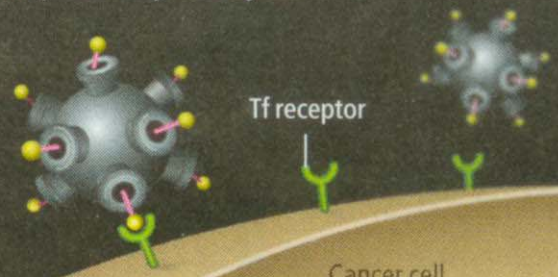


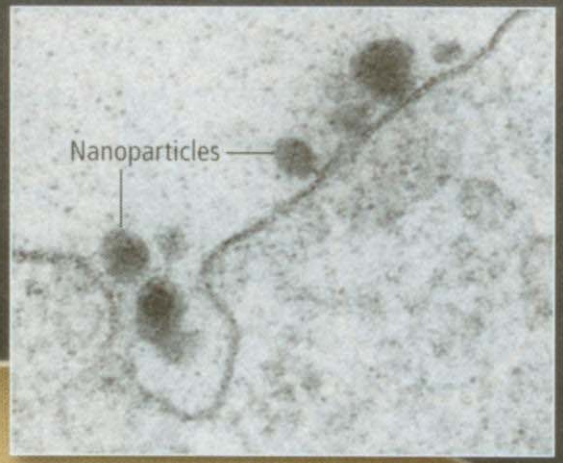
PASSIVE TUMOR TARGETING

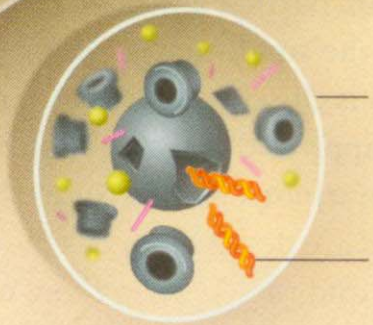
When the particles enter a patient's bloodstream, they circulate freely but cannot penetrate most blood vessel walls. Tumor vessels are abnormally leaky, with large pores that allow nanoparticles to pass through and accumulate in the tumor tissue.

ACTIVE TUMOR TARGETING

Transferrin receptors on the surface of a cancer cell bind to the transferrin protein on the nanoparticle, causing the cell to internalize the nanoparticle by endocytosis.







CONTROLLED RELEASE

Once inside the cell, a chemical sensor within the nanoparticle responds to the low pH within the endocytotic vesicle by simultaneously triggering disassembly of the nanoparticle and release of the siRNA molecules that will block a gene's instructions from being translated into a protein the cancer cell needs to survive.

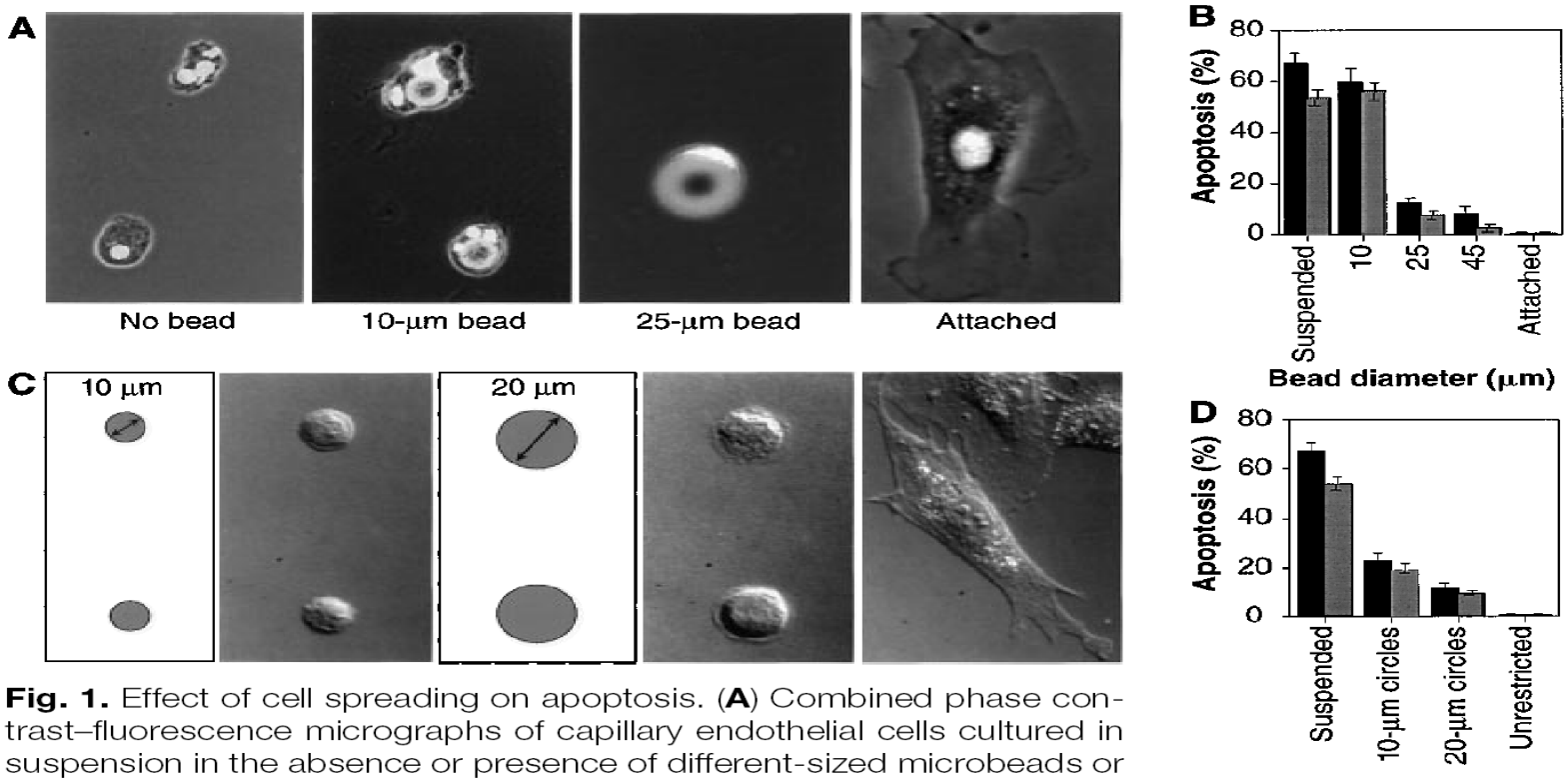
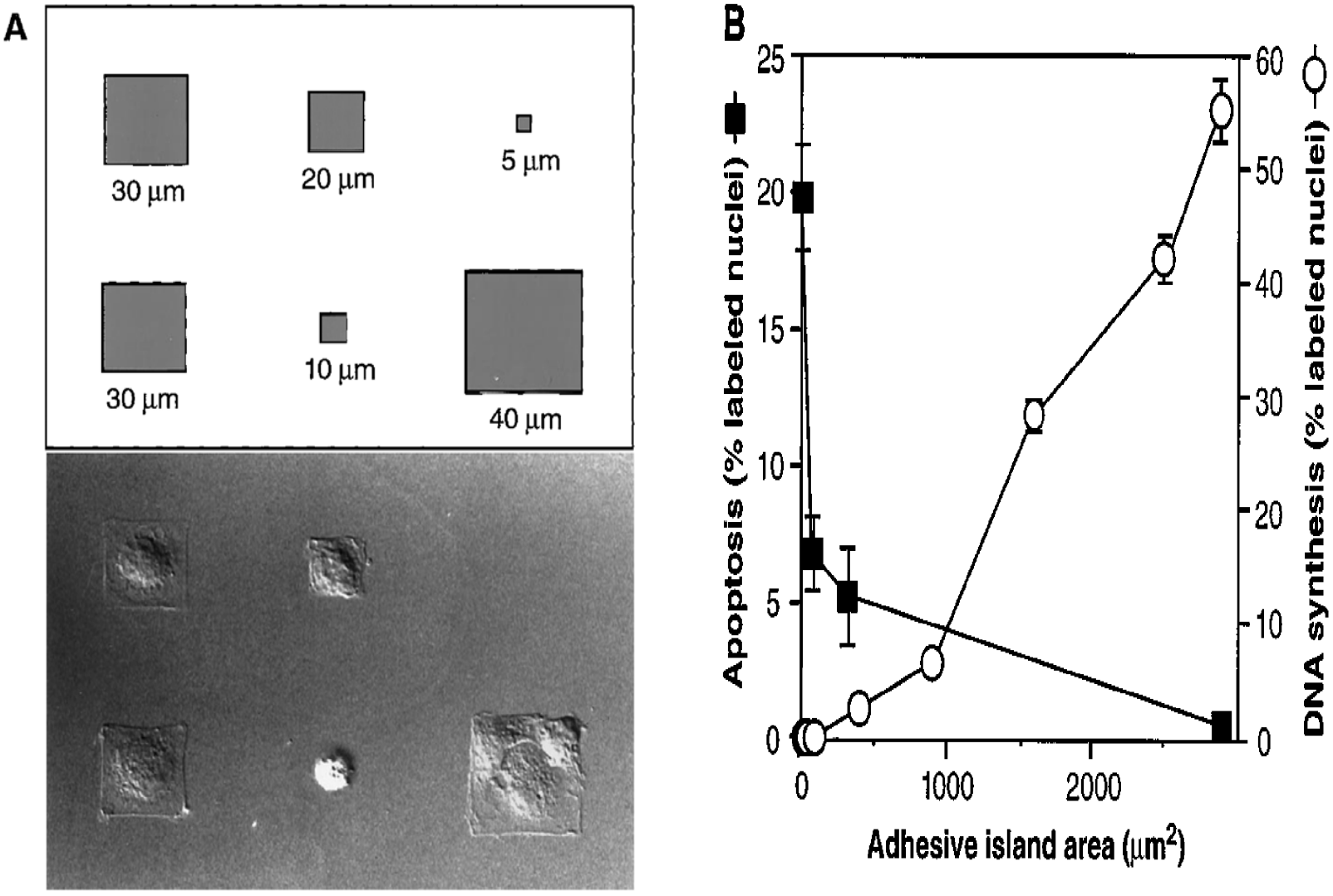


Fig. 1. Effect of cell spreading on apoptosis. (**A**) Combined phase contrast–fluorescence micrographs of capillary endothelial cells cultured in suspension in the absence or presence of different-sized microbeads or attached to a planar culture dish coated with FN for 24 hours (*28*). In the highly spread cell on the 25-μm bead, only the flattened 4′,6′-diamidino-2-phenylindole (DAPI)–stained nucleus is clearly visible. (**B**) Apoptosis in cells attached to different-sized beads, in suspension, or attached to a dish. The apoptotic index was quantitated by measuring the percentage of cells exhibiting positive TUNEL staining (black bars) (Boehringer Mannheim), which detects DNA fragmentation; similar results were obtained by analyzing changes in nuclear condensation and fragmentation in cells stained with DAPI at 24 hours (gray bars). Apoptotic indices were determined only within single cells bound to single beads. Error bars indicate SEM. (**C**) Differential interference-contrast micrographs of cells plated on substrates micropatterned with 10- or 20-μm-diameter circles coated with FN (left), by a microcontact printing method (*29*) or on a similarly coated unpatterned substrate (right). (**D**) Apoptotic index of cells attached to different-sized adhesive islands coated with a constant density of FN for 24 hours; similar results were obtained with human and bovine capillary endothelial cells (*28*). Bars same as in (B).


A
30 μm
20 μm
5 μm
30 μm
10 μm
40 μm
B
Apoptosis (% labeled nuclei)
DNA synthesis (% labeled nuclei)
Adhesive island area (μm²)
0
5
10
15
20
25
0
10
20
30
40
50
60
0
1000
2000

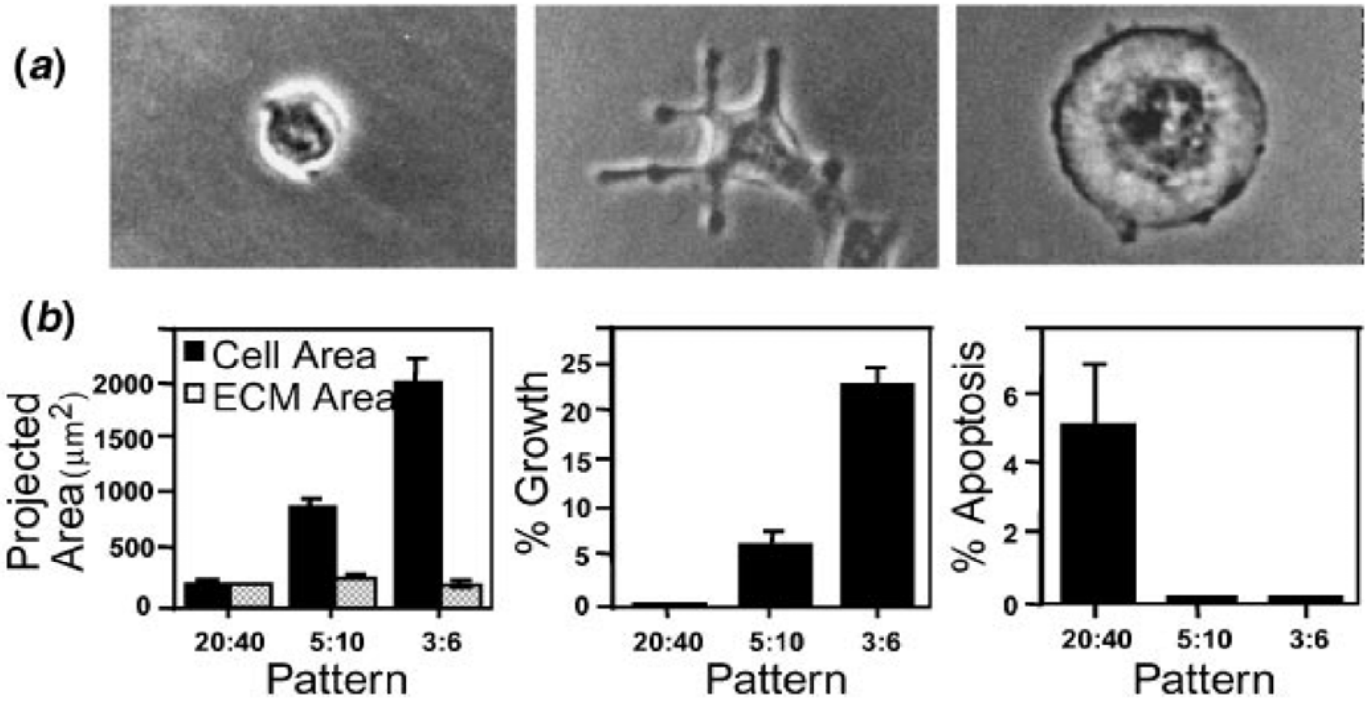
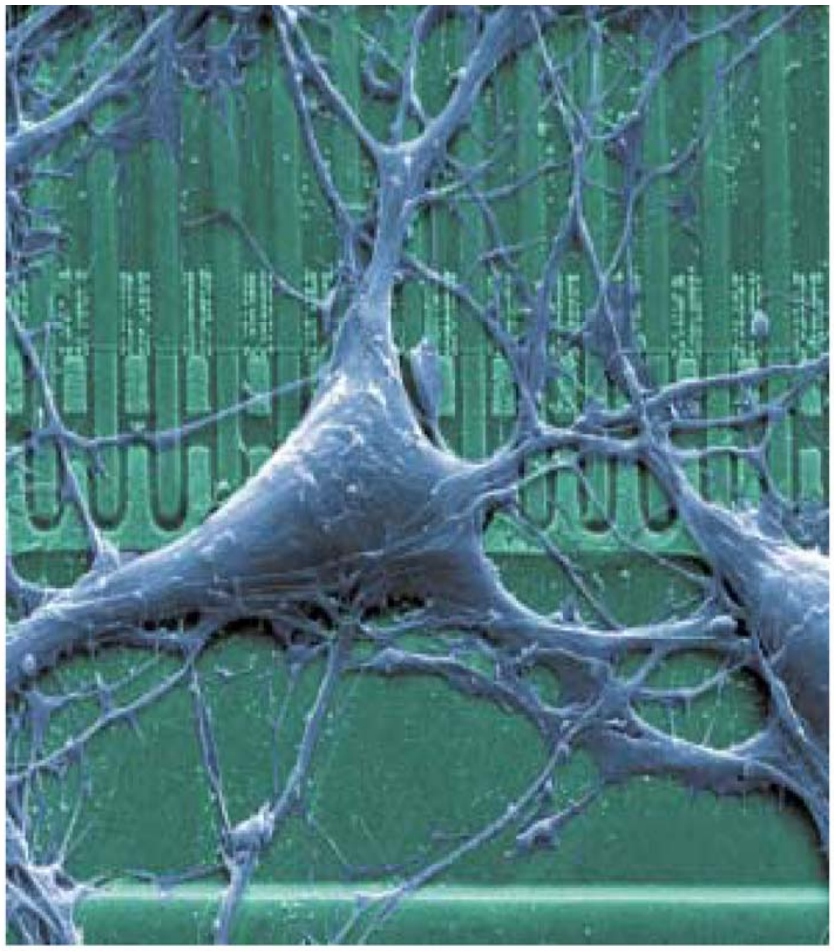
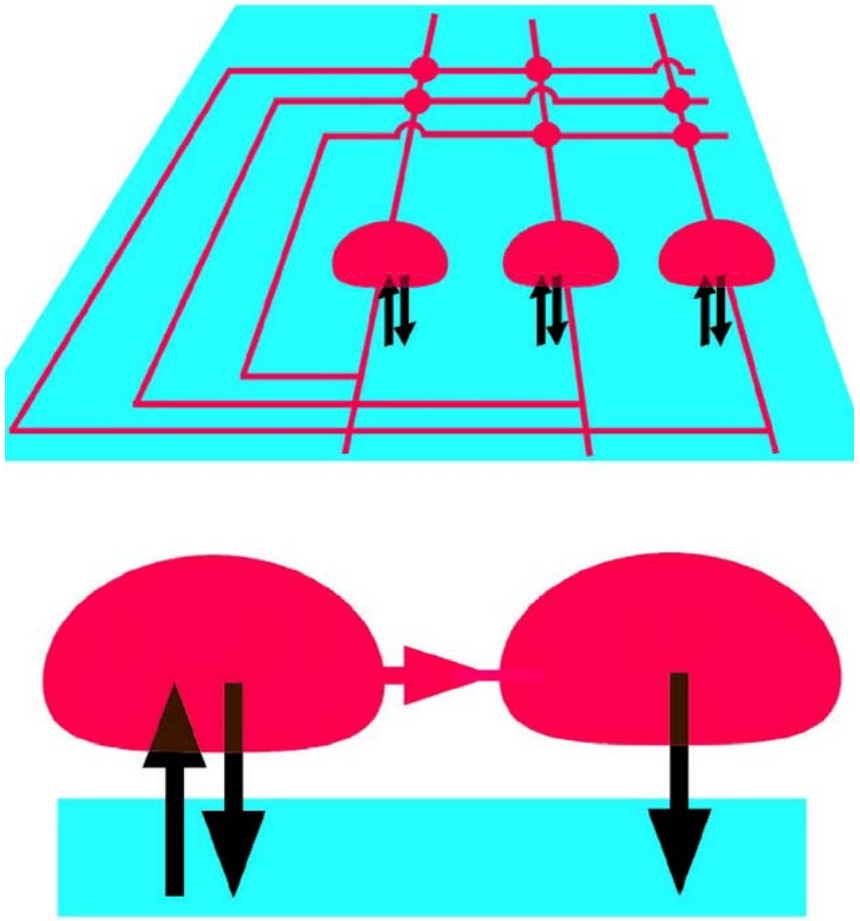
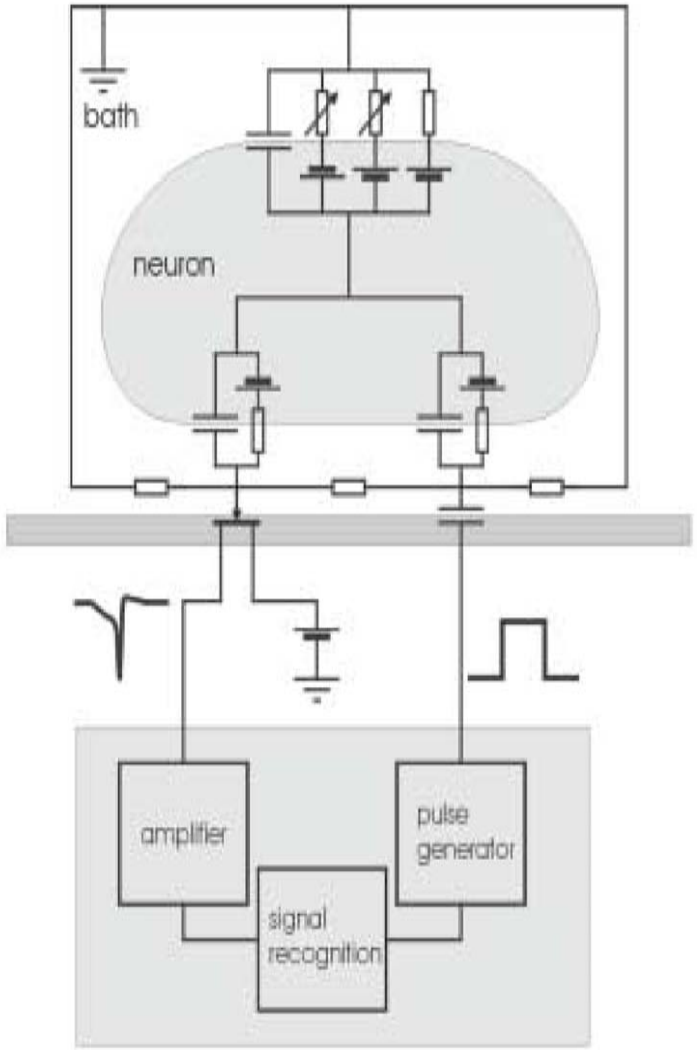


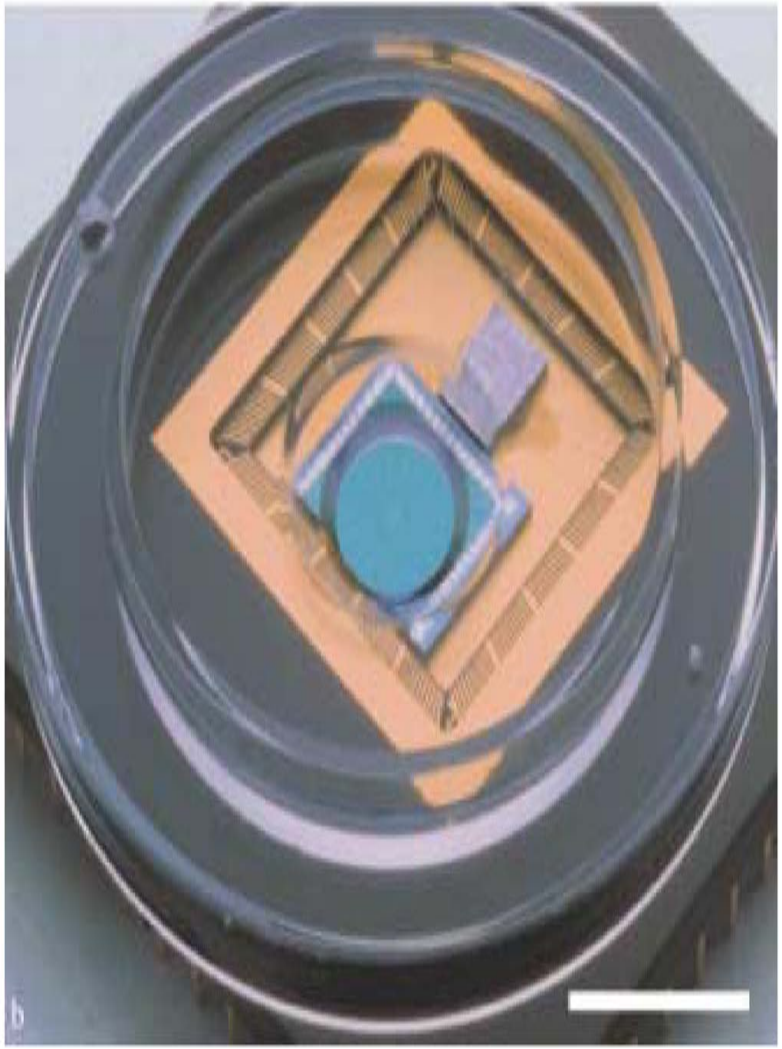
Figure 8 The extent of cell spreading determines the genetic programs engaged by a bovine capillary endothelial (BCE) cell. (*a*) Micrographs of BCE cells attached to individual 20- or 50-μm-diameter islands, or to multiple 5-μm-diameter islands patterned with microcontact printing. (*b*) Plots of the values of the extracellular matrix contact area and projected cell area, the percentage of cells in the growth phase, and the percentage of cells entering apoptosis for cells patterned on circular areas with diameters of 20, 5, and 3 μm, separated by 40, 10, and 6 μm, respectively.

Rat brain’s nerve cell on a silicon chip






bath
neuron
amplifier
signal
recognition
pulse
generator


b

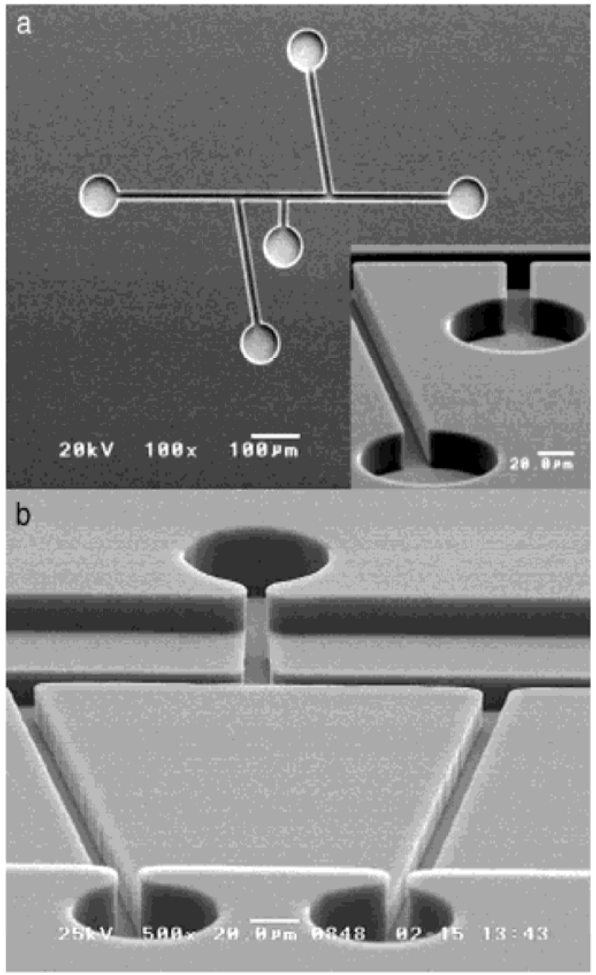


Fig. 1. Scanning electron micrographs of topographical polyester structures. a) One-layer structure with five pits and connecting grooves. The diameter of the pits is 80 µm, the width of the grooves is 15 µm, and the height of the structures 20 µm. b) Two-layer structure. Both layers are about 15 µm thick.

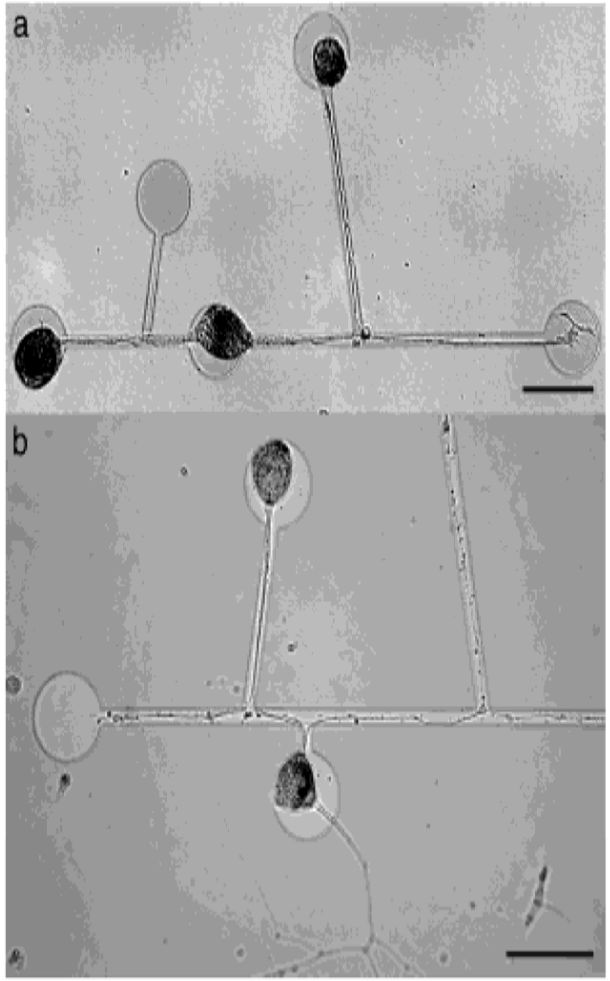
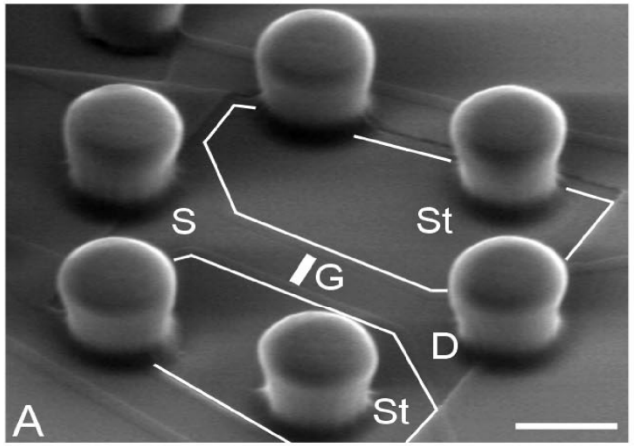
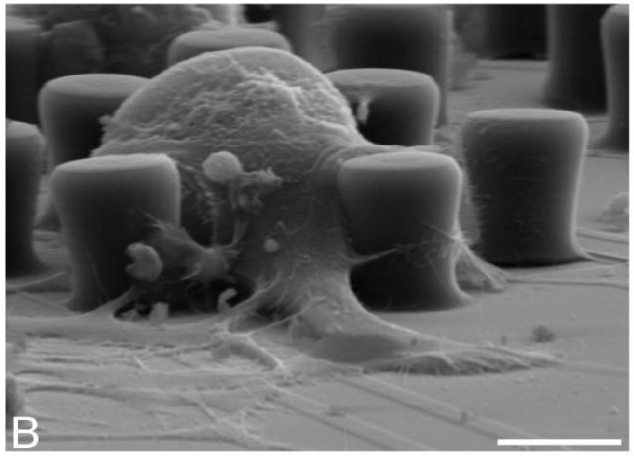
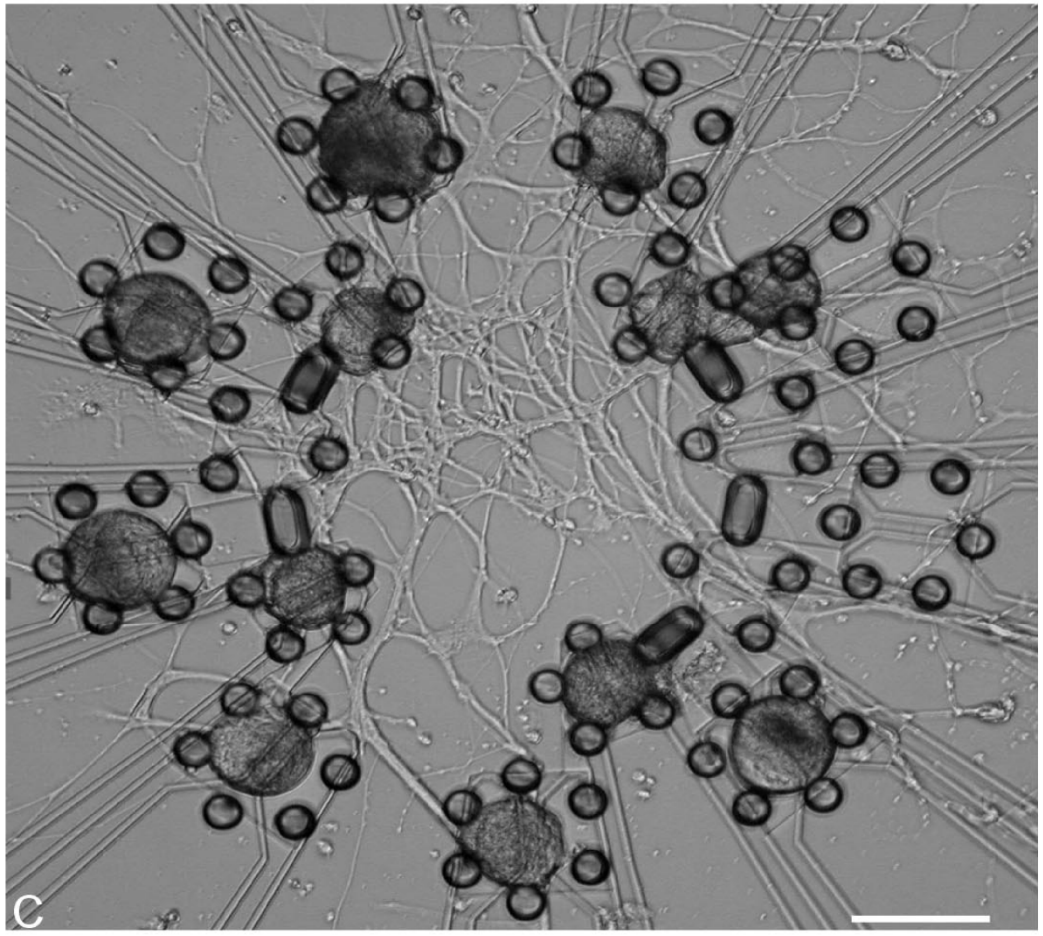


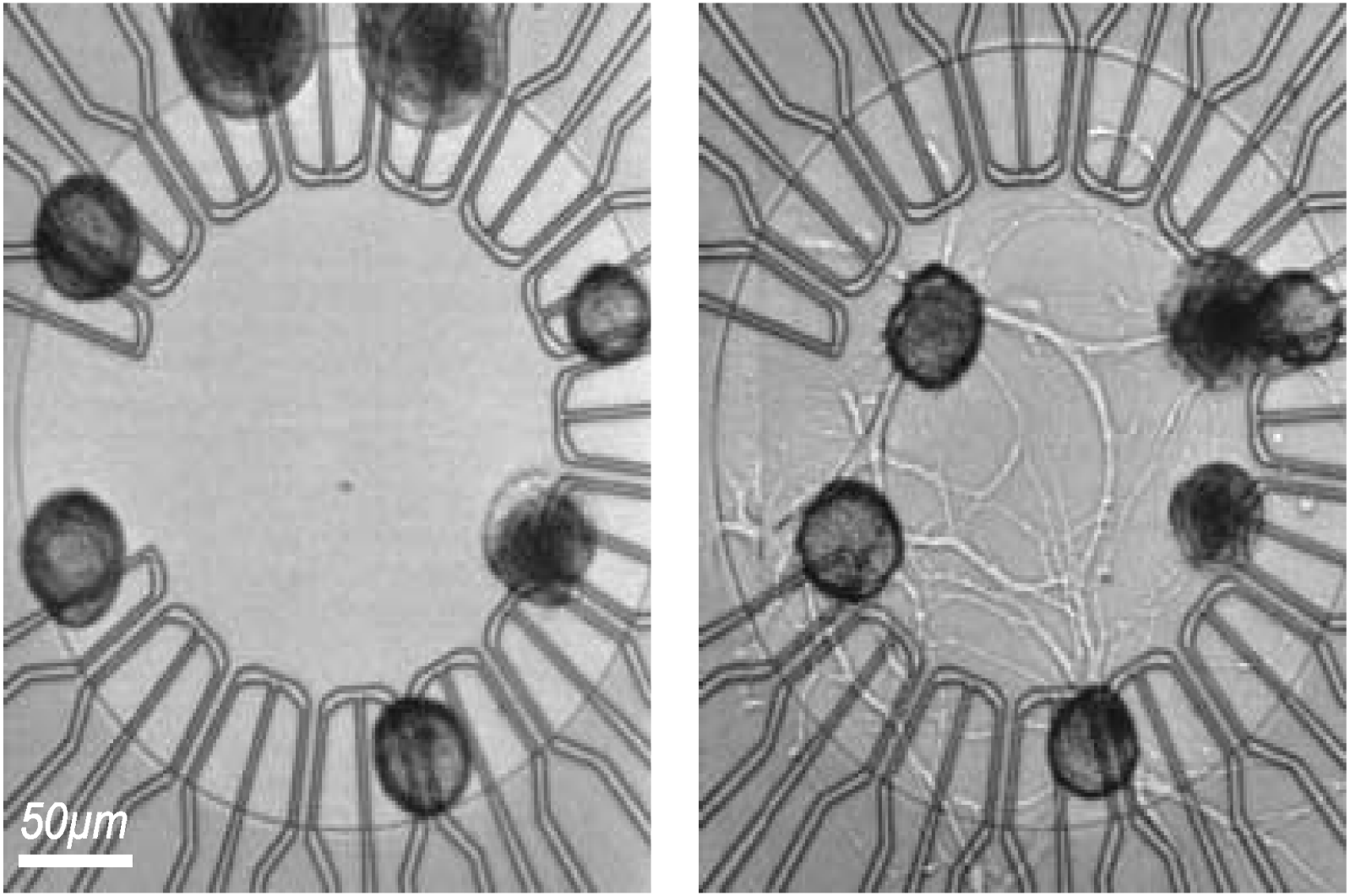
Fig. 2. Topographical guidance of snail neurons in one-layer polyester structures. a) Net of three neurons with perfect guidance of the neurites. b) Two neurons where one neurite in a pit passes the guiding structure. Scale bars are 100 µm.

Neuron silicon chip








50μm

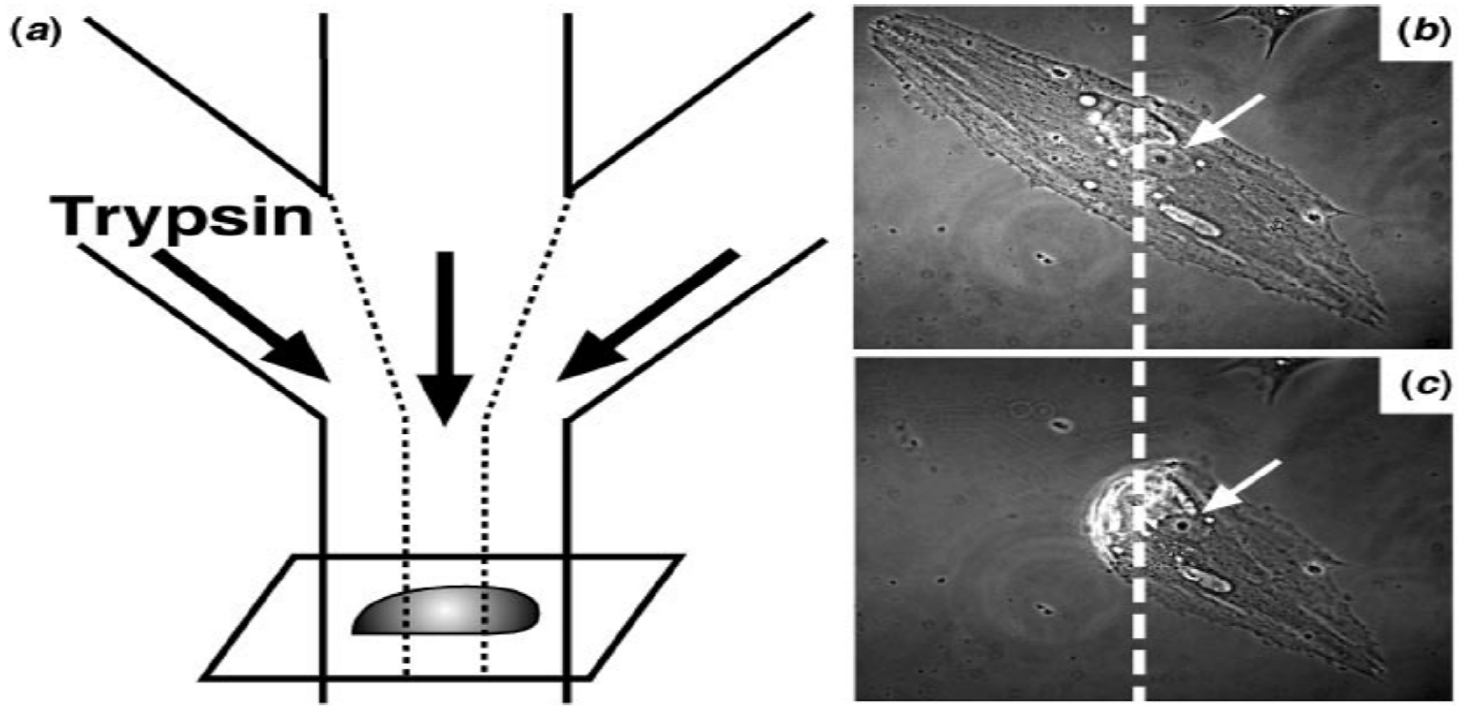
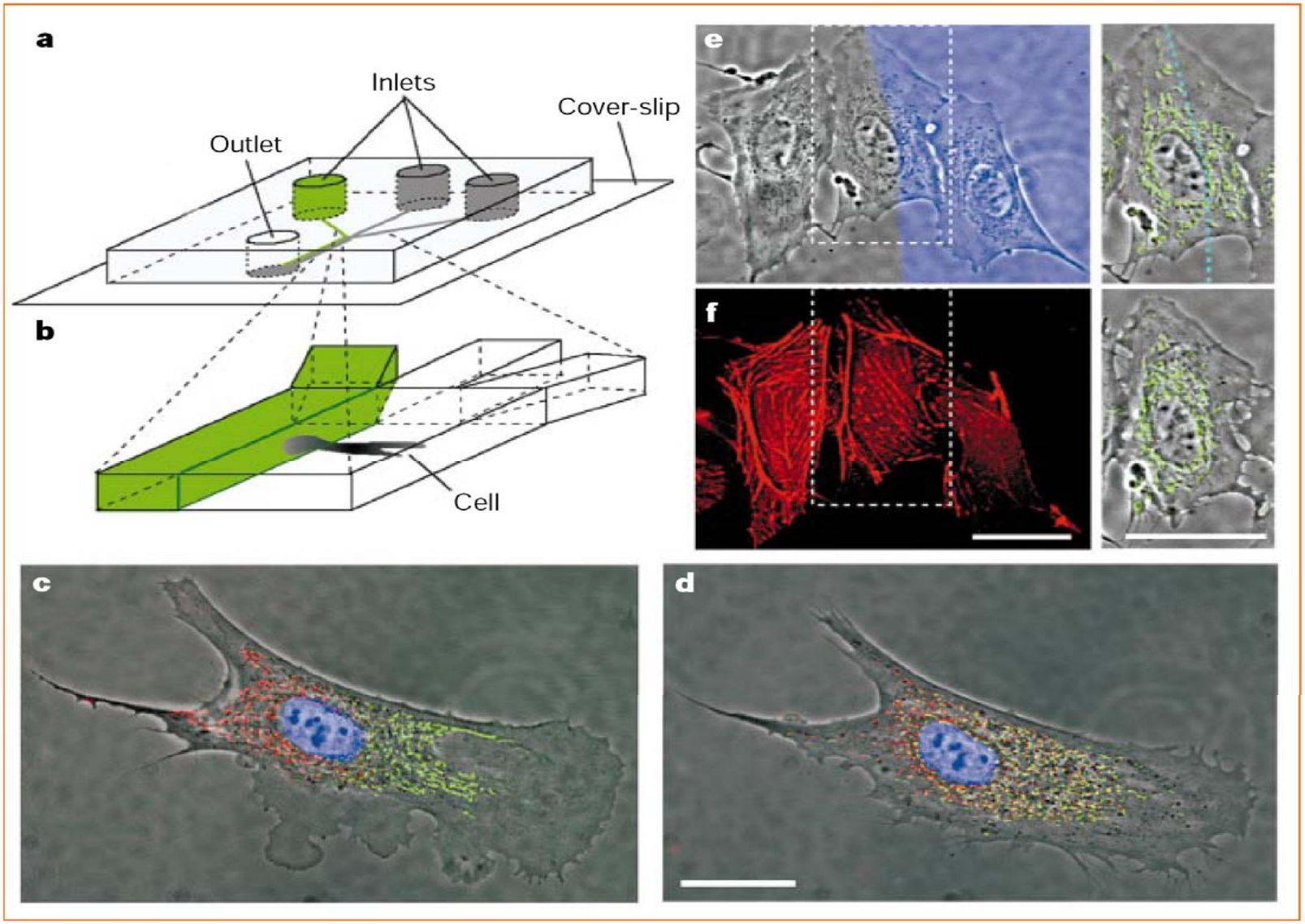
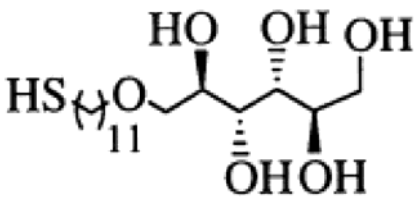
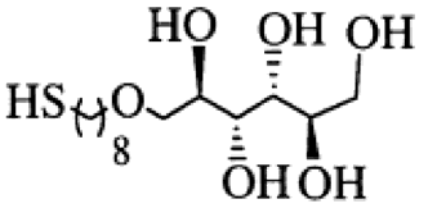
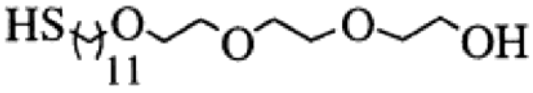


Figure 10 PARTCELL (partial treatment of cells using laminar flow) makes it possible to treat parts of cells selectively with small molecules as well as with proteins. (*a*) Schematic illustration of a typical PARTCELL experiment. Flows of different fluids (trypsin-EDTA and culture media) are positioned over different parts of a single, live bovine capillary endothelial (BCE) cell. (*b*) The BCE cell before trypsin treatment. (*c*) The same BCE cell after 5 min of trypsin treatment over the left side of the cell. The matrix proteins that maintain cell attachment were digested in the trypsin-treated side, causing cell detachment. The untreated side of the cell remained practically unchanged. Note that the position of the nucleus (*arrows*) does change after treatment of the cell with trypsin.


a
Inlets
Cover-slip
Outlet
b
Cell
e
f
c
d


HO
OH
OH
HS
O
11
OH
OH


HO
OH
OH
HS
O
8
OH
OH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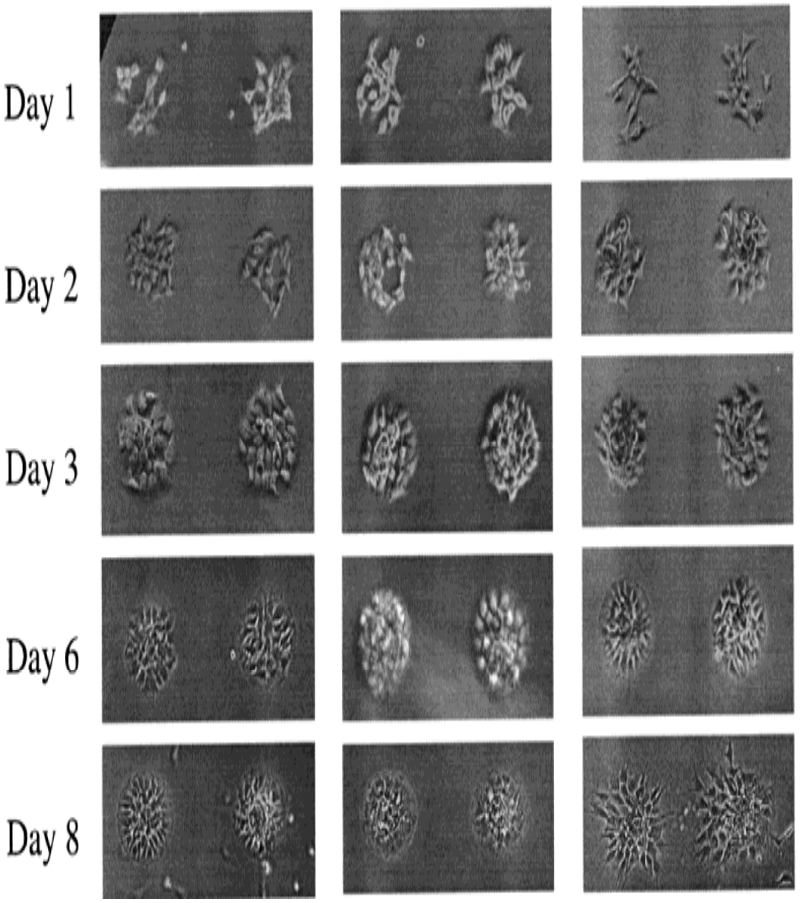
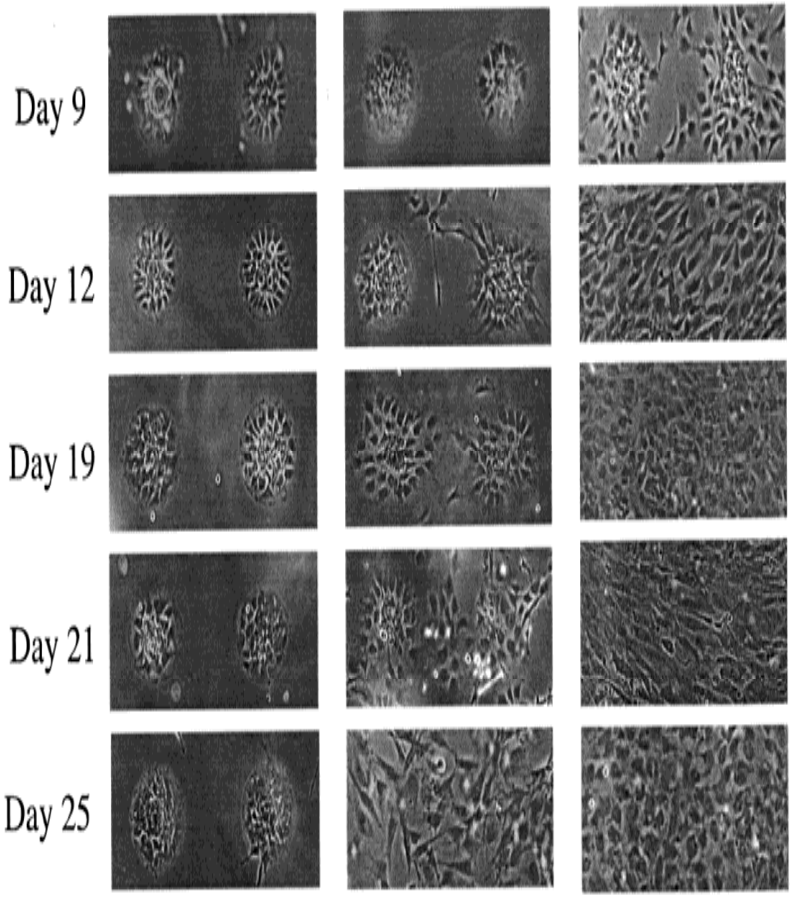
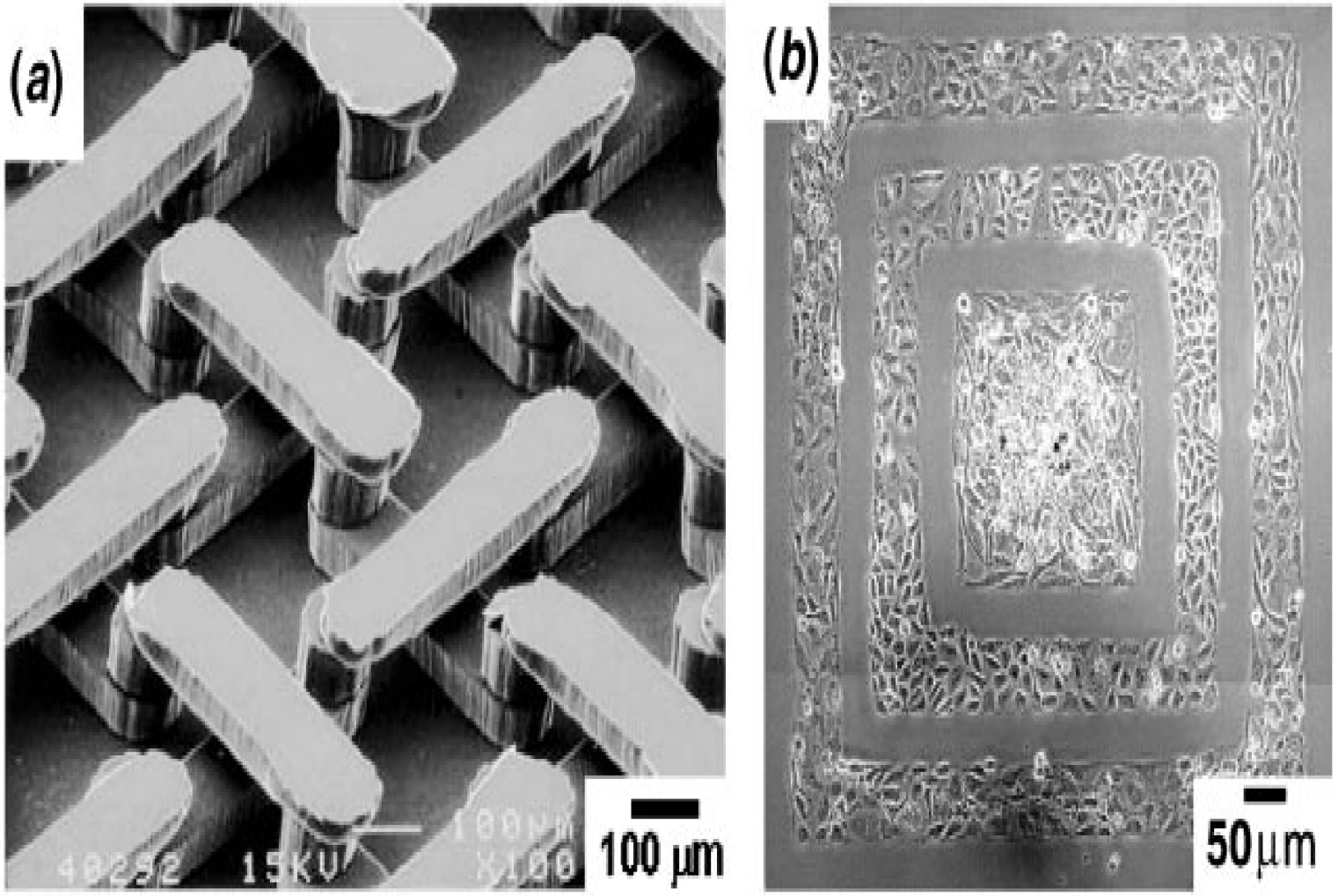

Day 1
Day 2
Day 3
Day 6
Day 8


Day 9
Day 12
Day 19
Day 21
Day 25


(a)
100 µm
(b)
50µm

Societal Implications of Nano

Key dimensions of the society:

1. Law
2. Politics
3. Economic and business
4. Public health and safety
5. National security
6. Education

For example, Human Genome Project (HGP):

- Identify and map all of the human genes, as well as determine the complete sequence of human DNA.
- Provide rich new ground for biological study and potential medical advances.
- Not feasible, an enormous waste of time and resource ?
- How genetic knowledge would be used
  Potential harms from the ability to manipulate & control
- The project of ethical, legal and social issues (ELSI)

The National Nanotechnology Initiative (NNI):

➡ Societal dimensions program component area:

(1) environmental, health, and safety (EHS) impacts of nano-technology development and risk assessment of such impacts

(2) education-related activities, such as the development of materials for schools and universities as well as public outreach

(3) Identification and quantification of the broad implications for society

Many, if not all, industries are anticipated to experience significant change in response to discoveries and applications of nanoscience. However, to fully understand the true extent of societal implications, one must also recognize connections branching into nearly every corner of the public sphere; general categories of societal impacts that have been raised as potential concerns range from safety and environmental impacts to workforce and global economic disruptions to controversial applications in medicine.

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Enhancing Soldier Survivability

HIGHLIGHTS 10.9.2009

Congratulations to ISN Director, Prof. John Joannopoulos, and ISN Faculty member Prof. Daniel Nocera on their elections to the **National Academy of Sciences**!

Congratulations to Prof. Ned Thomas, Founding Director of the ISN and head of MIT's DMSE, on his election as a Fellow of the **American Academy of Arts and Sciences**!

Congratulations to Prof. Vladimir Bulovic on being named a **MacVicar Fellow**!

Congratulations to Prof. Ned Thomas, Founding Director of the ISN and head of MIT's DMSE, on his election to the **National Academy of Engineering**!

ISN Faculty member Marin Soljacic awarded prestigious **MacArthur Fellowship**.

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WASTEWATER WOES New technologies may be needed to remove nanoparticles such as nanosilver from wastewater.

ALEX PARUNI, PEN

This nanosilver-containing toothpaste is approved by the U.S. Food and Drug Administration, but nanosilver used in washing machines is regulated under certain conditions by EPA.

Insurers scrutinize nanotechnology

On September 24, 2008, the U.S. insurance company Continental Western Group (CWG) issued a statement noting that it would exclude nanotubes and nanotechnology from its coverage. The statement has since disappeared from the CWG website, and fears of similar decisions by other insurance companies are as yet unrealized. But although CWG's decision to exclude nanotechnology was criticized by many as hasty and ill-informed, experts note that it represents the increasing concern among insurers about the emerging risks of nanotechnology.

"Nanotechnology is a big problem because the technology is moving much faster, as we all know, than information on health and environmental safety," says Robert Blaunstein of Nanotechnology Risk Management, a firm that advises industries, insurers, and investors on how to best manage the risks of nanotechnology.

The technology has already revolutionized electronics—our computers, iPods, and cell phones all contain nanomaterials. Physicians and pharmaceutical companies are using nanotechnology to devise smarter ways to deliver drugs. From sunscreens and bed-

trated by a recent report by the National Research Council, is that risk of nanotechnology is poorly understood and risk research is grossly underfunded.

And insurance companies agree. Lloyd's (U.K.), the world's oldest insurance firm and one of the larg-

ALEX PARLUNI, PROJECT ON EMERGING NANOTECHNOLOGIES

Carbon nanotubes have been shown to have asbestos-like impacts on mice.

est companies, along with other influential insurance companies, has listed nanotechnology at the top of its "emerging risks" list. "The biggest challenge facing insurers may be the diverse nature of nano-

ing risks in risk engineering services at Swiss Re, one of the world's largest reinsurance companies. "Because risk is our business, nanotechnology is up front ... subject to risk consideration." Reinsurance companies insure insurance companies and often cover risks no one else wants to handle.

As early as 2002, Munich Re, the world's largest reinsurance company, released a report stating that it expects a "new dimension in claims for personal injury, material damage, and financial loss, as well as liability risks in product, environment, and public liability." Swiss Re itself released a report on nanotechnology in 2004 and has since organized conferences as venues for manufacturers, insurance companies, scientists, nonprofit organizations, and government agencies to talk about and understand the potential risks of nanotechnology.

Insurers rely on hard data and calculable risks to provide coverage to companies and individuals. "If I was insuring you for death, [with] life insurance, I know lots of statistics, lots of numbers [that estimate] when I or you or anyone might pass away," explains Blaunstein, who has spent many years in the insurance industry. "It's easy for me to get a really good idea when that might hap-

Thank you

for your attention.