實驗室晶片導論

液珠式微流體晶片之研發與應用

Droplet-Based Biochips

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BEAM Lab

蓮葉與玫瑰花的啟發暨生醫應用

Mimicrying lotus and rose and the inspired bio-application

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液珠式微流體晶片之研發與應用

大綱

液珠做為工作流體之流體晶片，除了可以改善連續流體因流道設計所造成的壓降能量損失，可降低元件複雜度與整合難度，亦可減少試劑的浪費殘留，達到更精準的反應控制。在微小尺度下，液珠具有高表面積與體積比的特性，能快速傳熱增加反應速率，在數位微流體系統中亦可容納少量樣本進行快速且多樣化的反應，實現高度平行化與獨立反應操控的目標，近年來已發展為微流體系統研究的重點。

本專題結合對生化分子自組裝技術、微液珠操控技術、接觸角與表面能階理論、微流體混合理論等領域，以及各種流體條件(表面張力、黏滯性)對液珠碰撞融合後流場及混合行為的關連等基礎學理與技術，討論流體混合行為與反應行為，進一步推展並完善開放式微液珠被動傳輸平台的設計，並將之應用於數位微流體生化反應調控的液珠式生醫檢測與液珠式生質柴油產製。

本次授課之主要內容是本研發團隊在液珠之相關研究成果，概分為三項:

(1) 液珠移動、碰撞、混合、反應之流體動態分析

(2) 液珠移動介面之分析 及 本實驗室所發展之幾種液珠操控技術

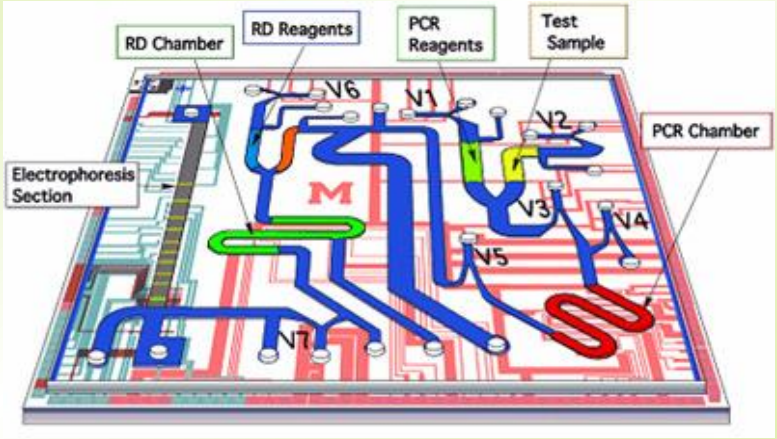
(3) 應用實例:生醫(可視化液珠式基因快篩技術)、個人化醫療檢測設計 (第11屆國家新創獎傑出學研新創技術)、能源 (液珠式高速率低耗能生質柴油產製系統) (12屆國家新創獎 傑出學研新創技術)、農業領域 (12屆國家新創獎 傑出學研新創技術)、藥物釋放設計

09美国《国家地理》全球摄影大赛优秀参赛作品
<荷塘趣事> 摄影：杨长荣
www.huaxia-ng.com


Film of Taro

Perspective

- **The rise of μ-TAS**
  - High surface to volume ratio : improve heat and mass transfer
  - Need only small quantities of reagents and sample
  - Potentially portable
  - High resolution and sensitivity
  - Suitable for biological assay



Pal *et al.*, *Lab Chip*. 2005

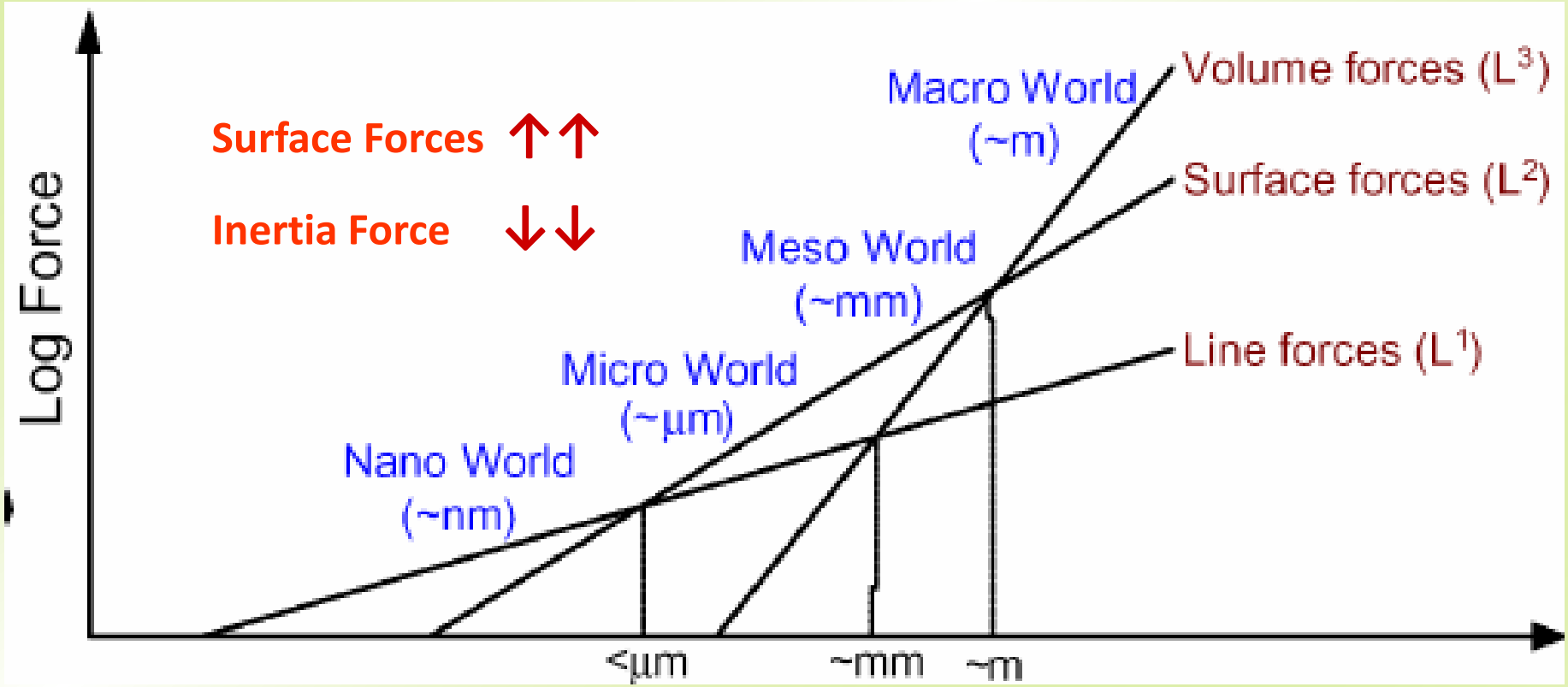
Extracted on 20121212 http://www.condenaststore.com/-sp/I-see-by-the-current-issue-of-Lab-News-Ridgeway-that-you-ve-been-work-New-Yorker-Cartoon-Prints_i8562947_.htm

微尺度效應

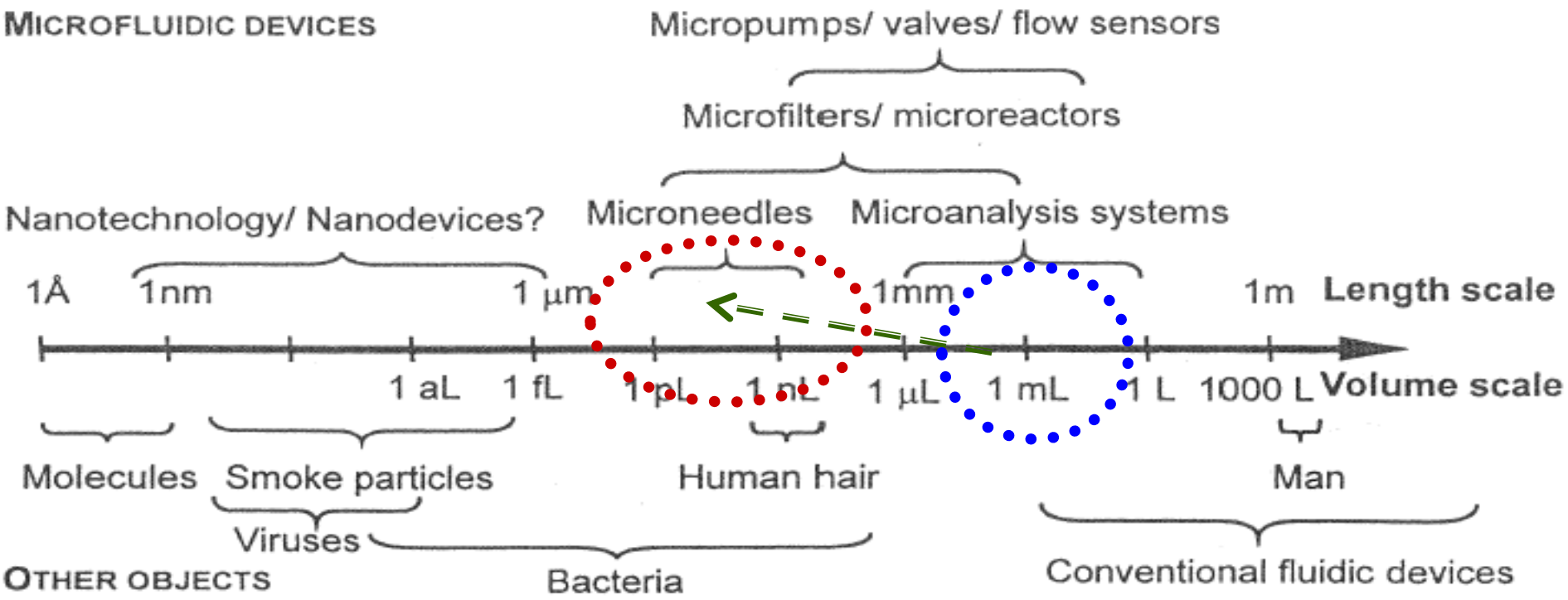
Volume force (mass) ~ d^3

Surface force (pressure, friction, electrostatic, diffusion) ~ d^2

Line force (surface tension) ~ d^1

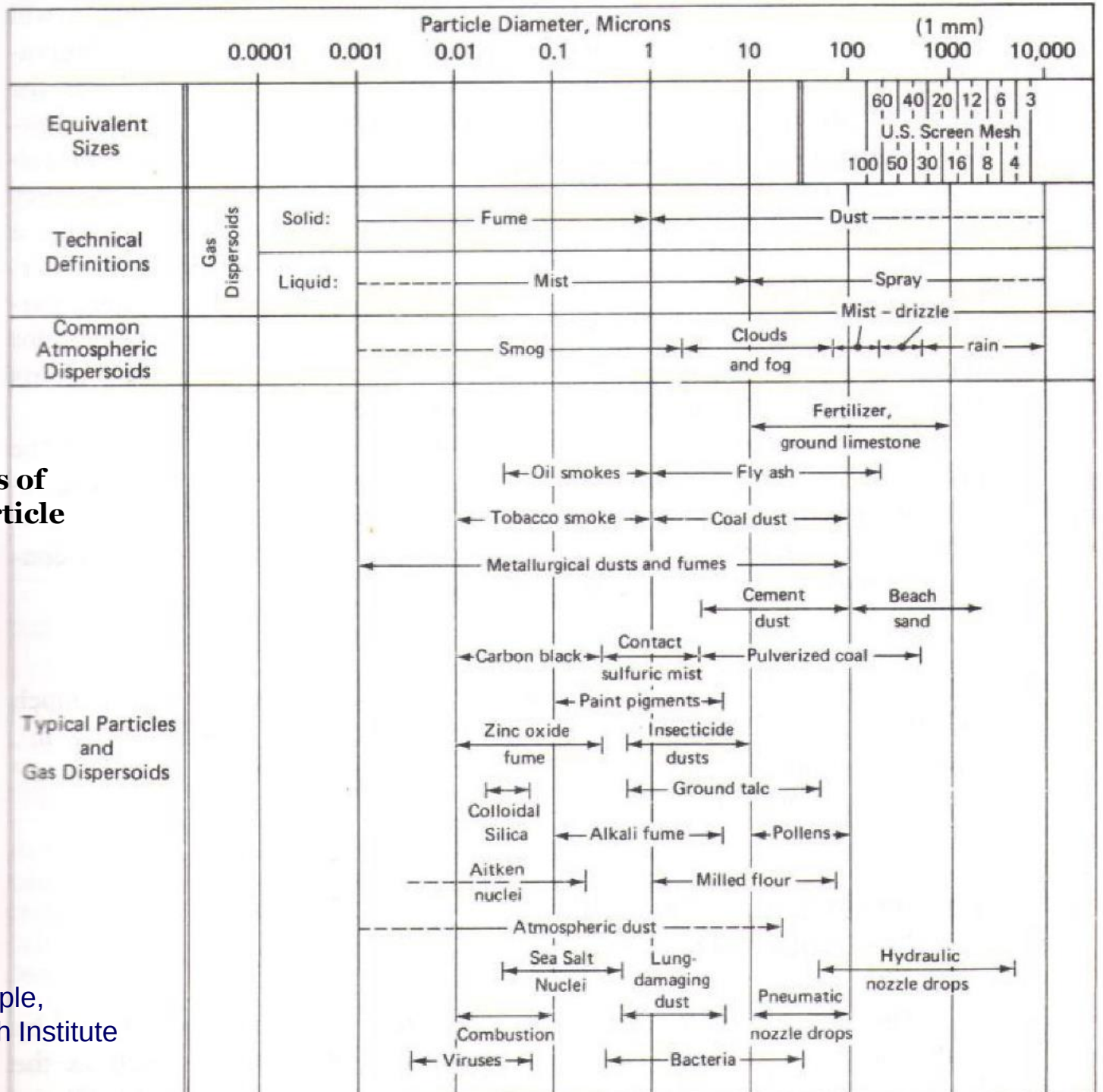


What is the volume of a droplets ?



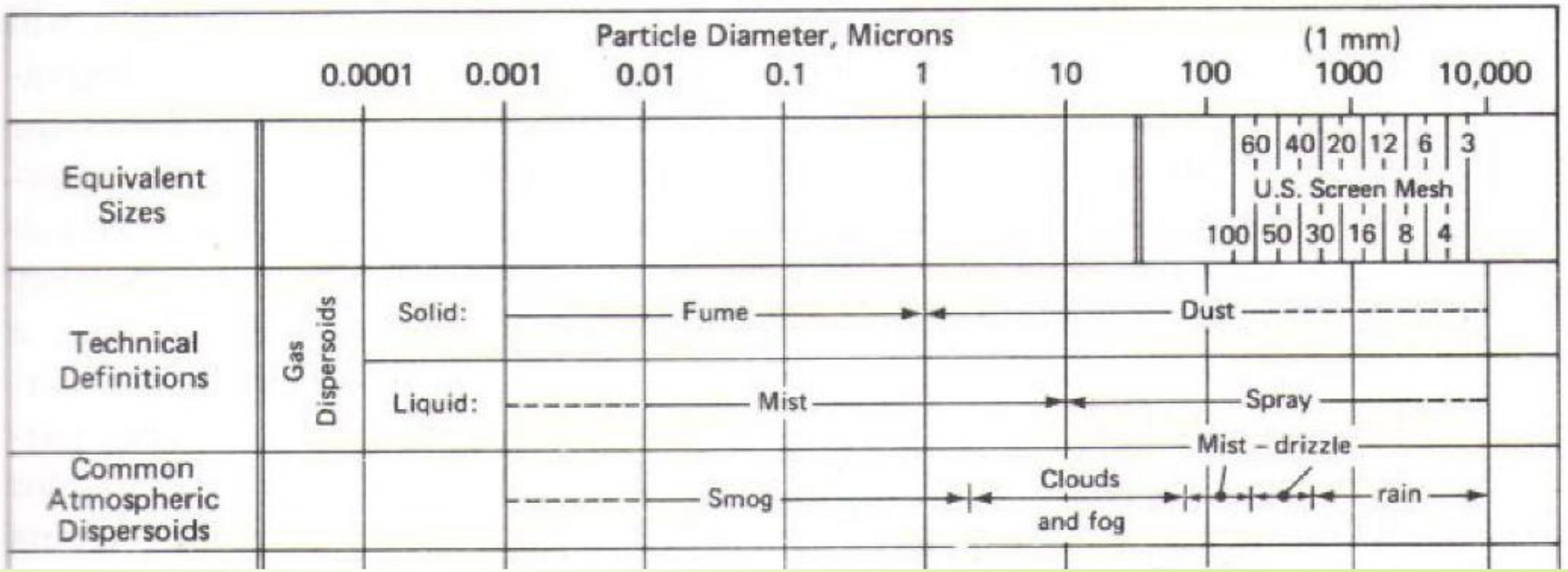
Nguyen and Wereley, 2003

Characterisitcs of particles & particle dispersoids



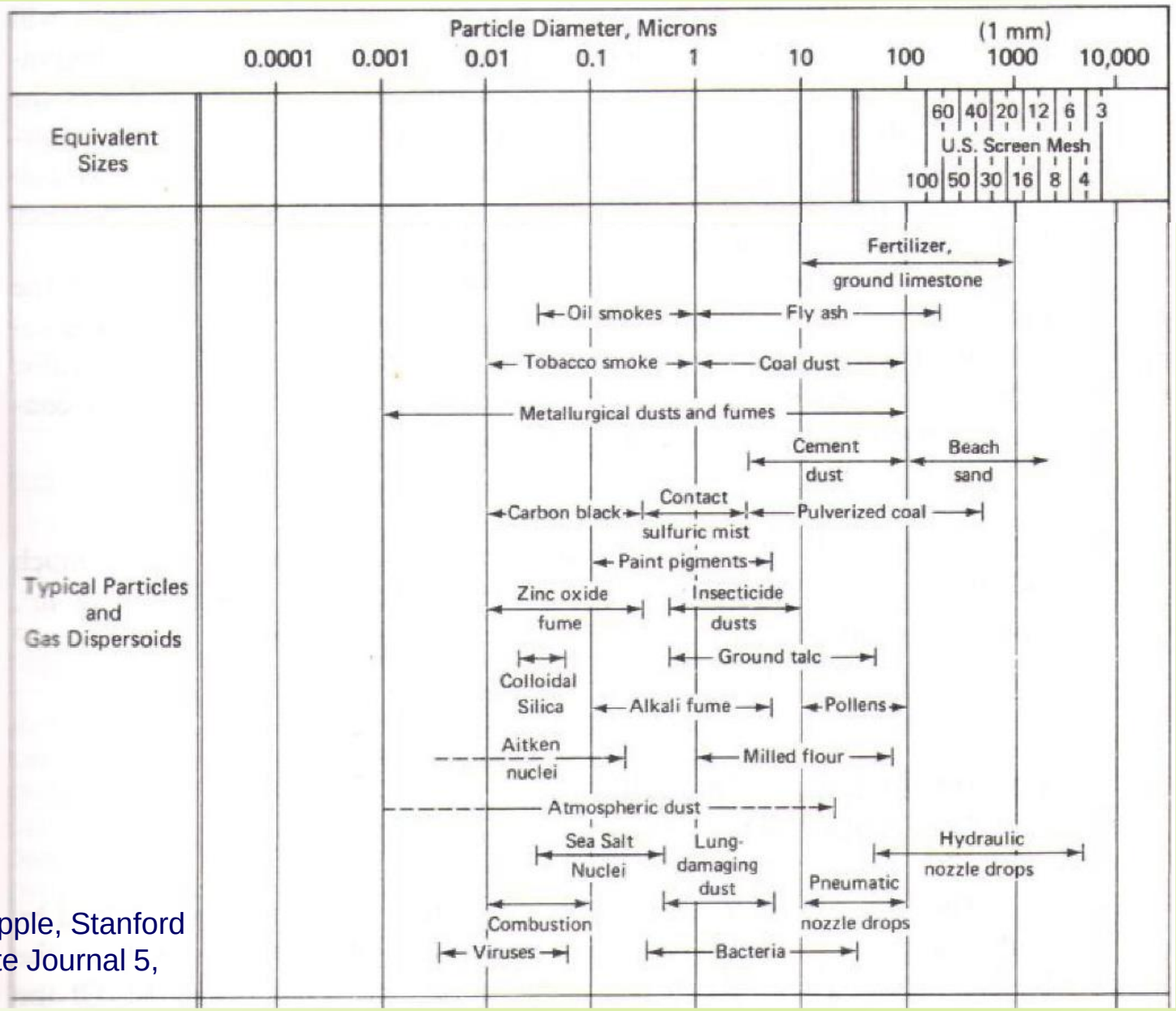
Source: C. E. Lapple, Stanford Research Institute Journal 5, 1961

Characterisitcs of particles & particle dispersoids



Source: C. E. Lapple, Stanford Research Institute Journal 5, 1961

Characterisitcs of particles & particle dispersoids



Source: C. E. Lapple, Stanford Research Institute Journal 5, 1961

Characterisitcs of particles & particle dispersoids

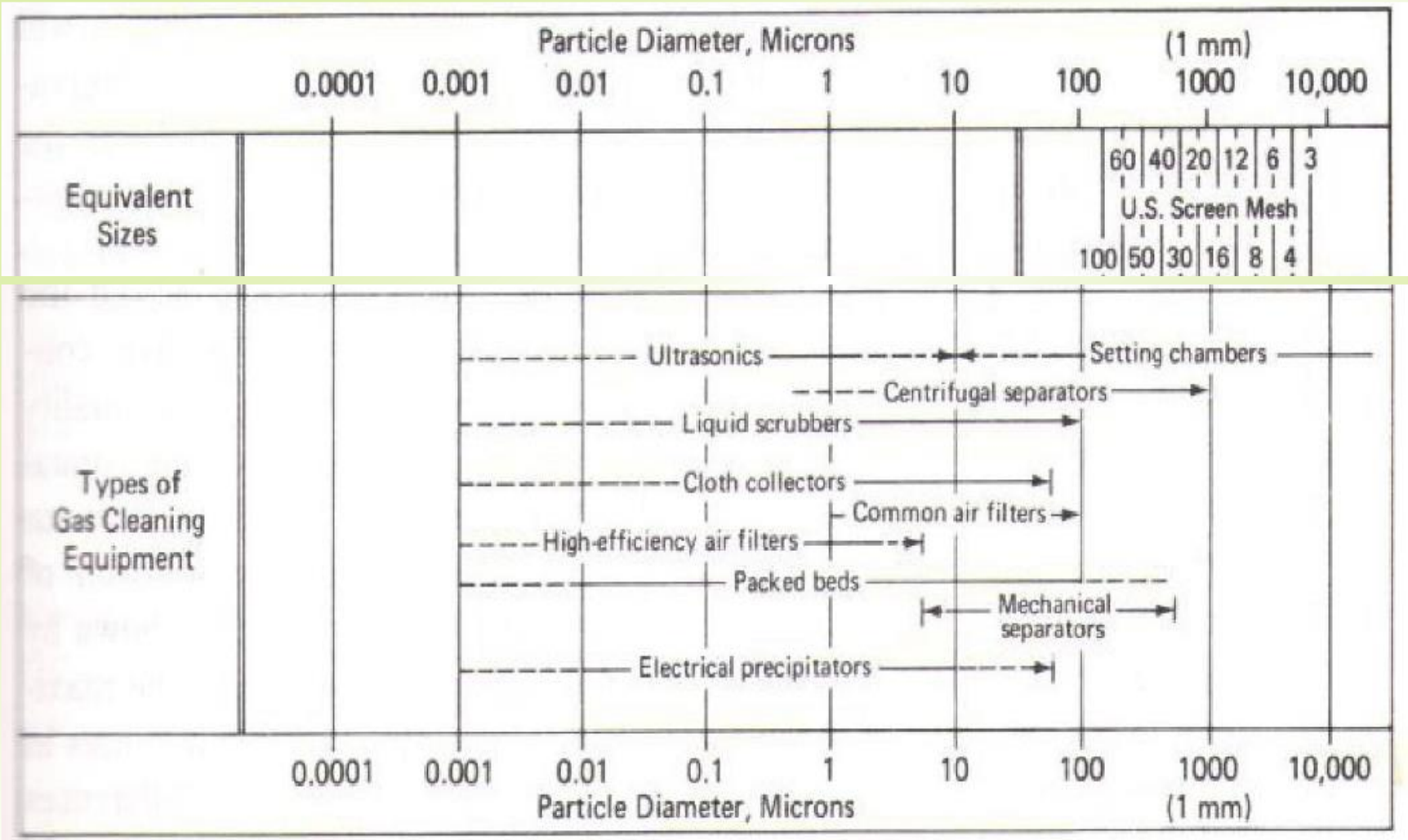
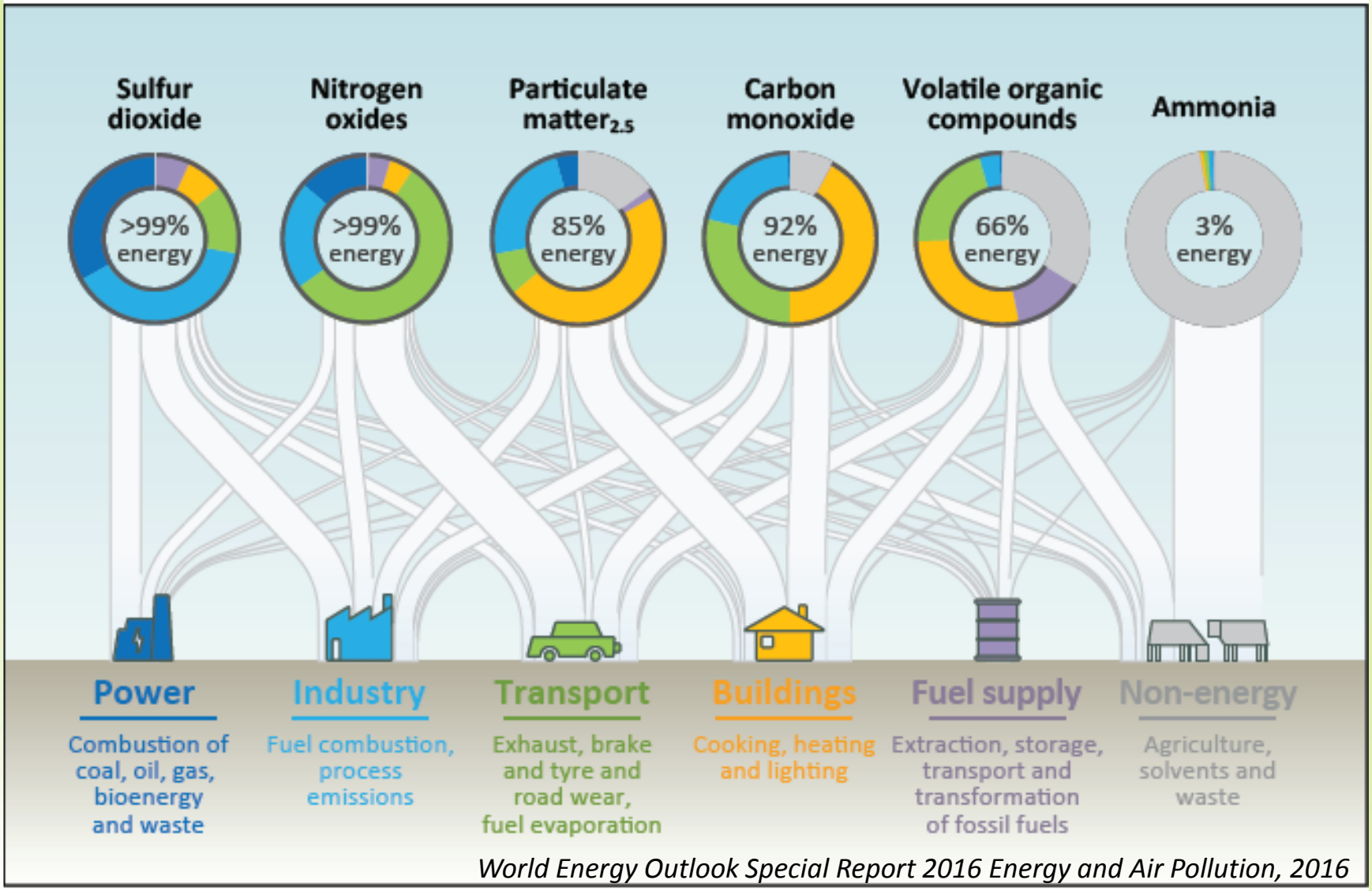


Figure 5-1 Characteristics of particles and particle dispersoids. (*Source:* C. E. Lapple. *Stanford Research Institute Journal* 5, 1961.)

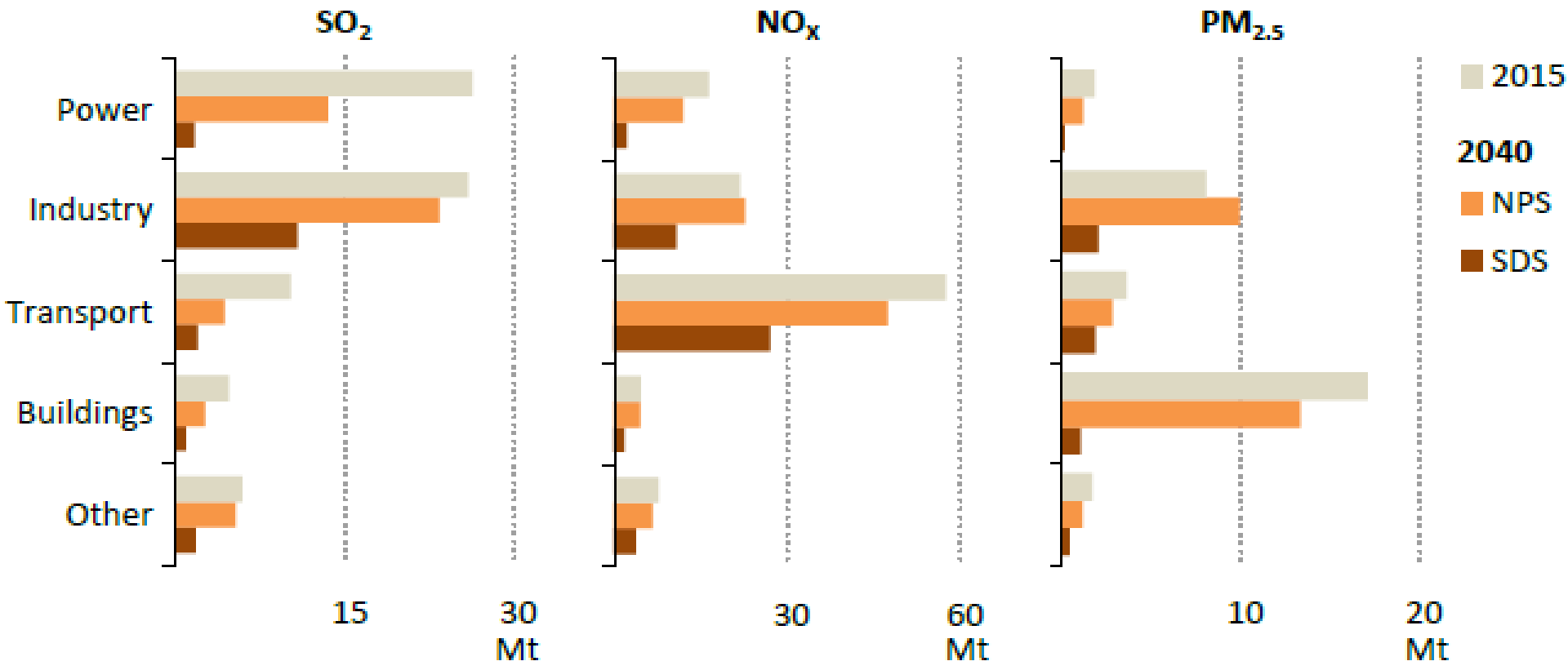
人為排放空氣汙染成分之來源分析-- 2015年
(Selected primary air pollutants and their sources, 2015)



World Energy Outlook Special Report 2016 Energy and Air Pollution, 2016

Air pollution emissions by sector and scenario, 2015 & 2040

IEA, World Energy Outlook-2018



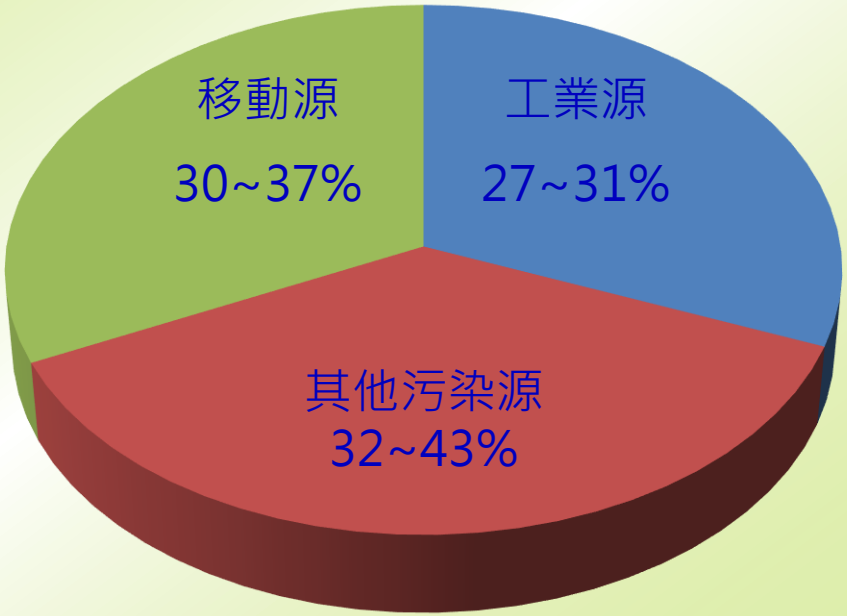
Pollutant emissions generally fall in the New Policies Scenario, but in most cases by much less than in the Sustainable Development Scenario

Notes: NPS = New Policies Scenario; SDS = Sustainable Development Scenario. Industry includes fuel combustion in the industry sector and transformation processes other than power generation.

Source: IEA analysis; International Institute for Applied Systems Analysis.

我國$PM_{2.5}$來源比率分析

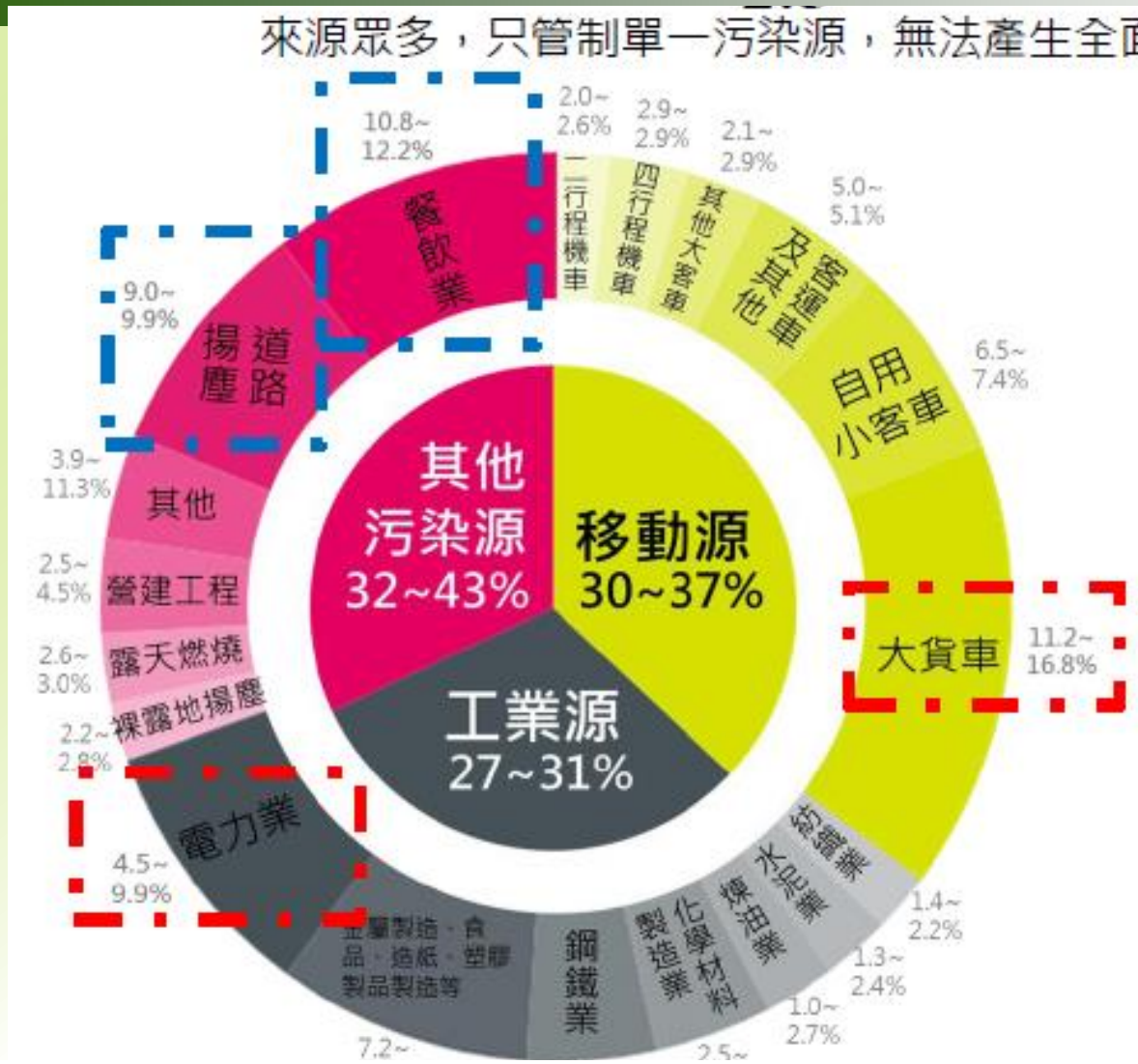
- 我國$PM_{2.5}$境外傳輸來源比率約為34~40%，境內污染源比率約為60~66%。
- 境內污染源中，移動源影響比率約為30~37%、工業源約為27~31%、其他污染源約為32~43%。



資料來源:環保署委託成功大學吳義林教授「台灣細懸浮微粒($PM_{2.5}$)成分與形成速率分析計畫」及雲林科技大學張艮輝教授「強化空氣品質模式制度計畫(第二年)」研究成果

註：依據排放清冊（TEDS 8.1版）估算

我國境內$PM_{2.5}$來源比例分析



我國$PM_{2.5}$

境外傳輸來源比率約為34~40%，

境內汙染源比率約為60~66%。

境內汙染源中，

移動源影響比率約為30~37%，

工業源約為27~31%，

其他汙染源約為32~43%。

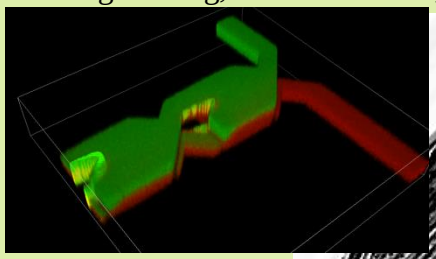
資料來源:環保署委託成功大學吳義林教授「台灣細懸浮微粒($PM_{2.5}$)成分與形成速率分析計畫」[性能評估結果：配對值分數偏差(Mean Fractional Bias, MFB)為$PM_{2.5}$=-12.8%，配對值絕對分數誤差(Mean Fractional Error, MFE)為$PM_{2.5}$=40.9%]及霧林科技大學張良輝教授「強化空氣品質模式制度計畫(第二年)」研究成果[性能評估結果：MFB為$PM_{2.5}$=-9.1%，MFE為$PM_{2.5}$=38.4%]

註：依據排放清冊（TEDS 8.1版）估算；網格模式模擬結果性能評估規範：配對值分數偏差MFB為$PM_{2.5}$= ±35%，配對值絕對分數誤差MFE 為$PM_{2.5}$= 55%以內。

連續式流場 vs. 液珠式晶片

Digital Microfluidics

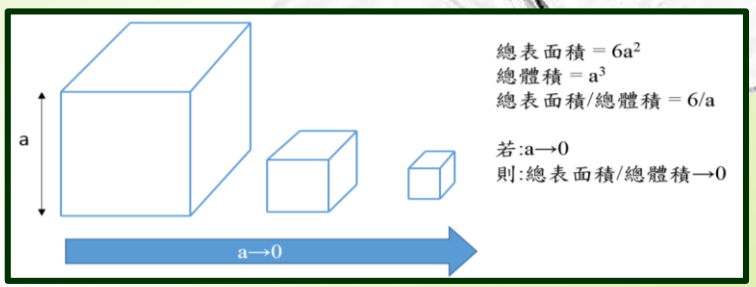
Fang & Yang, *Sens. Actuators, B*, 2009



Continuous flow

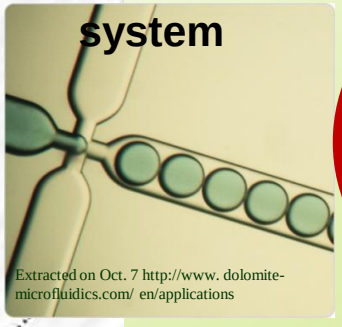
Extracted on Oct. 23
http://blogs.rsc.org/chipsandtips/2010/06/18/connector-less-manipulation-of-small-liquid-volumes-in-microchannels/

Droplet/plug flow
(digital flow)



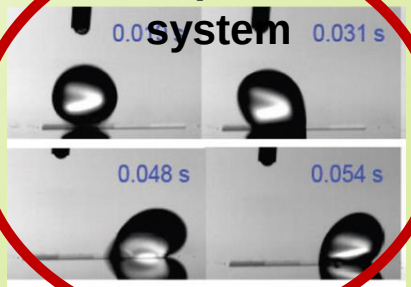
- ✓ Eliminate micropumps and valves
- ✓ Controllability
- ✓ Accurate dose control
- ✓ **Surface area to volume ratio**

closed system



Extracted on Oct. 7 http://www. dolomite-microfluidics.com/ en/applications

open system



Yang, *et al.*, *Langmuir*, 2008

- ✘ Unlimited to microchannels
- ✘ Maneuverability
- ✘ Vaporize

Science

J. T. Yang, 20081116

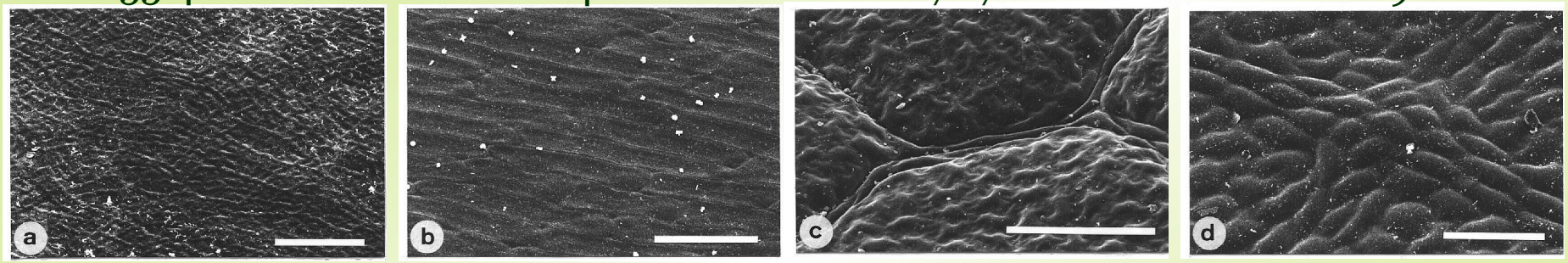
芋葉之出淤泥而不染

J. T. Yang, 20081116

Hydrophilic and Hydrophobic Features of Leaves

wetted plant leaf

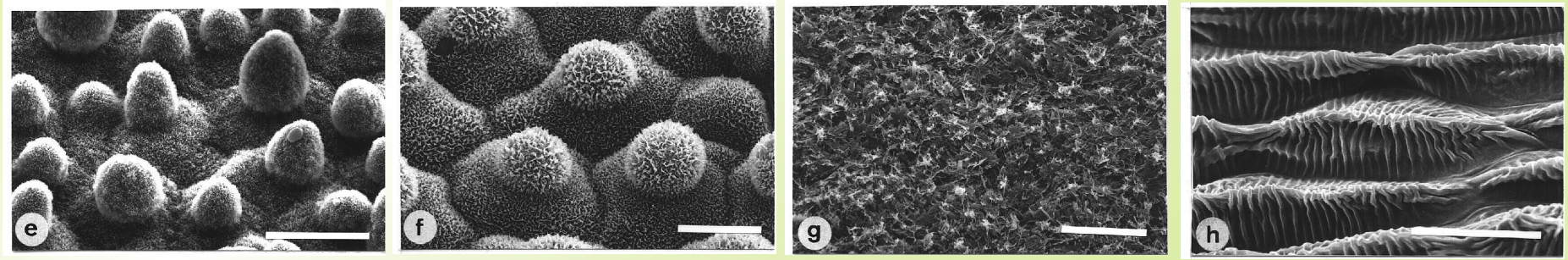
55.4 ° 28.4 ° 71.7 ° 88.9 °



Gnetum gnemon *Heliconia densiflora* *Fagus sylvatica* *Magnolia denudata*

non-wetted plant leaf

160.4 ° 159.7 ° 160.3 ° 128.4 °



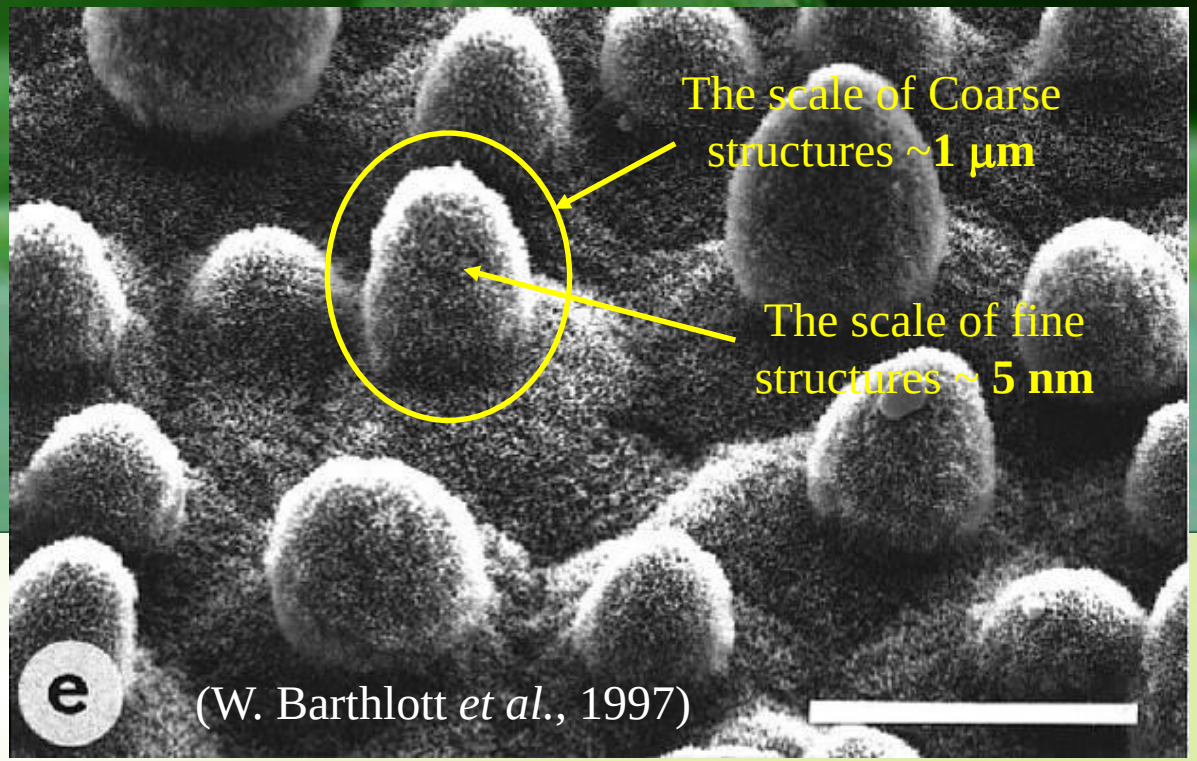
Nelumbo nucifera *Colocasia esculenta* *Brassica oleracea* *Mutisia decurrens*

(Barthlott *et al.*, 1997)

Lotus leaf

Lotus leaf, Super-hydrophobic surface

Apparent contact angle, θ_c ~160.4 °

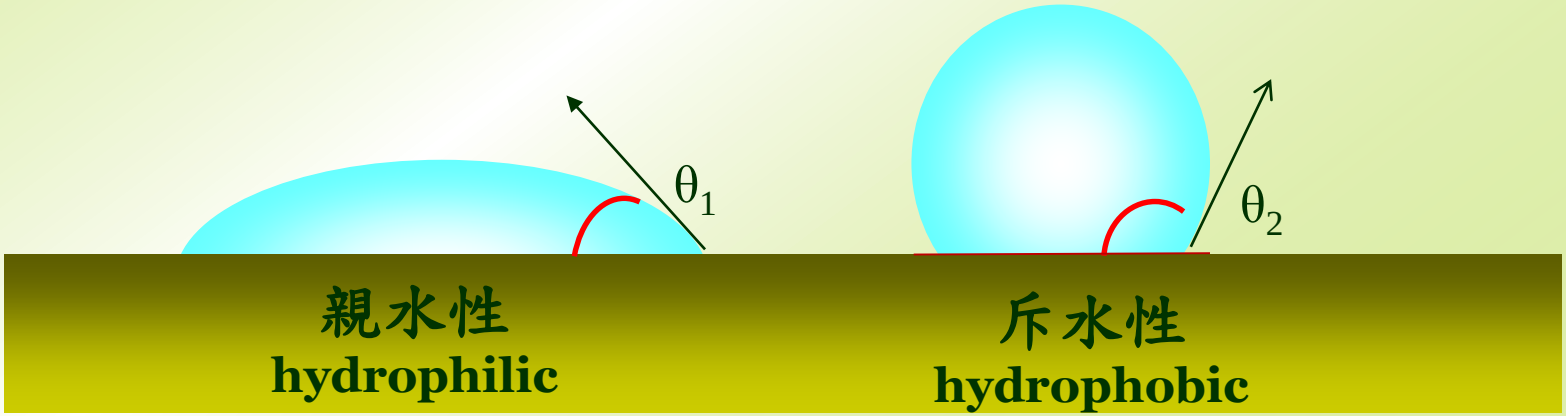


(W. Barthlott *et al.*, 1997)

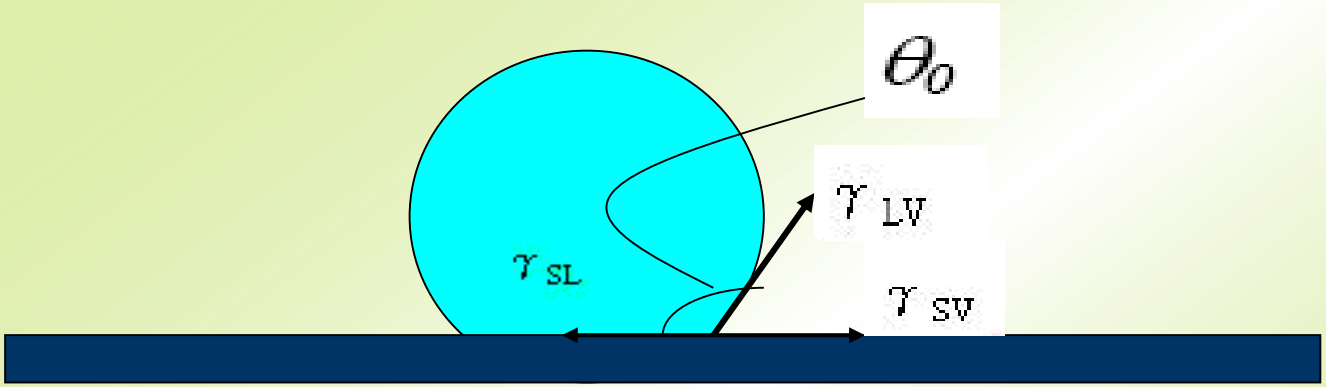
親水性與疏水性

- 由水滴與表面之接觸角作為其親、疏水性之判斷：

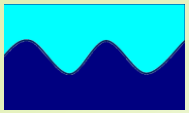
- 接觸角 < 90° ⟹ 親水性(hydrophilic)表面，如θ_1
- 接觸角 > 90° ⟹ 斥水性(hydrophobic)表面，如θ_2



親、疏水性與接觸角

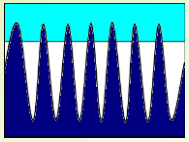


Young's Equation: $\cos\theta_0 = \dfrac{\gamma_{SV} - \gamma_{SL}}{\gamma_{LV}}$



Wenzel's Equation (1936): $\cos\theta_{app} = \dfrac{r(\gamma_{SV} - \gamma_{SL})}{\gamma_{LV}} = r\cos\theta_0$

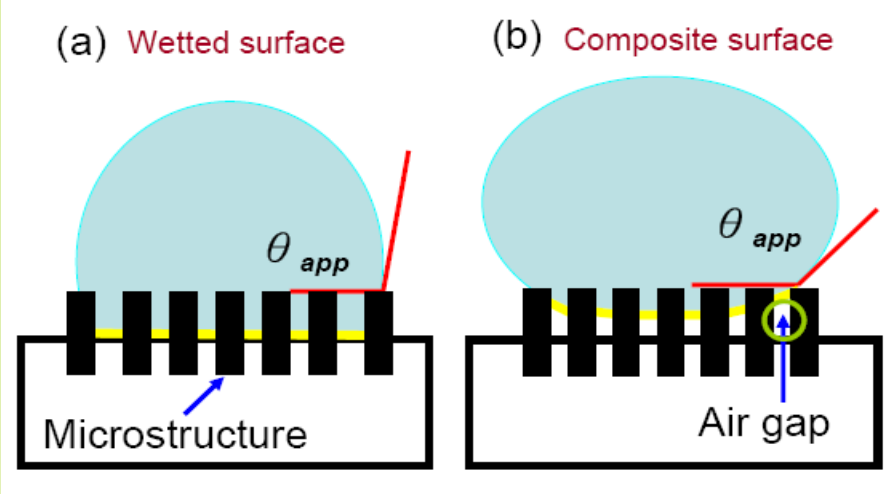
$r = \dfrac{A_{actual}}{A_{projected}}$



Cassie & Baxter Equation: $\cos\theta_{app} = f_1\cos\theta_1 + f_2\cos\theta_2$

f_1: 固液界面佔總表面積之比例、f_2：氣液界面佔總表面積之比例，
θ_1：固液之本質接觸角（即前文的θ_0）、θ_2：氣液之本質接觸角。

Schematics of Surface Effects



■ $\theta = 110^o$

Smooth surface

■ 5-10 μm roughness $\theta \sim 135^o$

Surface with micro-structure

■ **Smooth surface**

Young equation

$$\cos\theta_o = (\gamma_{SV} - \gamma_{SL})/\gamma_{LV}$$

■ **Wetted surface**

Wenzel equation

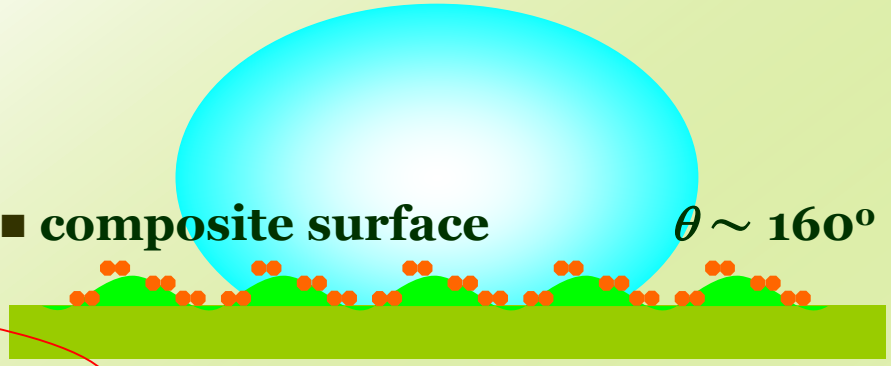
$$\cos\theta_{app} = r\cos\theta_0$$

■ **Composite surface**

Cassie and Baxter Eq.

$$\cos\theta_{app} = f_1\cos\theta_1 + f_2\cos\theta_2$$

■ composite surface $\theta \sim 160^o$



Surface with hybrid structure

Objectives inspired by lotus leaf

Mimicking lotus leaf

N/MEMS, SAM

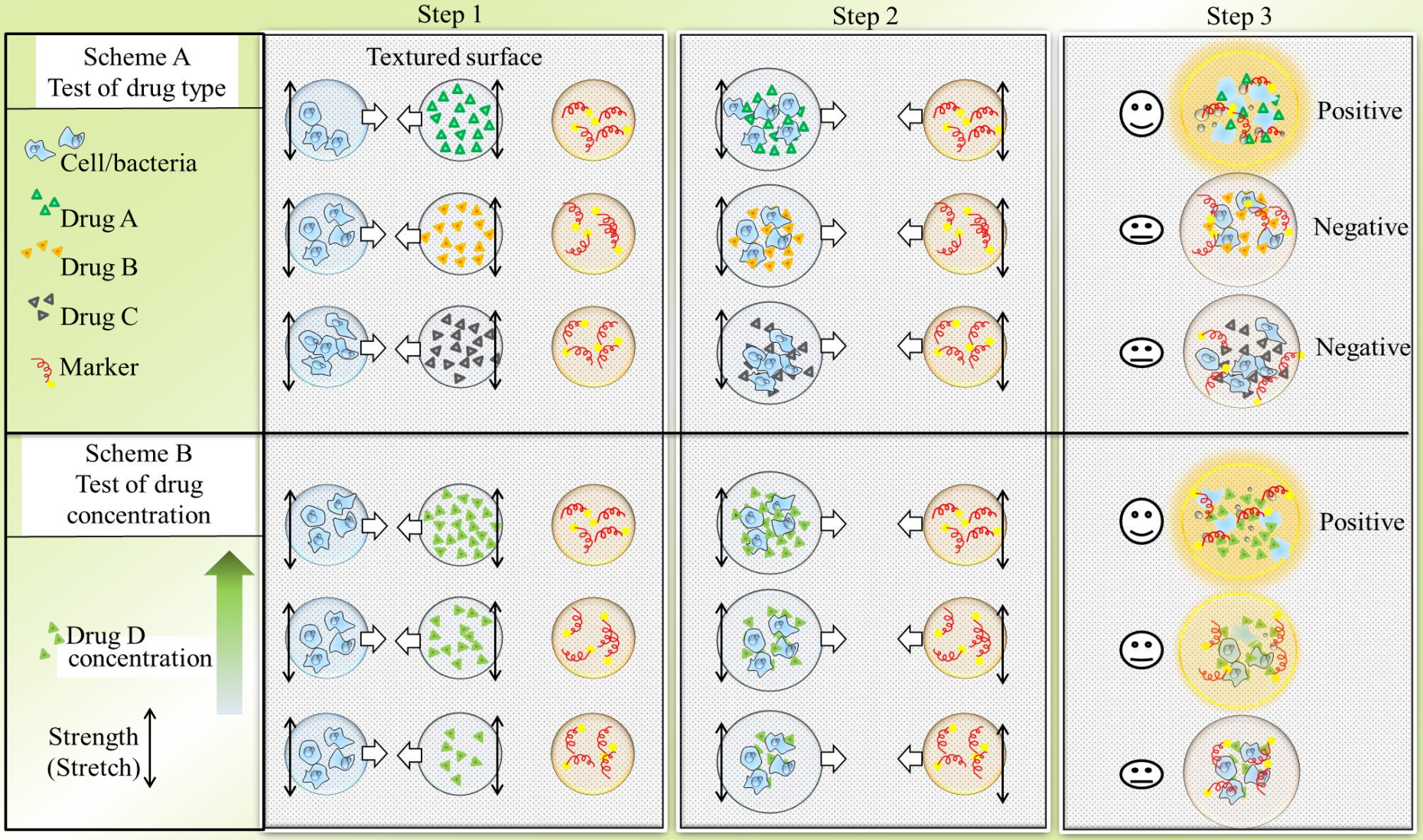
Ultra-hydrophobic surface

J. MEMS, 2006; *Langmuir*, 2008
JMM, 2009; *Lab Chip*, 2010a, 2010b, ...

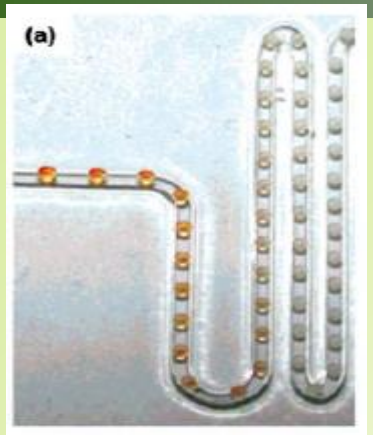
Gradient surface

國家新創獎，2007

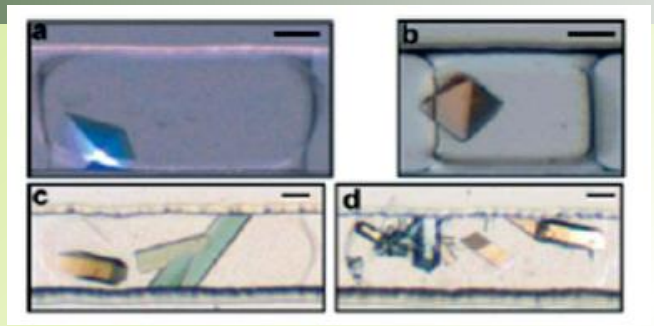
Droplet spontaneous moving and reacting on a microchip


Step 1
Step 2
Step 3
Scheme A
Test of drug type
Textured surface
Cell/bacteria
Drug A
Drug B
Drug C
Marker
Positive
Negative
Negative
Scheme B
Test of drug
concentration
Drug D
concentration
Strength
(Stretch)
Positive

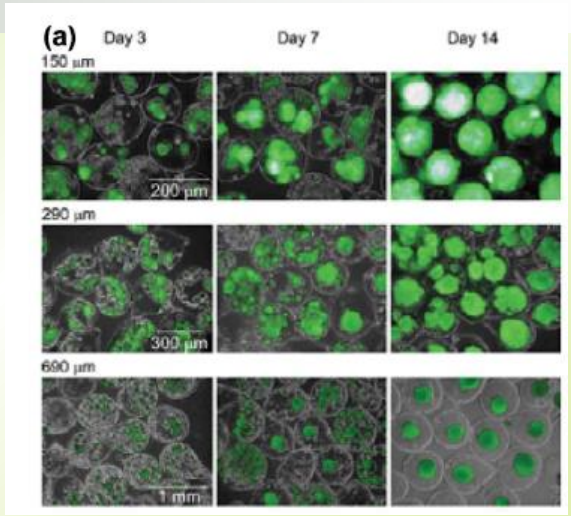
Droplet Applications



Cygan *et al.*, *Langmuir*, 2005



Hatakeyama *et al.*, *J. Am. Chem. Soc.*, 2006



Sugiura *et al.*, *Biomed. Microdev.*, 2007

Drug discovery

Chemical reactions

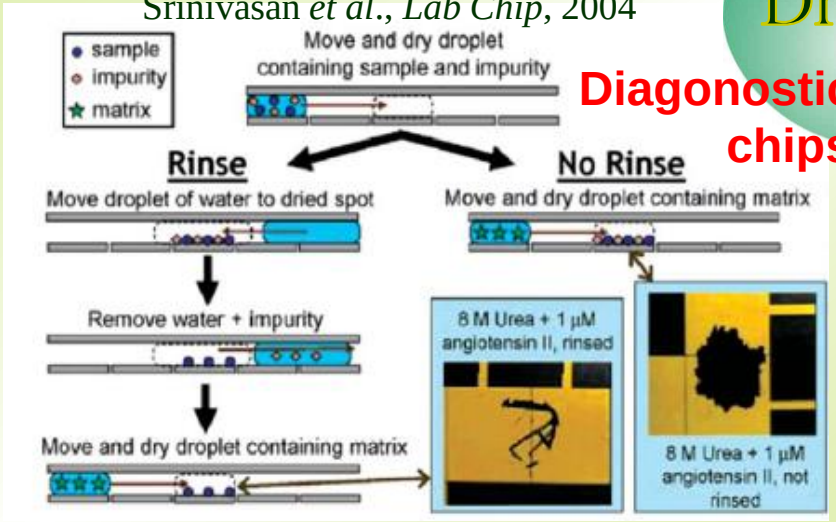
Therapeutic agent delivery

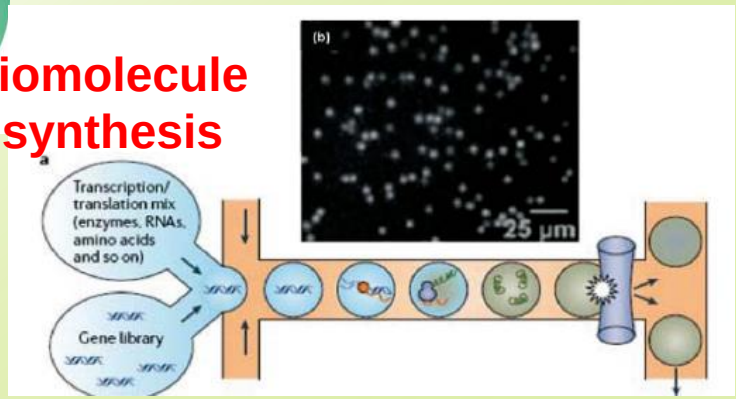
Droplet

Diagonostic chips

Biomolecule synthesis

Srinivasan *et al.*, *Lab Chip*, 2004



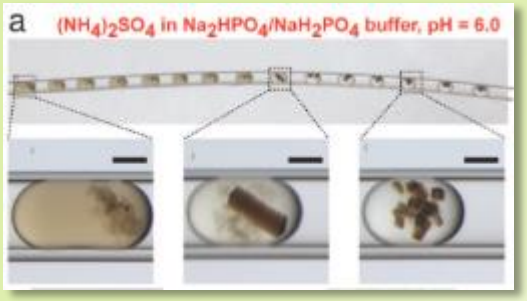


(a) Dittrich *et al.*, *Nat. Rev. Drug Discovery*, 2006
(b) Dittrich *et al.*, *ChemBioChem*, 2005

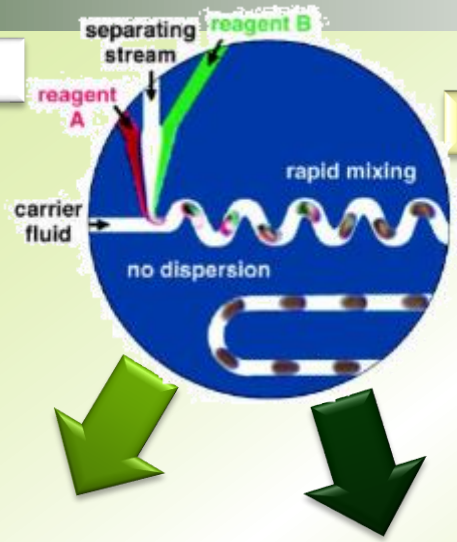
Teh *et al.*,"Droplet microfluidics," *Lab Chip*, 2008.

流道內液珠式微流體系統應用

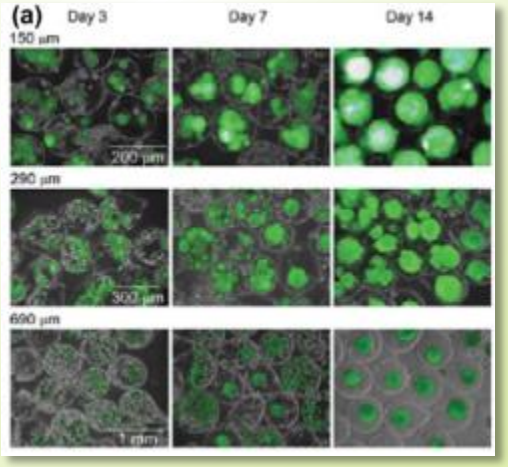
蛋白質合成監控



/9Li *et al.*, *P. Natl. Acad.. Sci. USA* , 2006/0

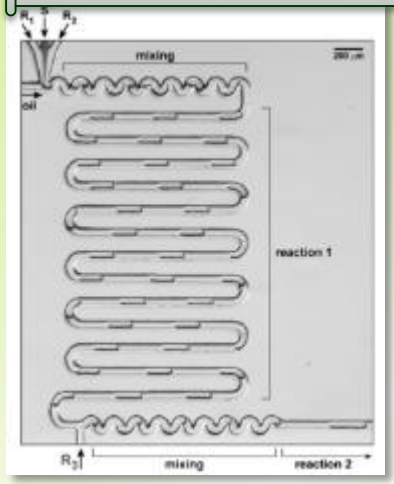


細胞包覆



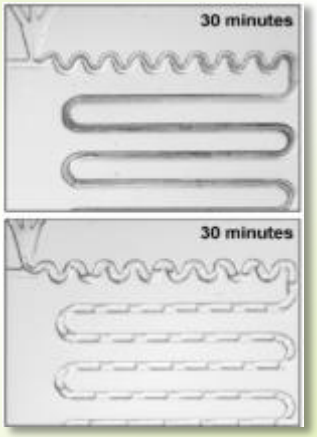
(Sugiura. *et al.*, *Biomed Microdev.*, 2007)

減少縱向擴散

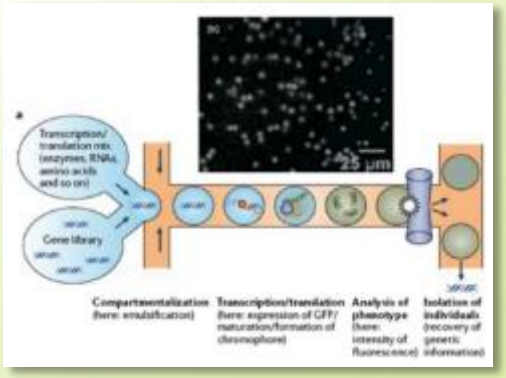


(Shestopalov *et al.*, *Lab Chip*, 2004)

奈米粒子合成

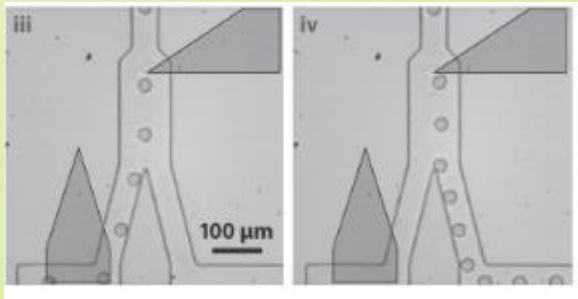


醫藥檢測篩選



(Dittrich *et al.*, *Nat. Rev.*, 2006)

高密閉性，可做細胞包覆，並平行監控。



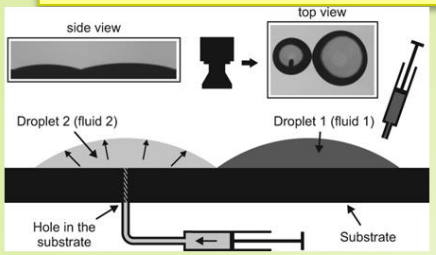
(Ahn *et al.*, *Appl. Phys. Lett.*, 2006)

液珠外有薄膜保護隔絕產物沾附流道壁面

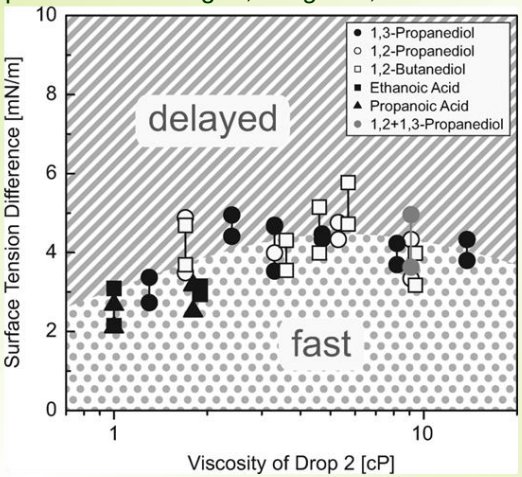
對個別液珠檢測篩選

微液珠碰撞與融合

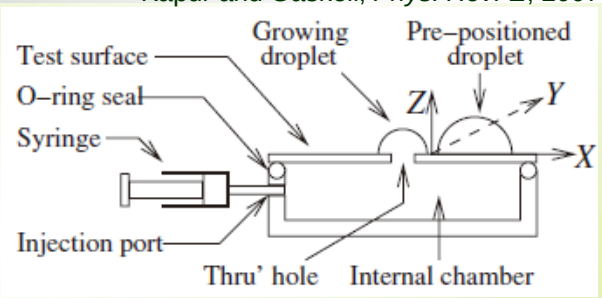
表面張力及黏滯性不同的液珠，接觸後的接合現像，可分為延遲接合與快速接合兩種。

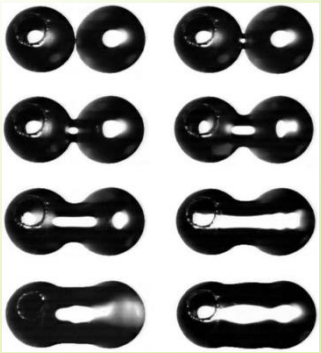


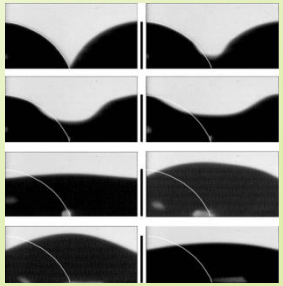
Karpitschka and Riegler, *Langmuir,* 2010

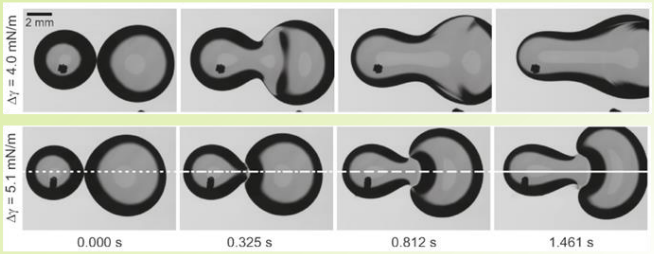


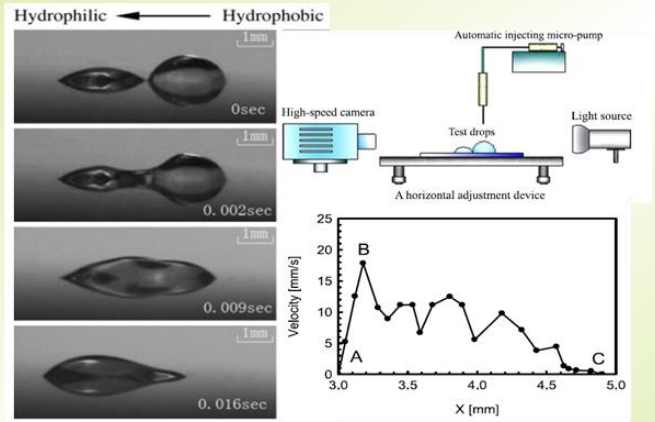
Kapur and Gaskell, *Phys. Rev. E*, 2007



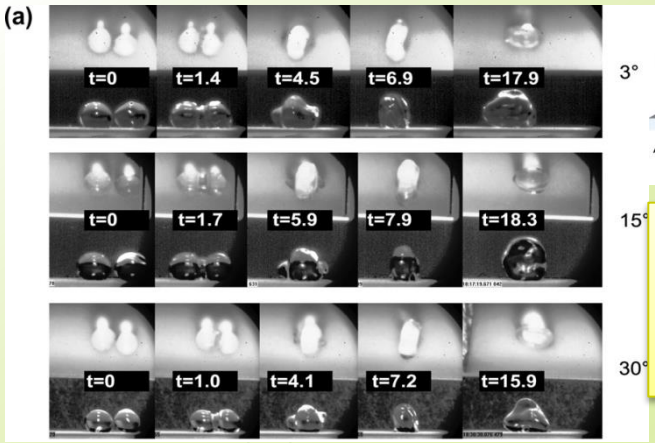


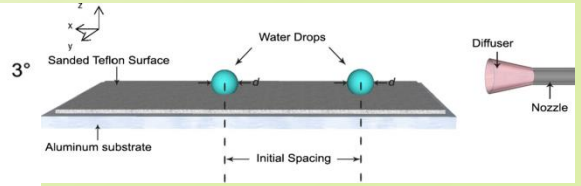






Wang *et al.*, J *Supercond Nov Magn*, 2010



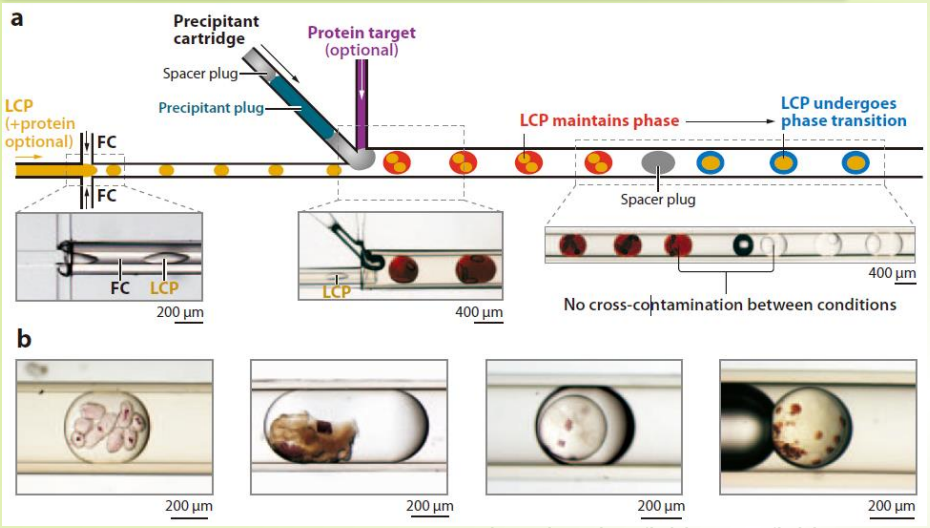


目前微液珠融合的相關研究，仍以輪廓變化以及流體混合為主

Nilsson and Rothstein, *J. Colloid interface Sci.*, 2011

液珠式微反應器

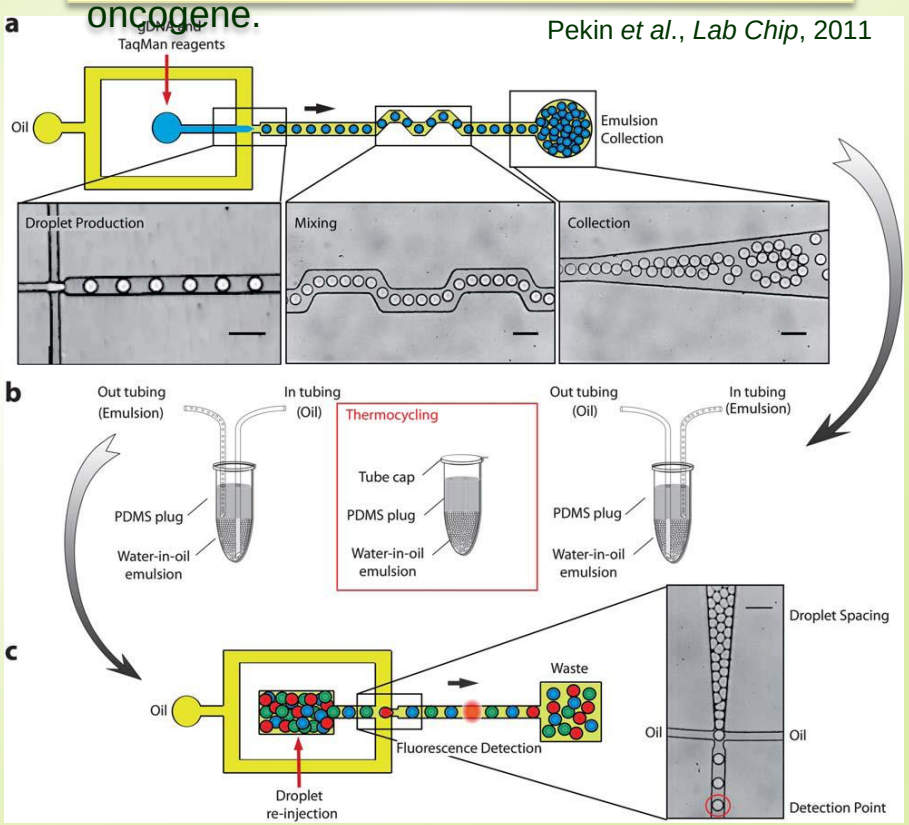
Droplet-based microfluidic system for membrane crystallization within lipidic mesophases

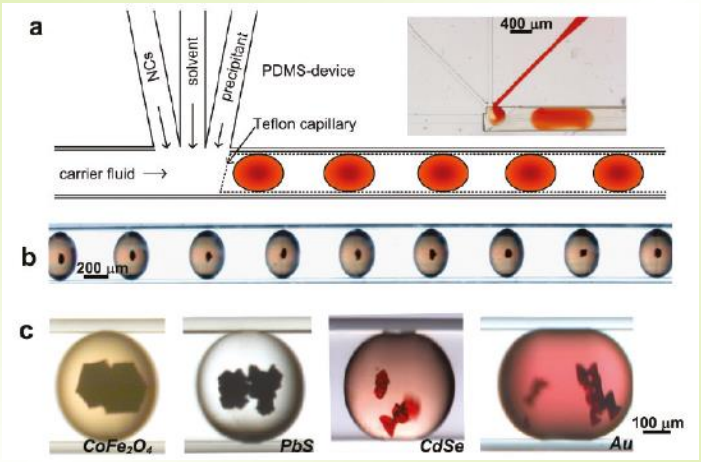


Li et al., *Microfluid. Nanofluid.*, 2010

Development and validation of a method to allowed the highly sensitive and quantitative detection of mutations in the KRAS oncogene.

Pekin *et al.*, *Lab Chip*, 2011



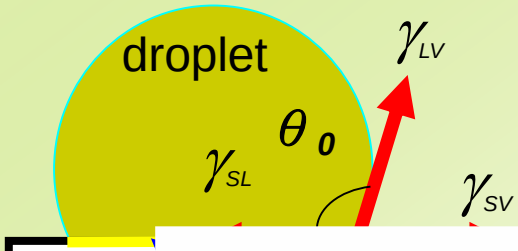


Bodnarchuk, *J. Am. Chem. Soc.*, 2011

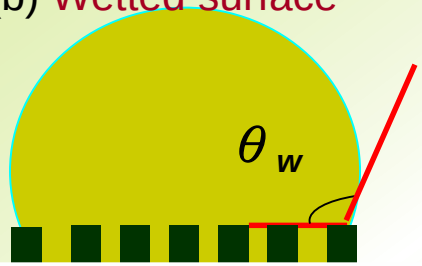
The self-assembly of inorganic nanocrystals (NCs) confined inside nanoliter droplets (plugs) into long-range ordered superlattices.

Contact Angle & Surface Wettability

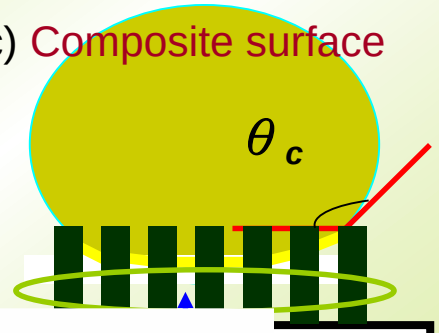
(a) Smooth surface



(b) Wetted surface



(c) Composite surface



Cor s

■ Smo rface

Your r Eq. (1944)

$\cos\theta$ $\vartheta_0 + f_1 - 1$

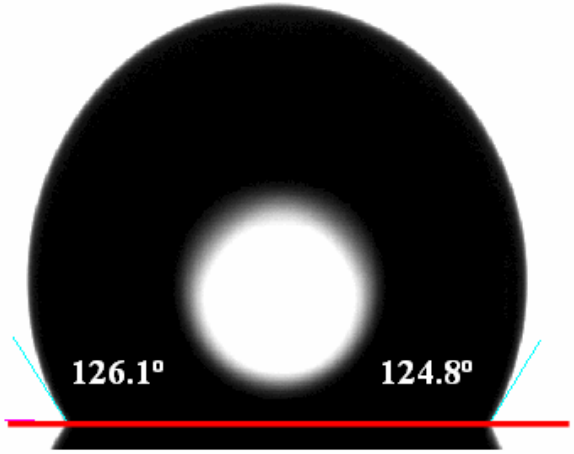
■ Jus parameter:

cor on of

les ensity of

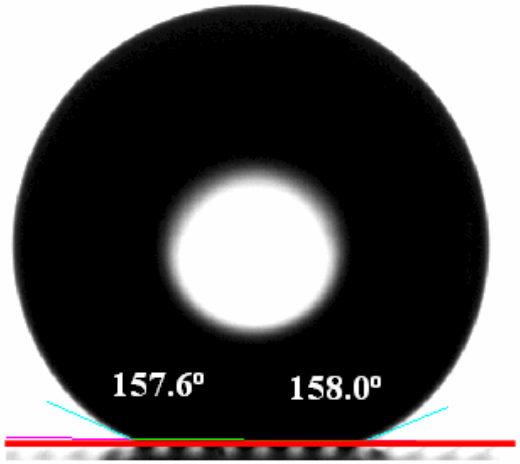
ures, f_1

(a) PPFC, microstructure stature of 3.2 μm



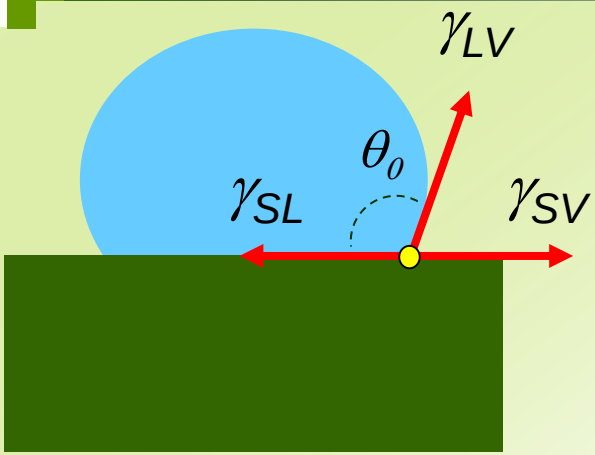
Collapsed droplet

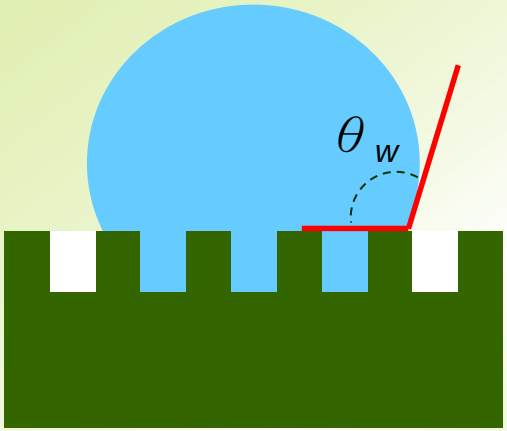
(b) PPFC, microstructure stature of 24.1 mm

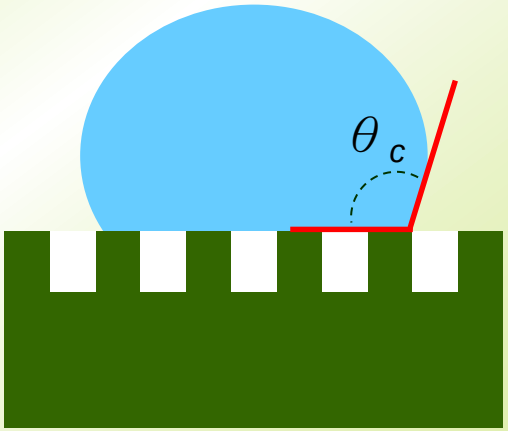


Suspended droplet

接觸角度與表面自由能







■ 平滑表面

Young equation

$$\cos\theta_0 = \frac{\gamma_{SV} - \gamma_{SL}}{\gamma_{LV}}$$

■ 潤濕表面

Wenzel equation

$$\cos\theta_w = \frac{r(\gamma_{SV} - \gamma_{SL})}{\gamma_{LV}} = r\cos\theta_0$$

■ 複合表面

Cassie and Baxter Equation

$$\cos\theta_C = f_1 \cdot \cos\theta_1 + f_2 \cdot \cos\theta_2$$

$$r = \frac{A_{actual}}{A_{projected}} \qquad f_1 = \frac{A_{S-L}}{A_{total}} \qquad f_2 = \frac{A_{V-L}}{A_{total}}$$

表面自由能

$$\frac{G_S}{\sqrt[3]{9\pi V^{2/3}\gamma_{LV}}} = (1-\cos\theta_r)^{2/3}(2+\cos\theta_r)^{1/3}$$

潤濕表面：$\theta_r \rightarrow \theta_w$

複合表面：$\theta_r \rightarrow \theta_c$

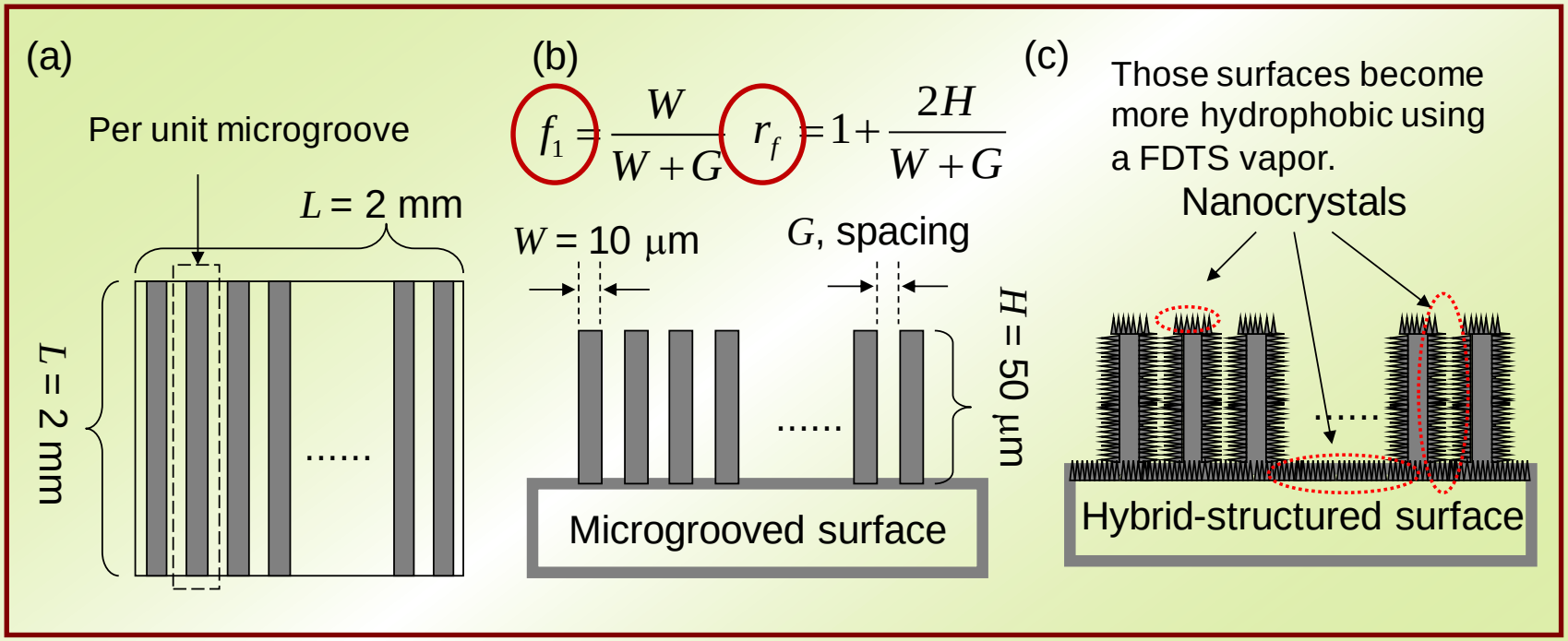
(Patankar, 2003)

接觸角度, θ → 表面自由能, G_s

Technology

J. T. Yang, 20081116

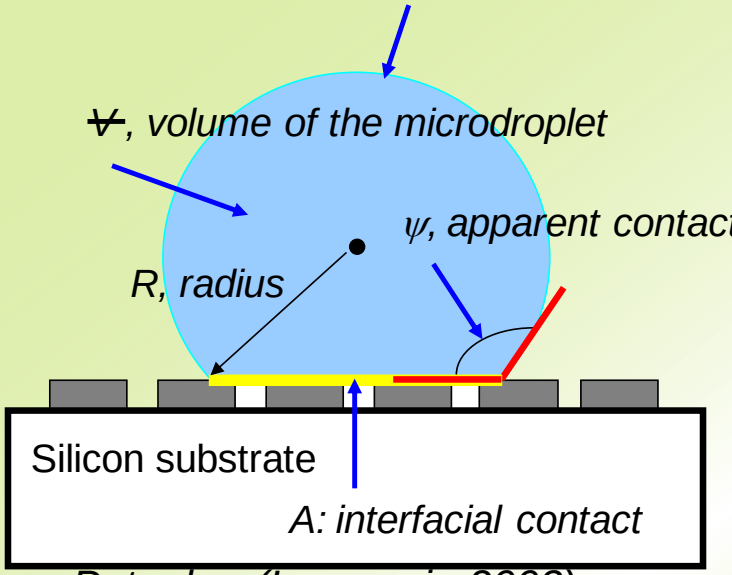
Design Parameters for Hybrid-structured Surfaces



- **The pattern density and roughness are functions of geometrical dimensions of microgrooves.**

Gibbs Surface Free Energy

S, interfacial area of the Liquid-vapor phase



Patankar (Langmuir, 2003)

$$G_0 = \gamma_{LV} \times \Omega_{LV-\min} = \gamma_{LV} \times 4\pi r^2 = 7.31\times10^{-7}\ \text{J}$$

$$\frac{G_S}{\sqrt[3]{9\pi V^{2/3}}\gamma_{LV}} = \left(1-\cos\theta_r\right)^{2/3}\left(2+\cos\theta_r\right)^{1/3}$$

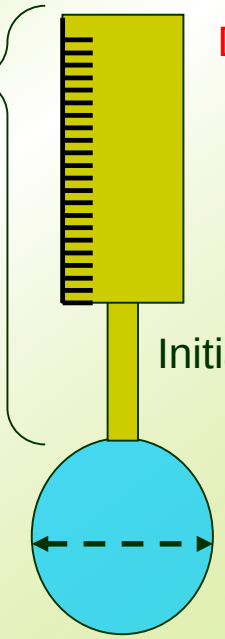
Lagrange multiplier method

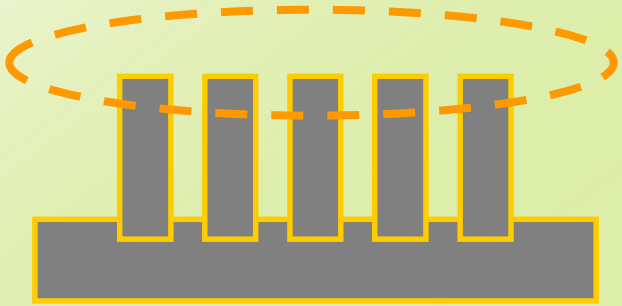
求解微液珠於穩態最小表面自由能。

V = 3 μL
D = 1.8 mm

Needle

由接觸角的量測計算出液珠穩定懸浮於微結構表面之表面自由能(G_s)





Droplet on a composite surface at the steady state

Micro/Nano-Fabrications
&
Experimental Measurement

Micro-fabrications & Microstructures

Photolithography and Pattern

(AZ 5214)

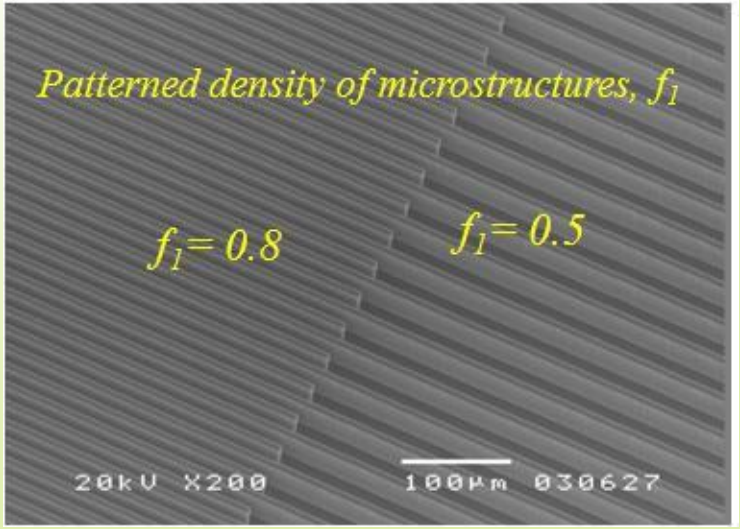
Development and Dry etching

(ICP)

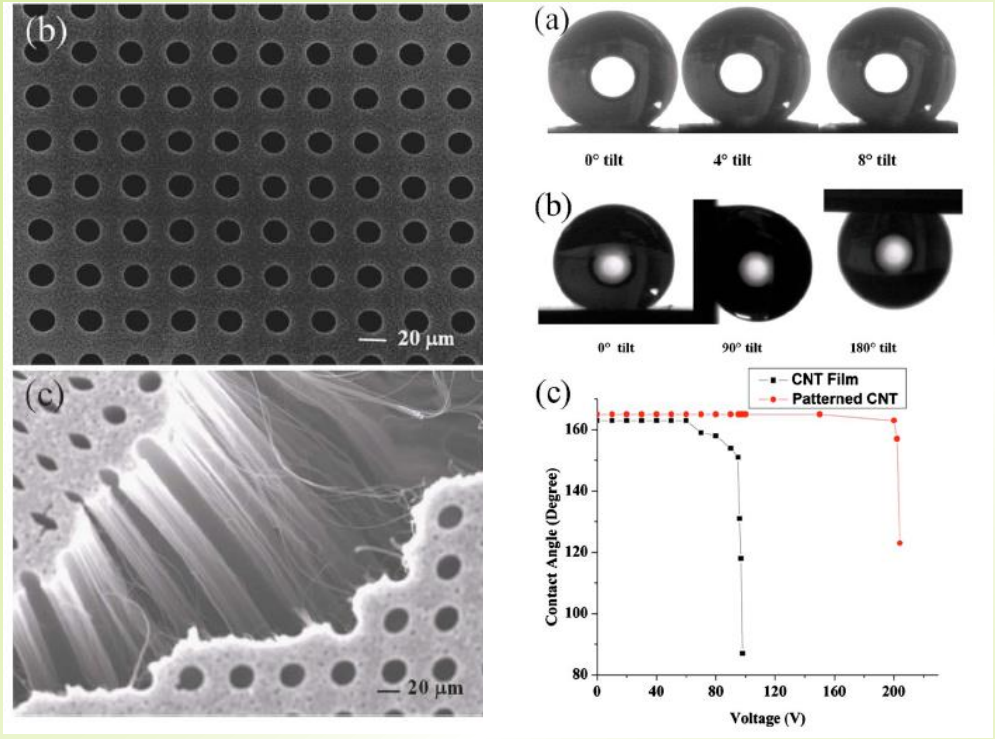
Coating a layer of hydrophobic film

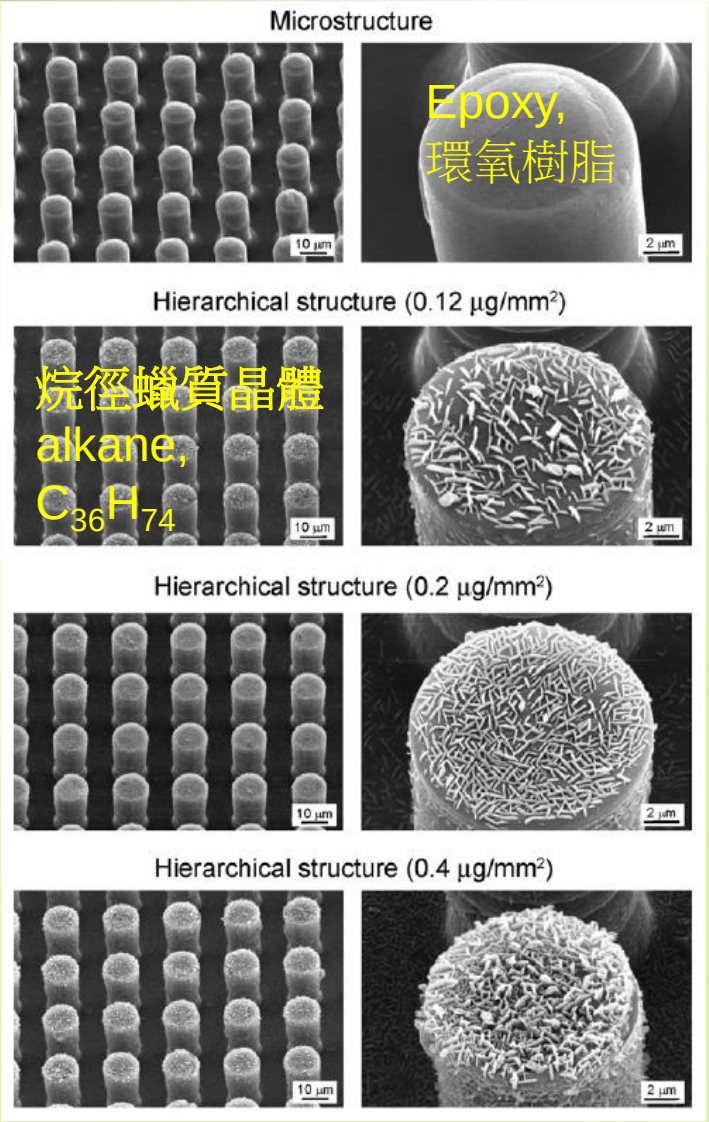
(FDTS monolayer)

The geometrical dimensions : 2000 μm in length, 10 μm in width, 50 μm in height.



Hybrid-structured surface (1)



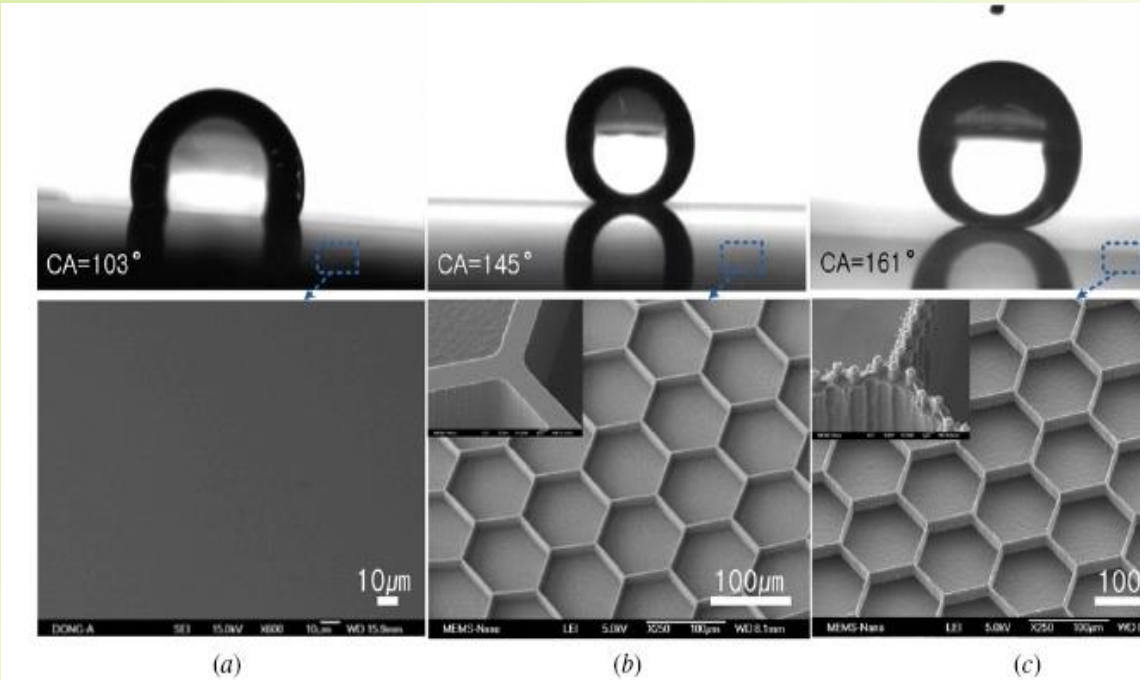


- **Wang, Z., Koratkar, N., Ci, L., and Ajayan, P. M. 2007. *Appl Phys Lett*, Vol. 90(14), pp. 143117.**

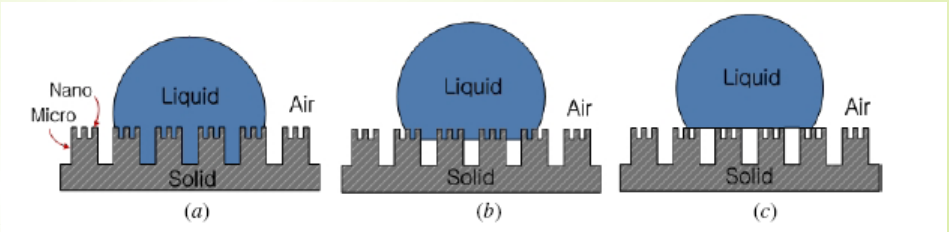
Bhushan, B., Koch, K., and Jung, Y. C. 2008., *Soft Matter*, Vol. 4(9), pp. 1799-1804.

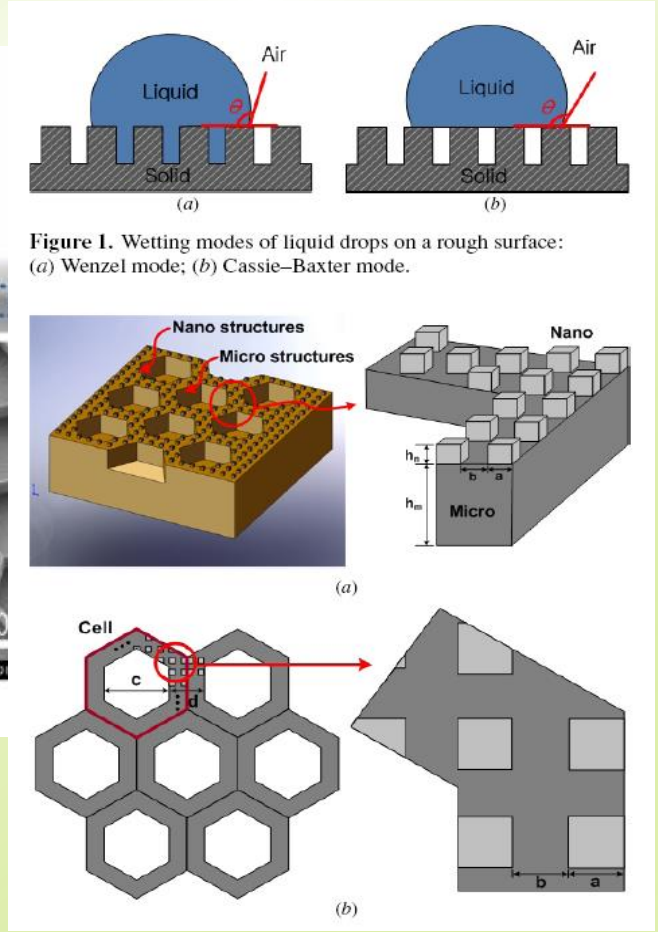
Hybrid-structured surface (2)

- Lee, S. M., Jung, I. D., and Ko, J. S. 2008. J Micromech Microeng, Vol. 18(12), pp. 125007.

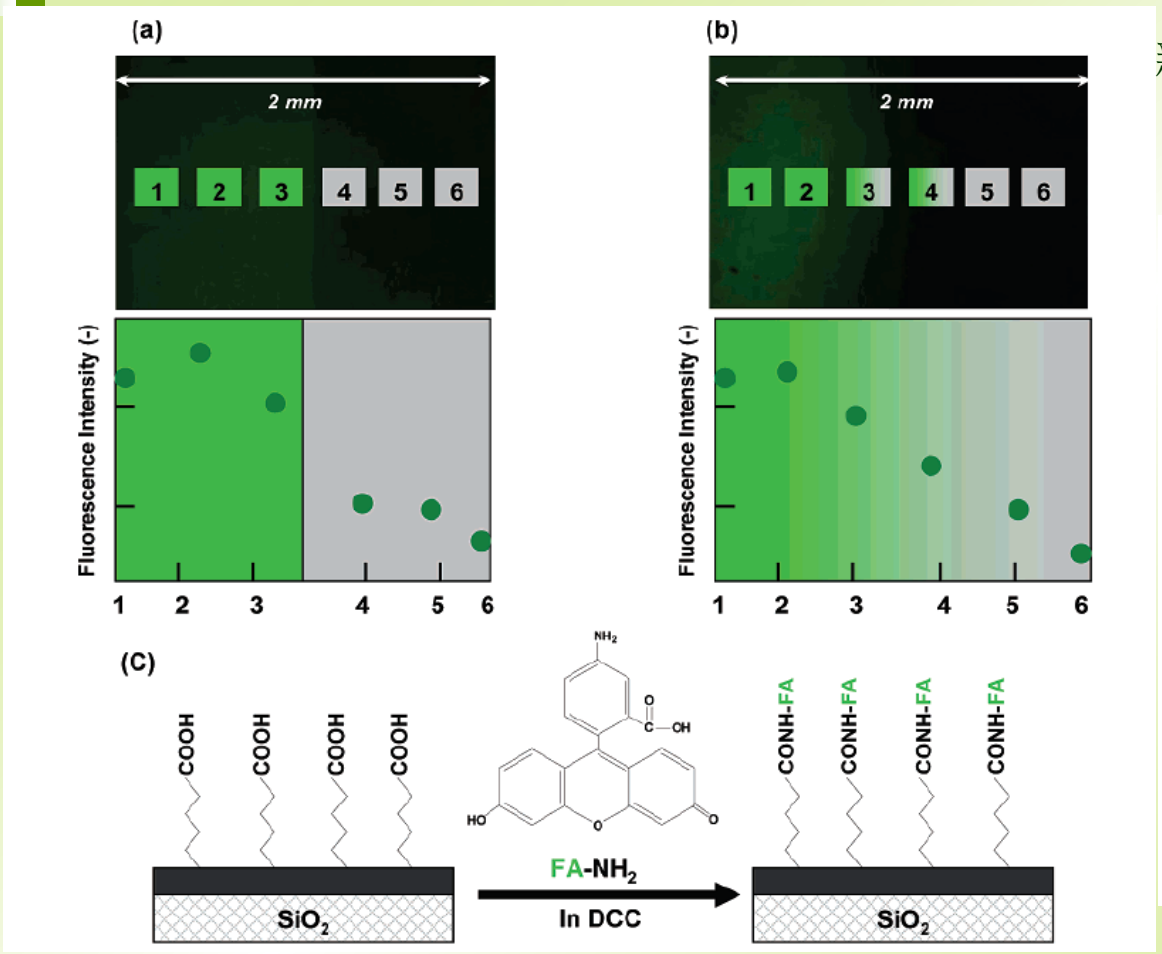


W-W model W-C model C-C model





Self-assembly method



親水端(-COOH)←斥水端（CH_3）

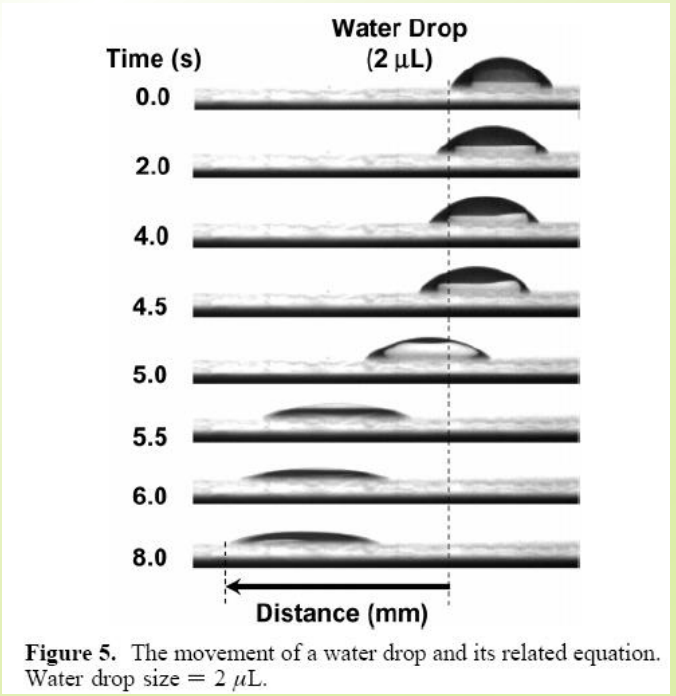
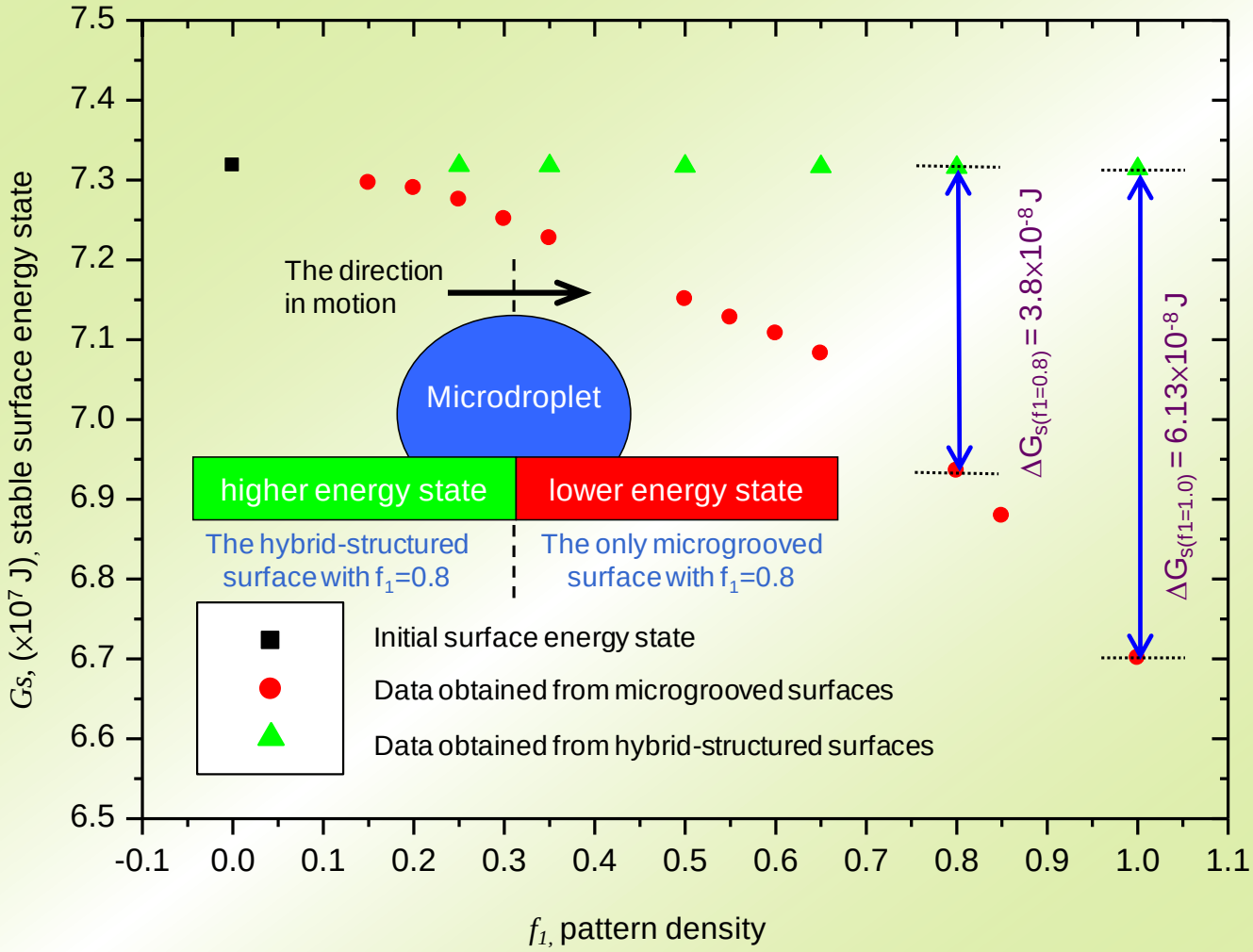


Figure 5. The movement of a water drop and its related equation. Water drop size = 2 μL.

Ito, Y., Heydari, M., Hashimoto, A., Konno, T., Hirasawa, A., Hori, S., Kurita, K., and Nakajima, A. 2007. *Langmuir*, Vol. 23(4), pp. 1845-1850.

Surface Energy State

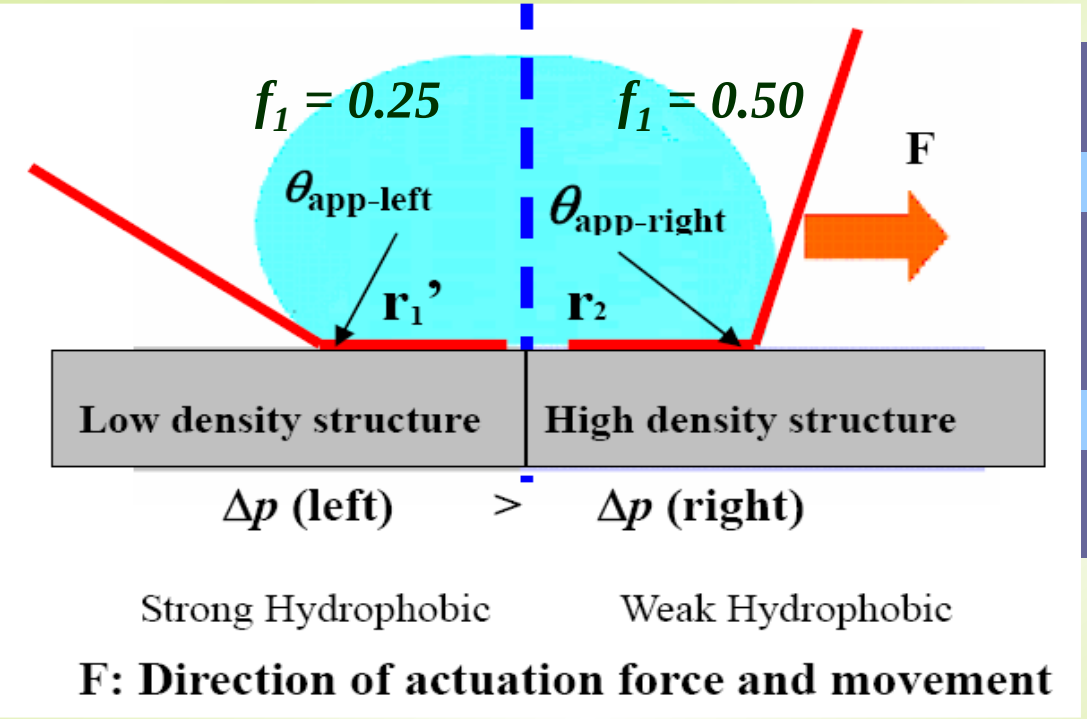


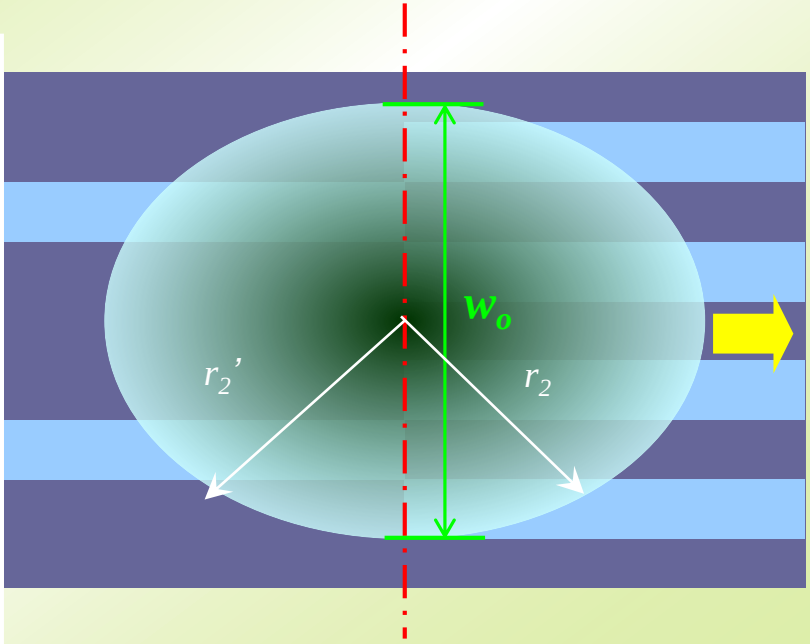
液珠於奈微複合表上有較高的表面自由能階，具有較低的遲滯效應且容易滾動。

獲得更大的表面自由能階梯度，因此增加液珠傳輸距離和速度。

液珠移動機制

Yang *et al.*, *J. MEMS*, 2006 (91)



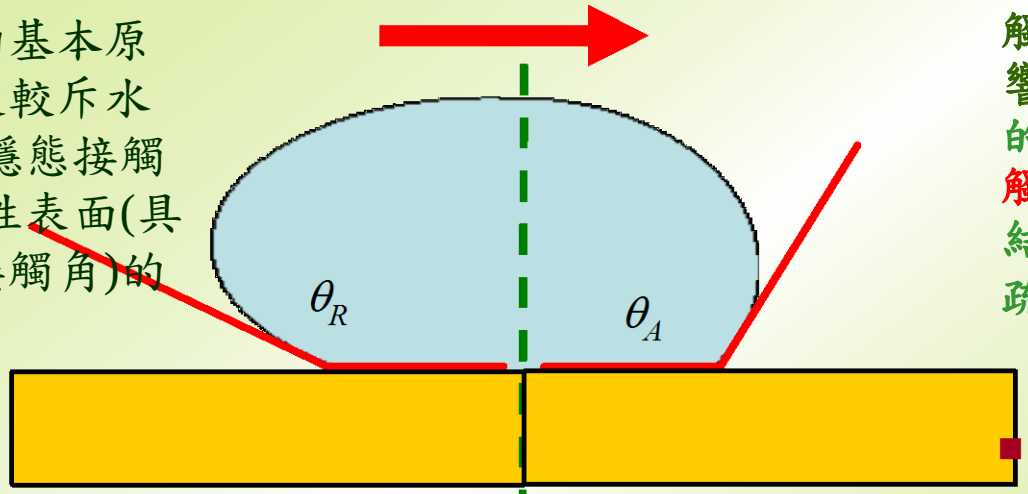


當液珠所受到驅動力大於阻滯力
液珠即可在表面移動。

J. T. Yang, J. H. Chen, K. J. Huang, and J. A. Yeh, 2006, "Droplet Manipulation over a Hydrophobic Surface with Roughened Pattern," *IEEE Journal of Microelectromechanical Systems*, Vol. 15, June, pp. 697-707.

液珠輸送及操控之方法彙整

- 微液珠傳輸的基本原則，液珠將從較斥水性(具有較大穩態接觸角)往較親水性表面(具有較小穩態接觸角)的方向傳輸。



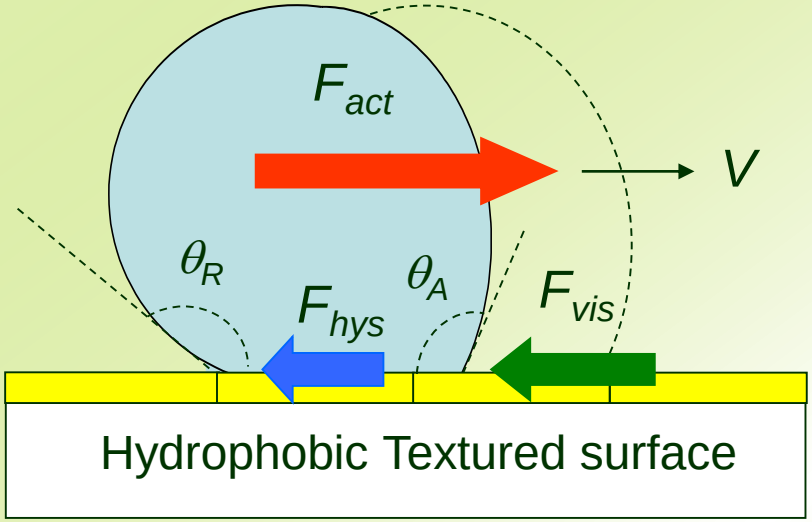
- 主要的驅動機制與原理，來自於液珠與壁面接觸時，因外界能量的影響(溫度、電壓與光能場的強度分佈)或是底部接觸表面特性改變(例如微結構密度和化學薄膜親疏水性)。

Basic Principle	More Hydrophobic surface Larger contact angle	More Hydrophilic surface smaller contact angle
Thermal method	Higher surface temperature	Lower surface temperature
Chemical method	lower free surface energy between solid and vapor, G_{SV}	Higher free surface energy between solid and vapor, G_{SV}
Electro-wetting method	Higher free surface energy between solid and liquid, G_{SL}	lower free surface energy between solid and liquid, G_{SL}
Microstructure method	Lower density structure, f_1	Higher density structure, f_1

而使液珠左半部與右半部介面上的氣液表面能自由能的不平衡，導致氣液介面的表面自由能階梯度變化(G_{LV})，而使微液珠沿梯度方向被驅動。

動力學分析 $\Sigma F = ma$

Yang *et al.*, *Langmuir*, 2008 (83)



$$F_{act} = -\frac{d\Delta G}{dx} \cong \pi R^2 \gamma_{LV} \left(\frac{d\cos\theta}{dx} \right)$$

在驅動力的部份，主要來自於表面微奈米結構密度梯度引發微液珠左右半部氣液介面上，表面自由能的梯度差所造成的驅動力。

$$-2\gamma_{LV} R\left(\cos\theta_{R_0} - \cos\theta_{A_0}\right)$$

因遲滯現象所造成的阻滯力，相當於靜摩擦力。

$$F_{vis} \cong 3\pi\eta RV \ln\left(\frac{X_{\max}}{X_{\min}}\right)$$

微液珠動態運動中液珠本身與接觸面的黏滯力，相當於動摩擦力。

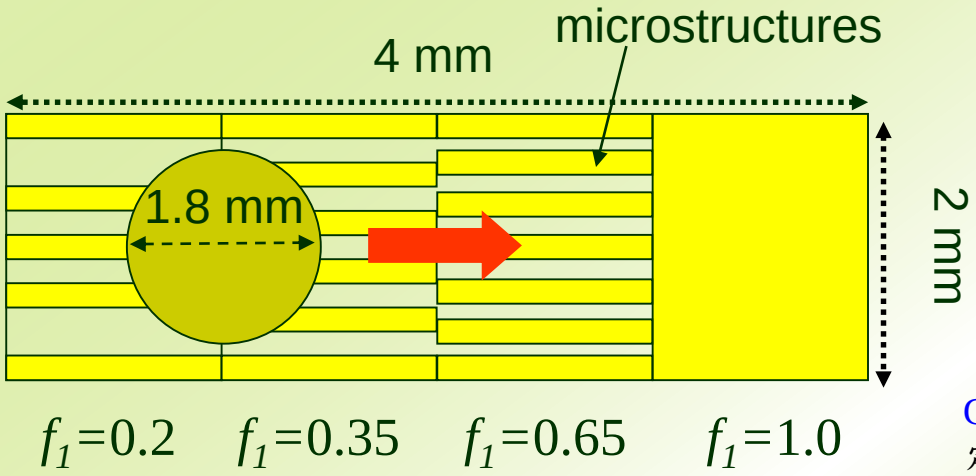
液珠於奈微米表面結構移動過程中，主要的力學作用機制包括驅動力(actuation force)、阻滯力(hysteresis force)和黏滯力(viscous force)，這三者的合力作用造成液珠的表面輪廓形變，並主宰微液珠於壁面路徑表面上的運動狀態與動力大小。

$$V \cong \frac{\gamma_{LV} R}{3\eta \ln(X_{\max} / X_{\min})} \left(\frac{d\cos\theta}{dx}\right)$$

微液珠於表面傳輸時的平均穩態速度

能量轉換 $E_K = \Delta G - W_{friction}$

Note:
根據能量守恆和表面自由能的觀點，去探討液珠在移動過程中的能量轉換機制。



f_1=0.2 f_1=0.35 f_1=0.65 f_1=1.0

f_1 :patterned density of microstructure

$$E_K = \Delta G - W_{friction}$$

ΔGs_{12}表示液珠在橫跨前後兩個具有不同微結構密度表面上，穩態表面自由的能階差。

G_{shape}是指運動的液珠當開始停止移動到達穩定靜止於表面上這段期間，液珠表面震盪所造成的能量損耗。

$$W_{vis} = F_{vis} \times \Delta x$$

Unknown, but …

$$\Delta Gs_{12} - G_b - W_{vis} - G_{shape} = \frac{1}{2} mv^2$$

Available (theory prediction and measurement)

藉由液珠在移動前後穩態表面自由能的轉換，扣除因遲滯力和黏滯力所造成的摩擦能損和液珠表面震盪的內能損耗，應該等於液珠移動時的平均動能。

Yang *et al.*, *Langmuir*, 2008 (83)

Design Parameters for Hybrid-structured Surfaces (Table 1)

Pad No.	f_1	r_f	G / μm	G/W	θ_w / deg	θ_c / deg	θ_m / deg
1	0.15	2.5	56.7	5.67	159.7	154.98	152.8
2	0.2	3	40	4	NA	151.04	150.85
3	0.25	3.5	30	3	NA	147.53	147.5
4	0.3	4	23.33	2.33	NA	144.33	143.4
5	0.35	4.5	18.57	1.86	NA	141.36	140.3
6	0.5	6	10	1	NA	133.42	133.15
7	0.55	6.5	8.18	0.82	NA	131	131.45
8	0.6	7	6.67	0.67	NA	128.66	130.1
9	0.65	7.5	5.38	0.54	NA	126.41	128.5
10	0.8	9	2.5	0.25	NA	119.98	120.9
11	0.85	9.5	1.76	0.18	NA	117.93	118.5
12	1	11	0	0	NA	112	112
Pad No.	f_1	$f_{1\text{-nano}}$	$r_{f\text{-nano}}$	θ_m / deg	θ_w / deg	θ_c / deg	θ_h / deg
13	0.25	2.54	0.08	150.85	NA	171.17	173.1
14	0.35	2.54	0.08	140.3	NA	170.09	170.5
15	0.5	2.54	0.08	133.15	NA	167.44	167.6
16	0.65	2.54	0.08	128.5	NA	166.27	166.2
17	0.8	2.54	0.08	120.9	NA	164.4	164.5
18	1	2.54	0.08	112	162.3	162.3	162.3

Research Actions inspired by Lotus Leaf and Plants
BEAM Lab at NTU

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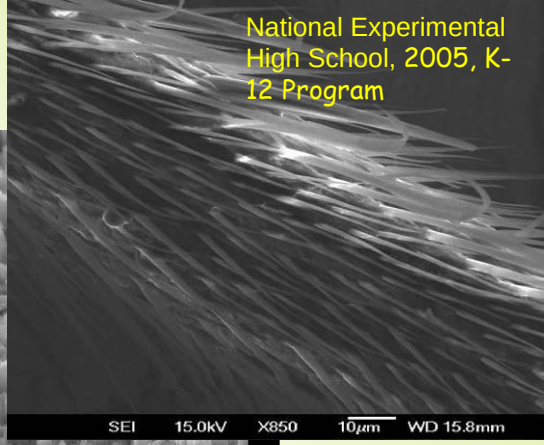
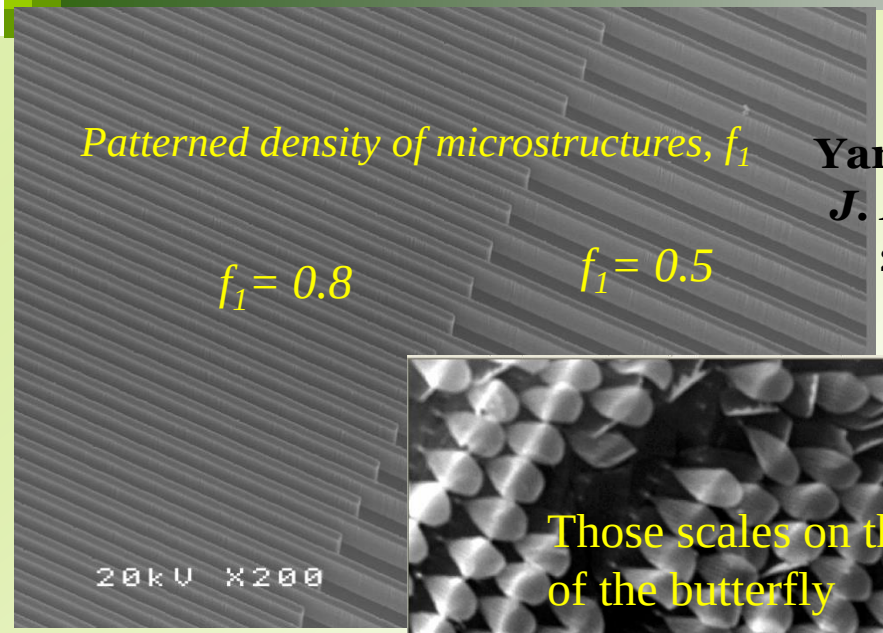
國立台灣大學 機械工程學系

國科會能源計畫辦公室主任

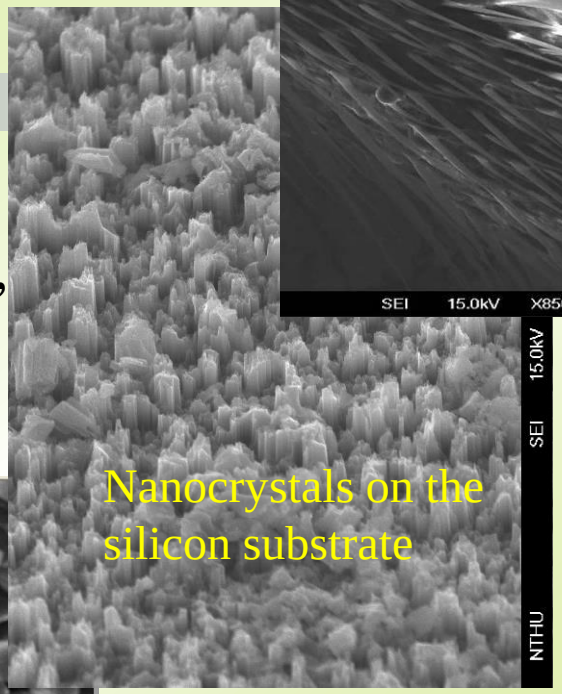
May 17th, 2010 @ Chungli

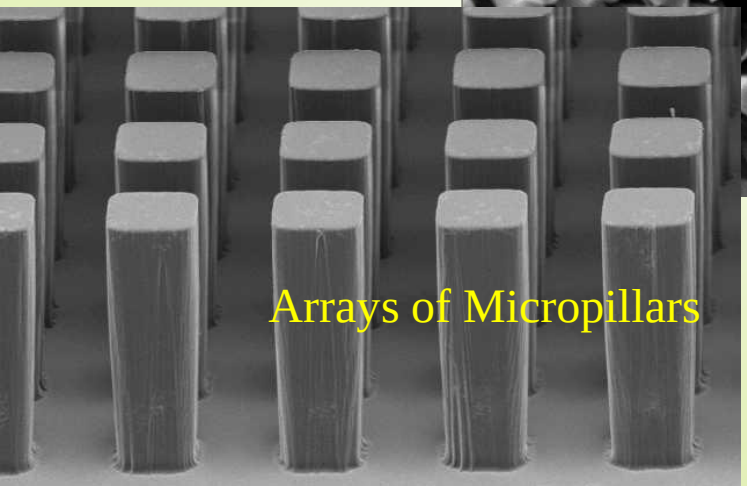
Surface Science & Art

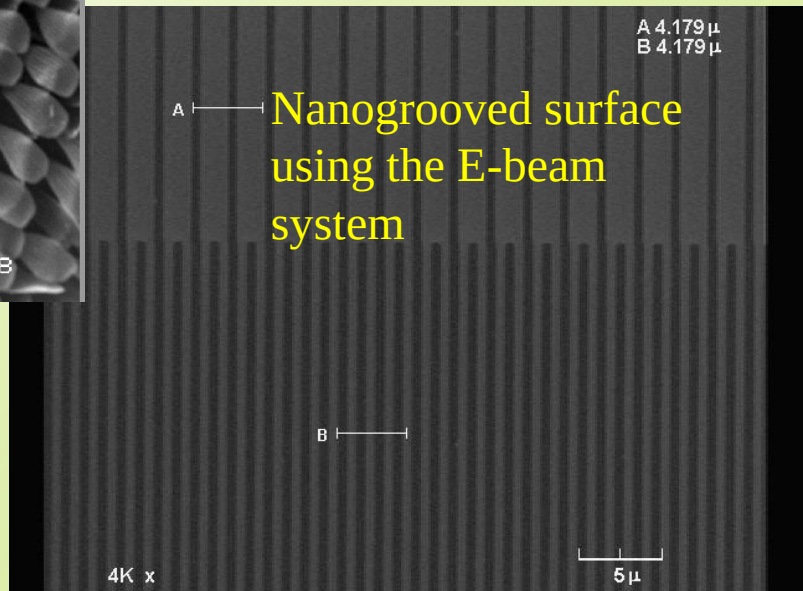




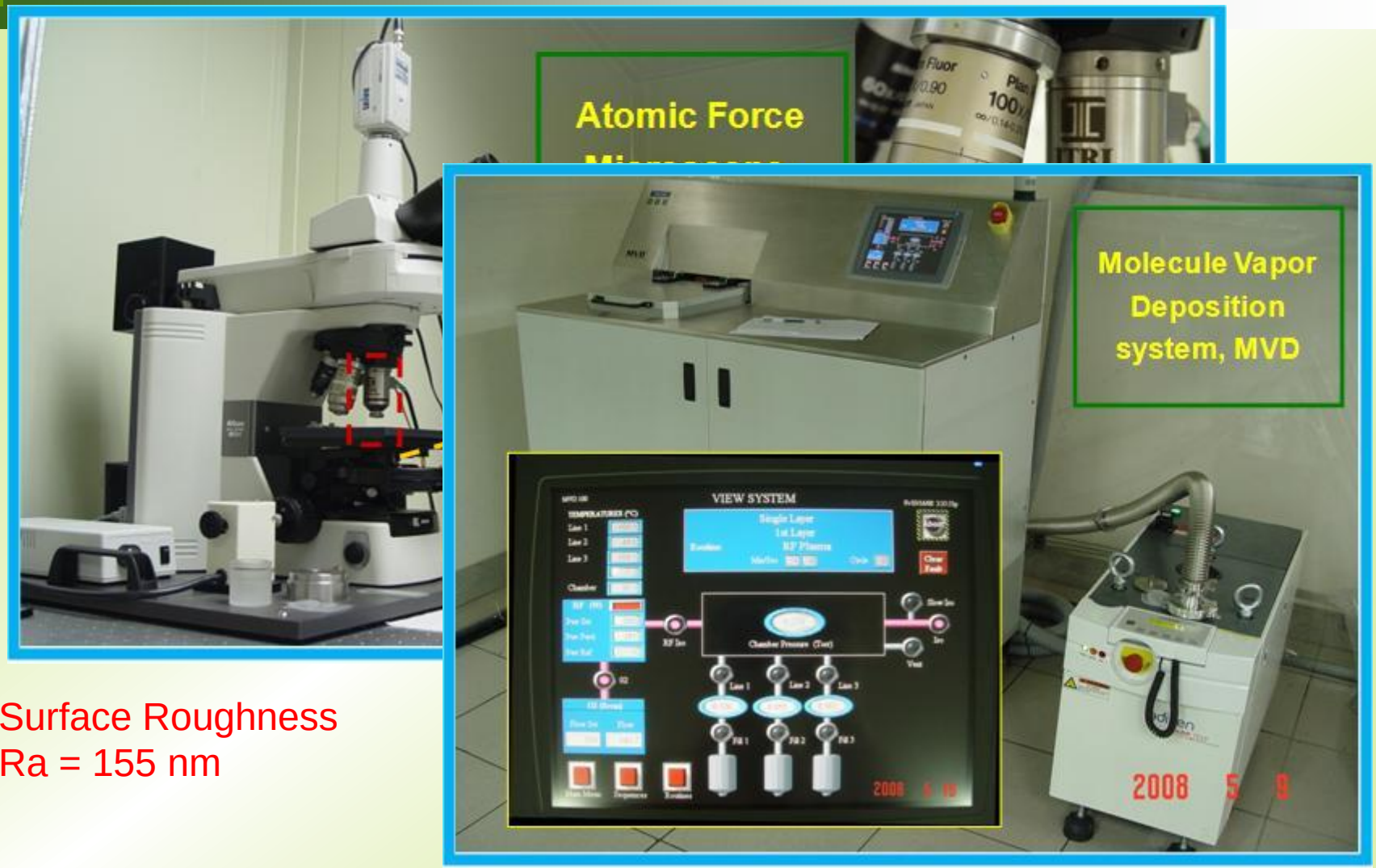
Yang et al., *J. MEMS*, 2006





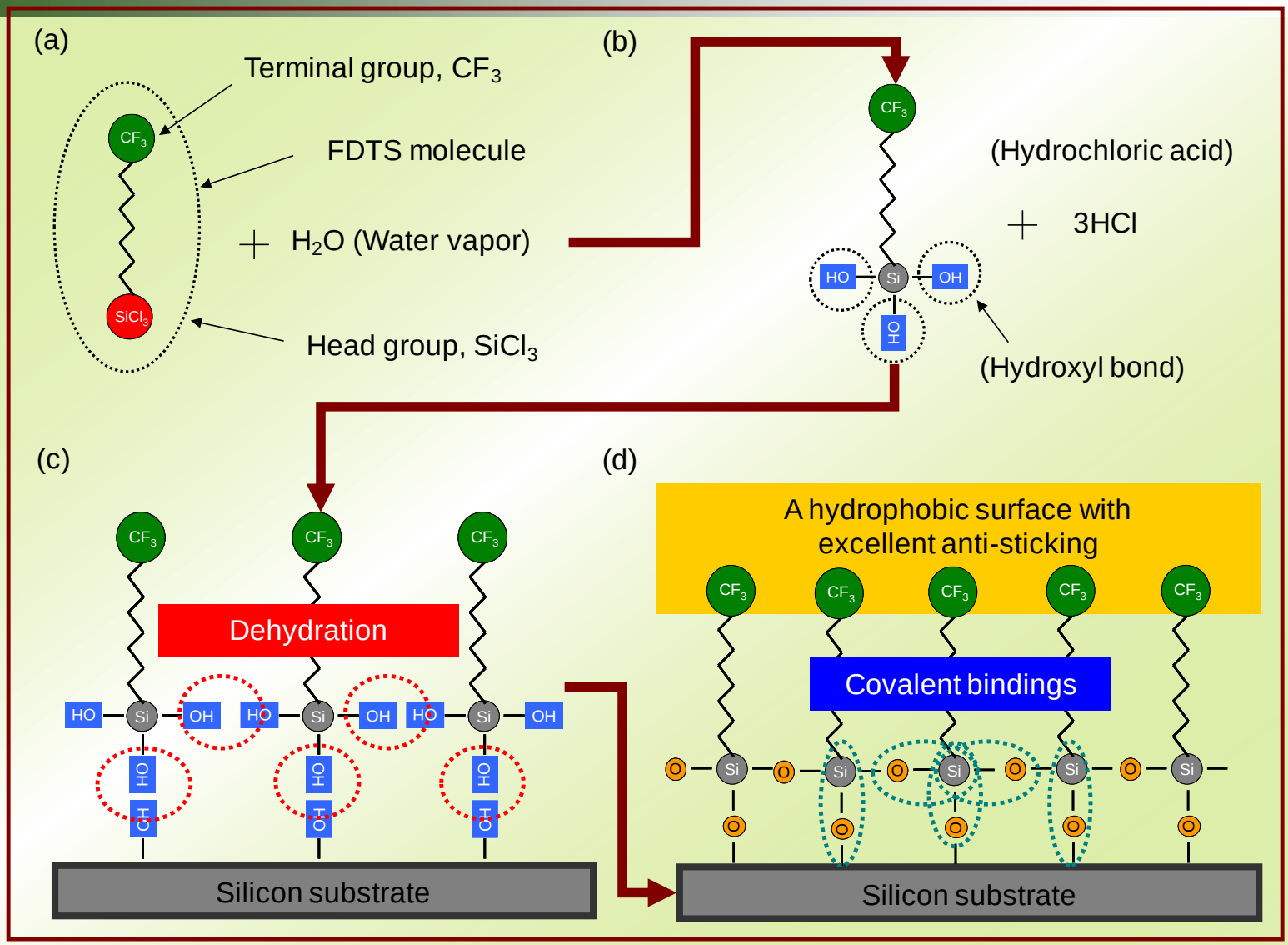


Morphology & Surface Modification



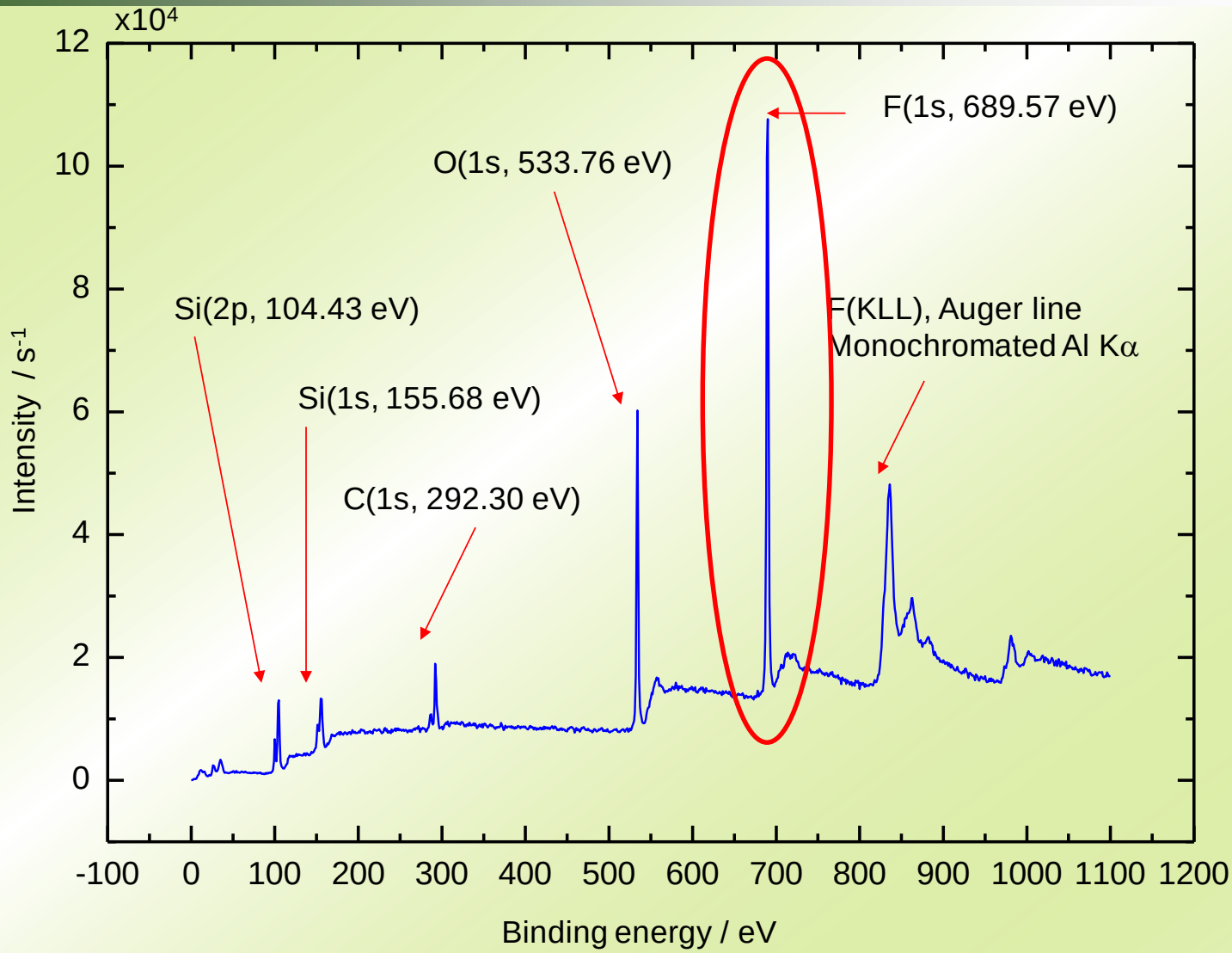
Surface Roughness
Ra = 155 nm

Mechanism of Self-Assembly Monolayer

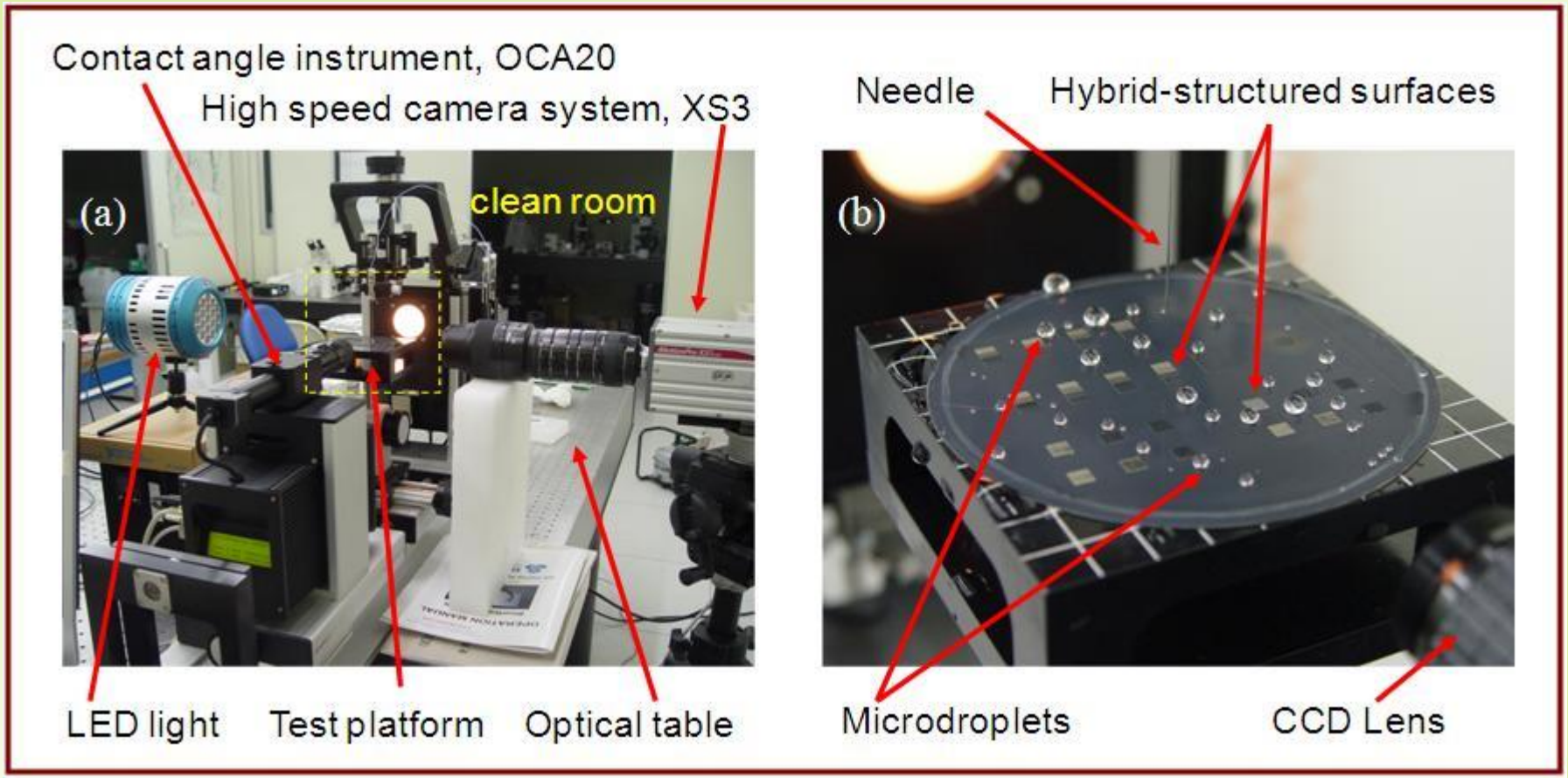


Spectrum for a FDTS Monolayer on the Hybrid-structured Surface

X-ray 光電子質譜分析儀(XPS)

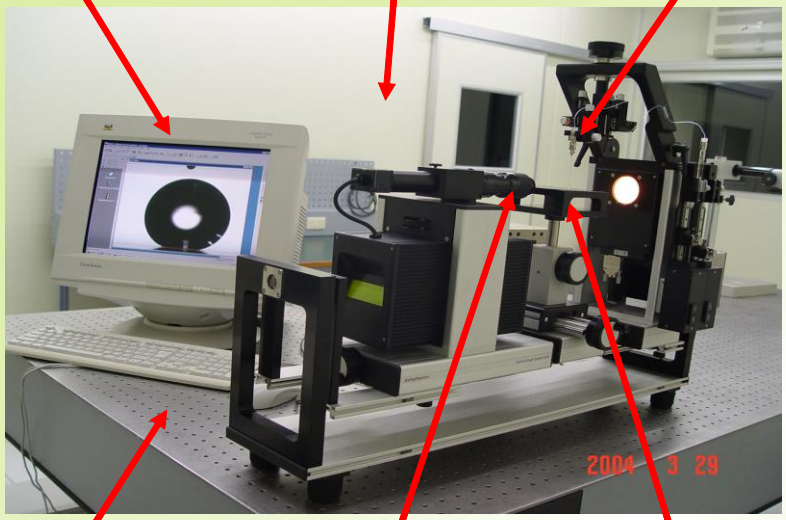


Measurement platform for the droplet Contact angle

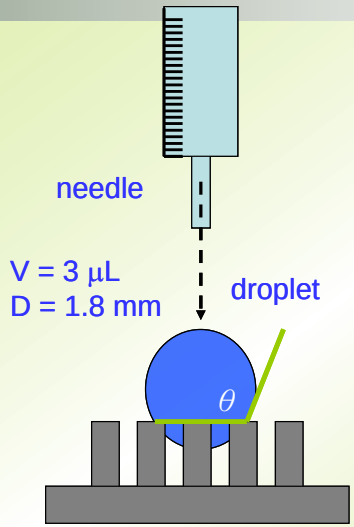


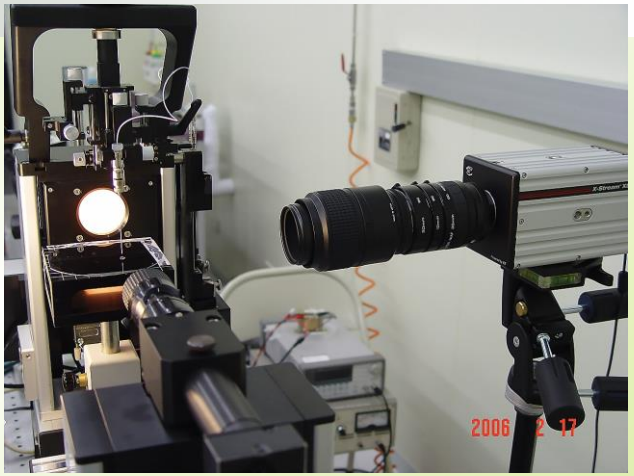
液珠實驗設備圖

影像擷取系統　class 1000 無塵室　微液珠產生器



氣壓式光學防震桌　CCD Lens　量測平台





Taking pictures of a single droplet on a composite surface at the steady state

Note:

Static measurement

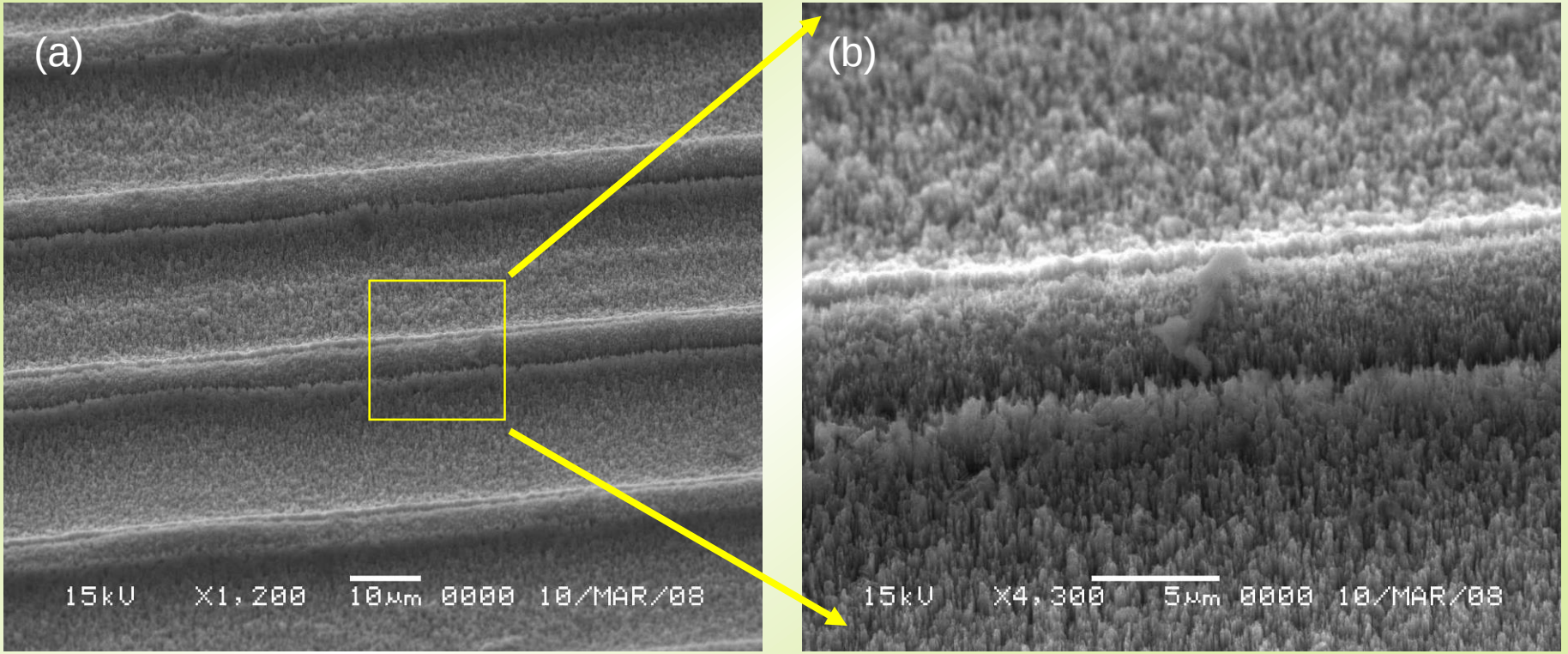
Contact angle, θ → G_s, G_b, V

Dynamic measurement

兩款微表面傳輸元件，其表面微結構分佈密度序列如下(A) 0.25、0.5、0.8、1 ;(B) 0.2、0.35、0.65、1。

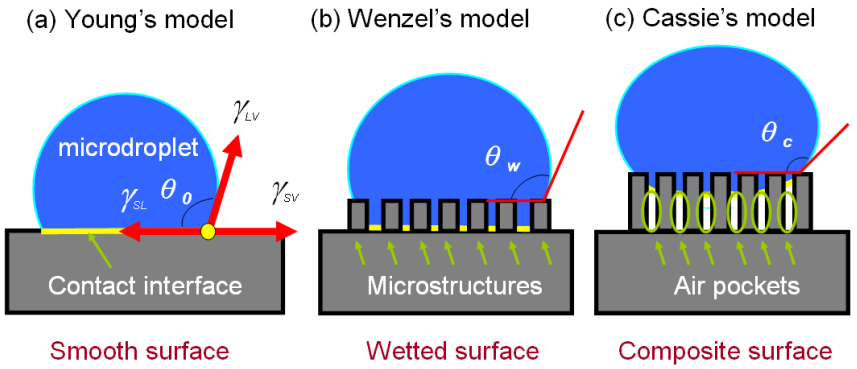
Hybrid structured surfaces

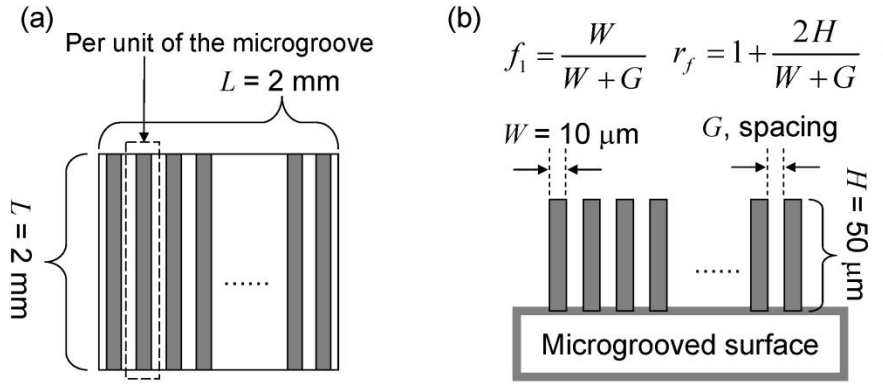
Yang et al., Highlights of JMM, 2009 (33)

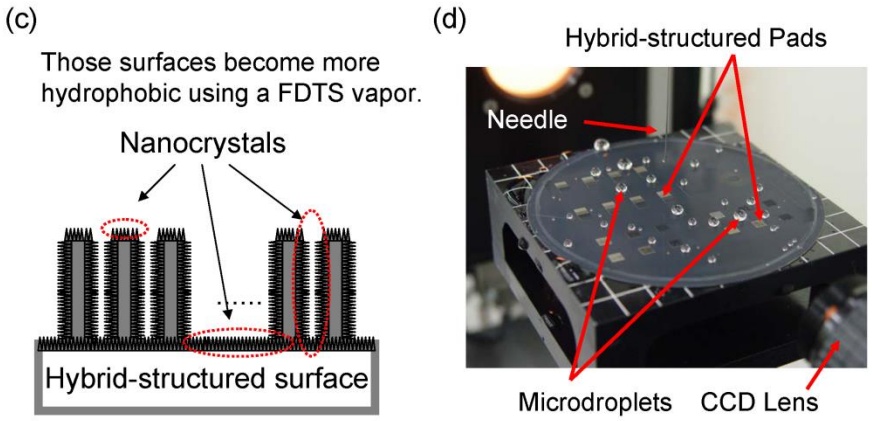


Photographic Scans of a Hybrid Structured Surface with a SEM: (a) The Sight Field at a Small Magnification; and (b) The Sight Field at an Increased Magnification

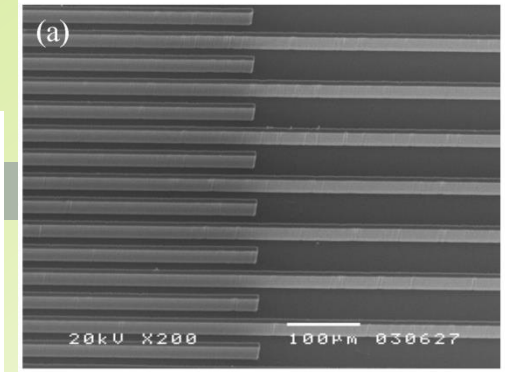
Ultra-Hydrophobic Surfaces

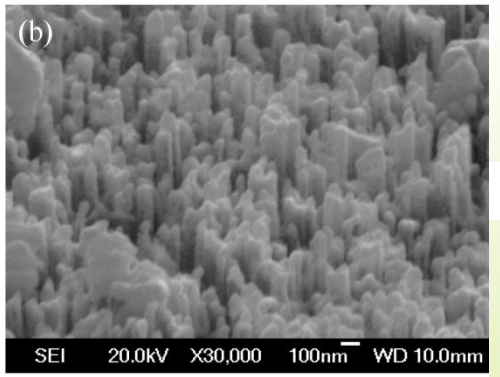


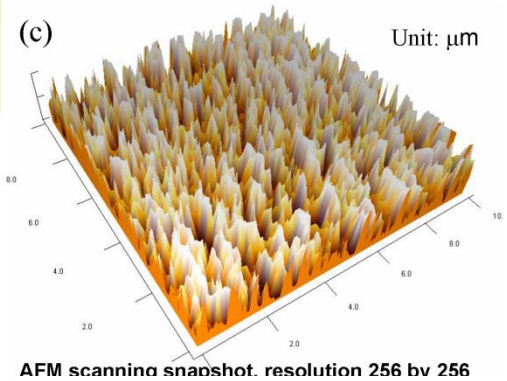


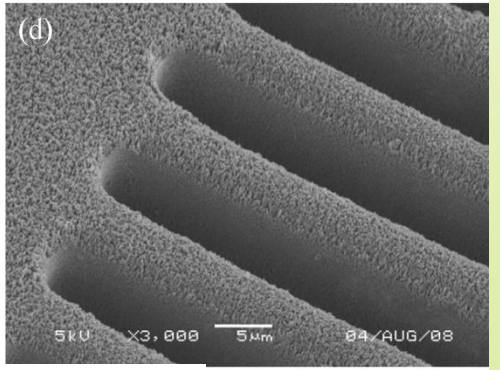


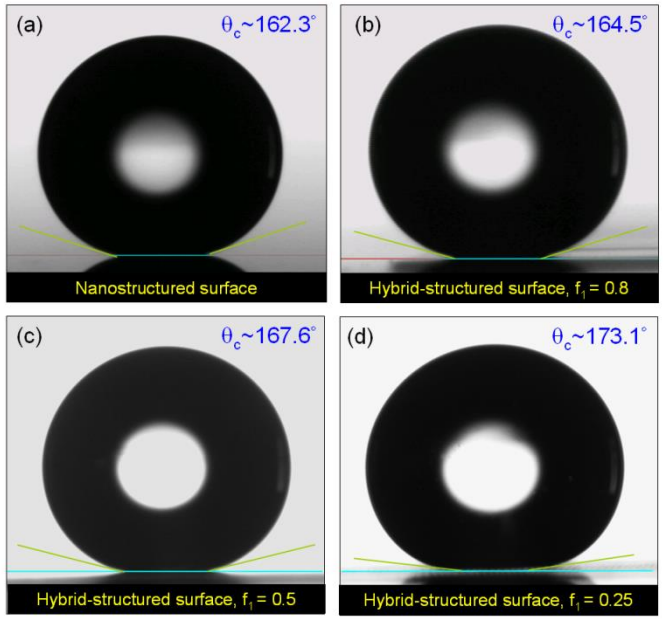
Yang et al., Highlights of JMM, 2009 (33)





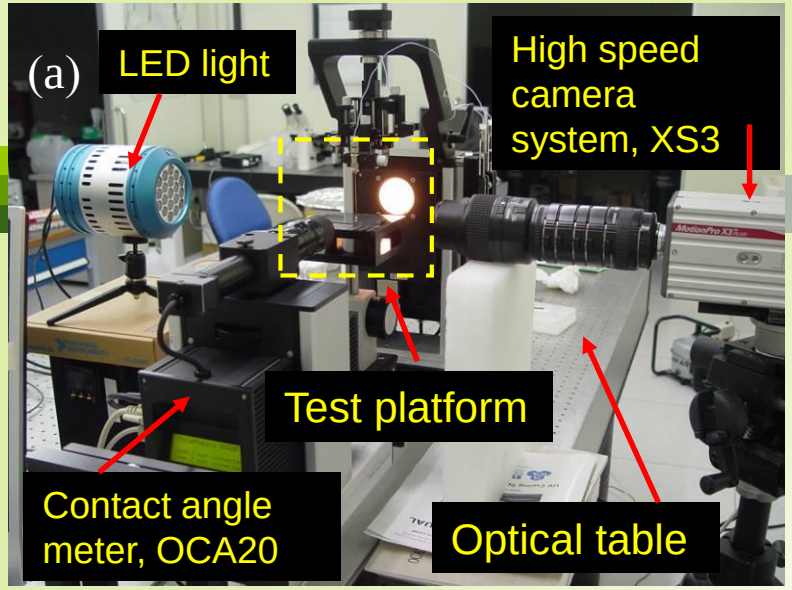


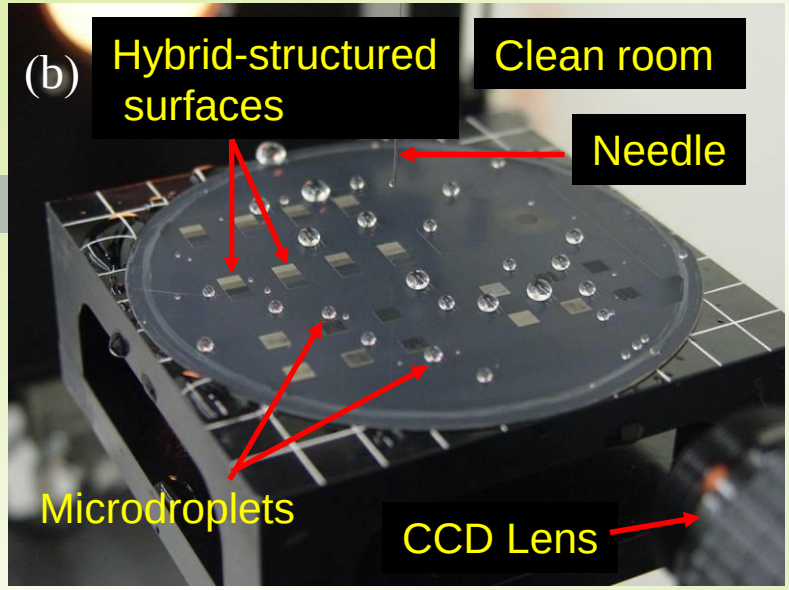


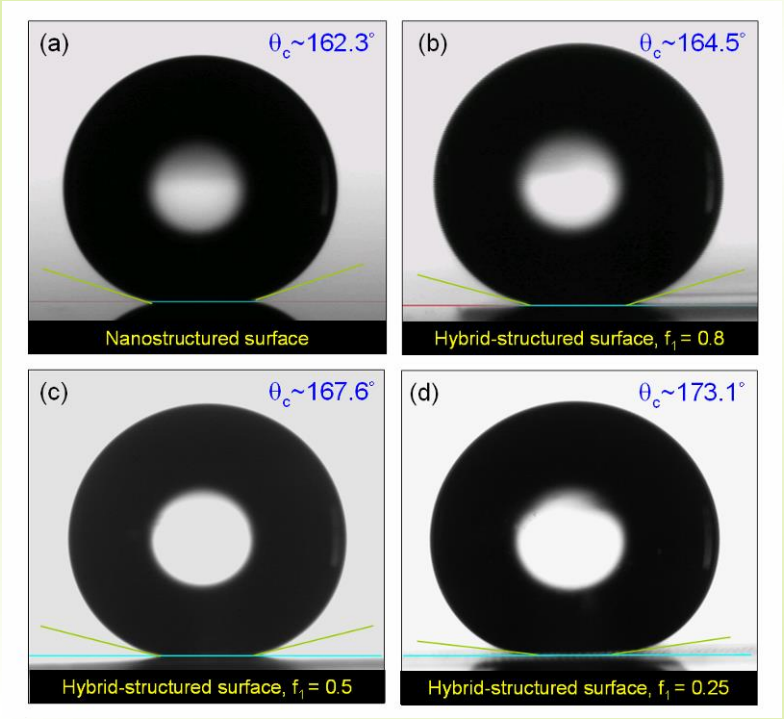


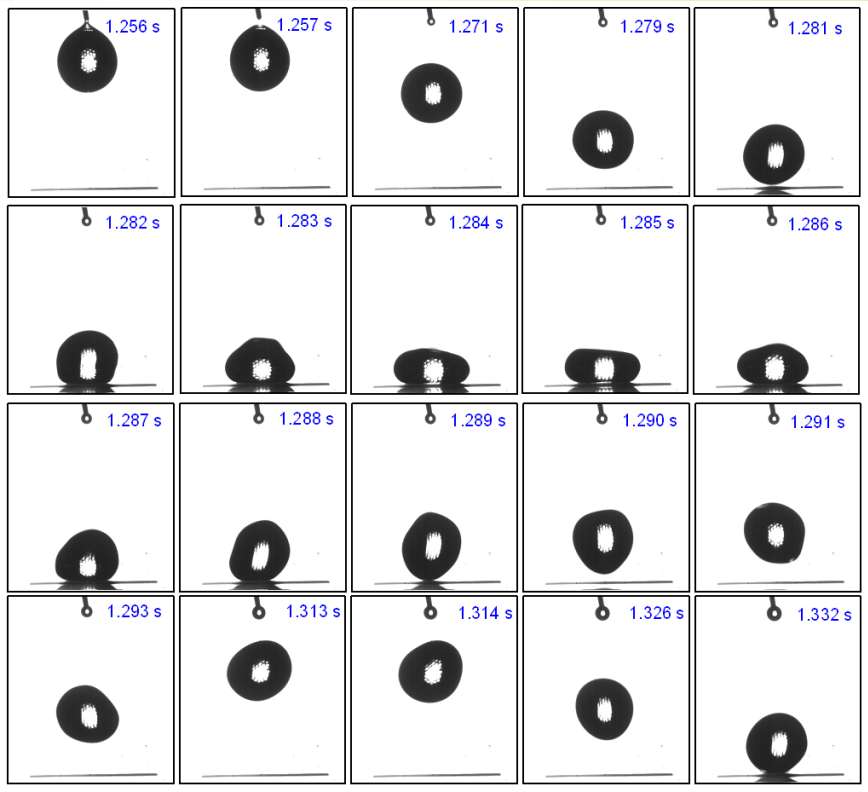
A droplet is falling on Si surface

J. T. Yang
Z. H. Yang,
C. Y. Yang
Dr. M. H. Hsu
Dr. Y. H. Lai
2009



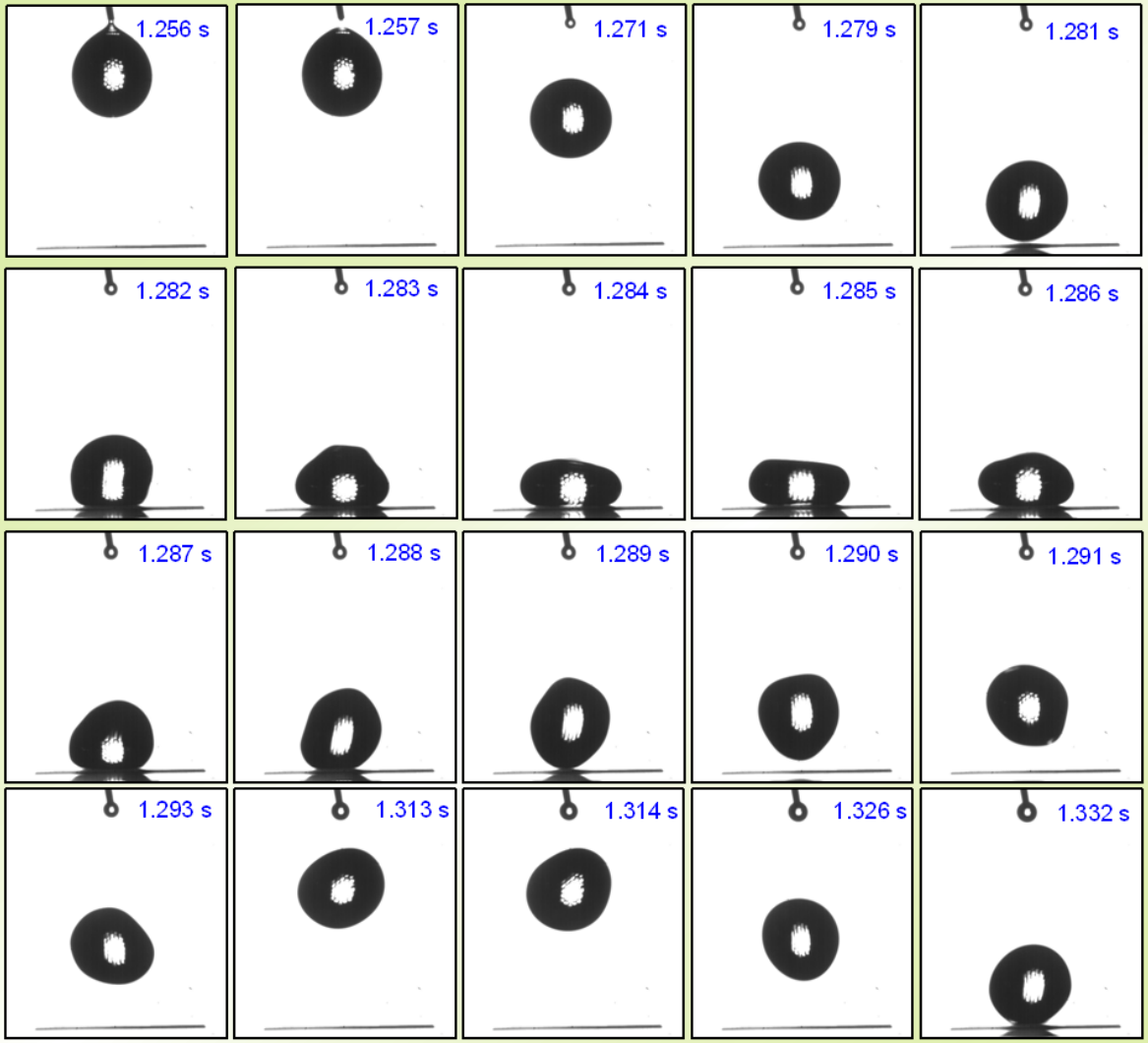






A droplet is falling on Si surface

Droplet bouncing off a hybrid surface



5 mL 的微液珠於f_1= 0.5s 奈微複合表面上彈跳 20次以上共歷時0.729 s 。

第一次彈跳高度即為最大彈跳高度3.29 mm。

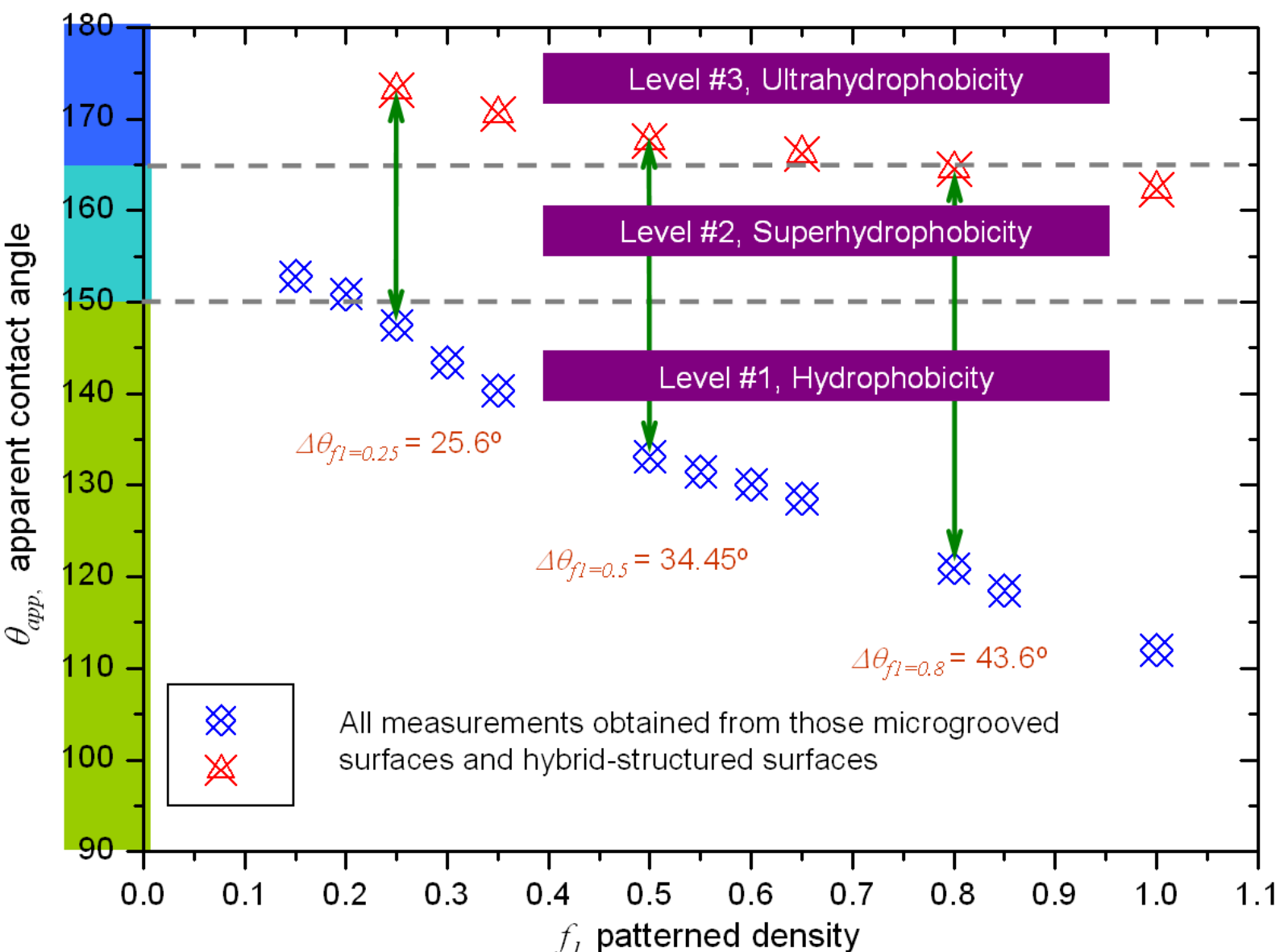
微液珠碰撞過程的能量轉換與液珠表面輪廓改變。

A drop falls on Polsihed_Si_surface

Surface Hydrophobicity of Three Levels

楊宗翰, 楊鏡堂

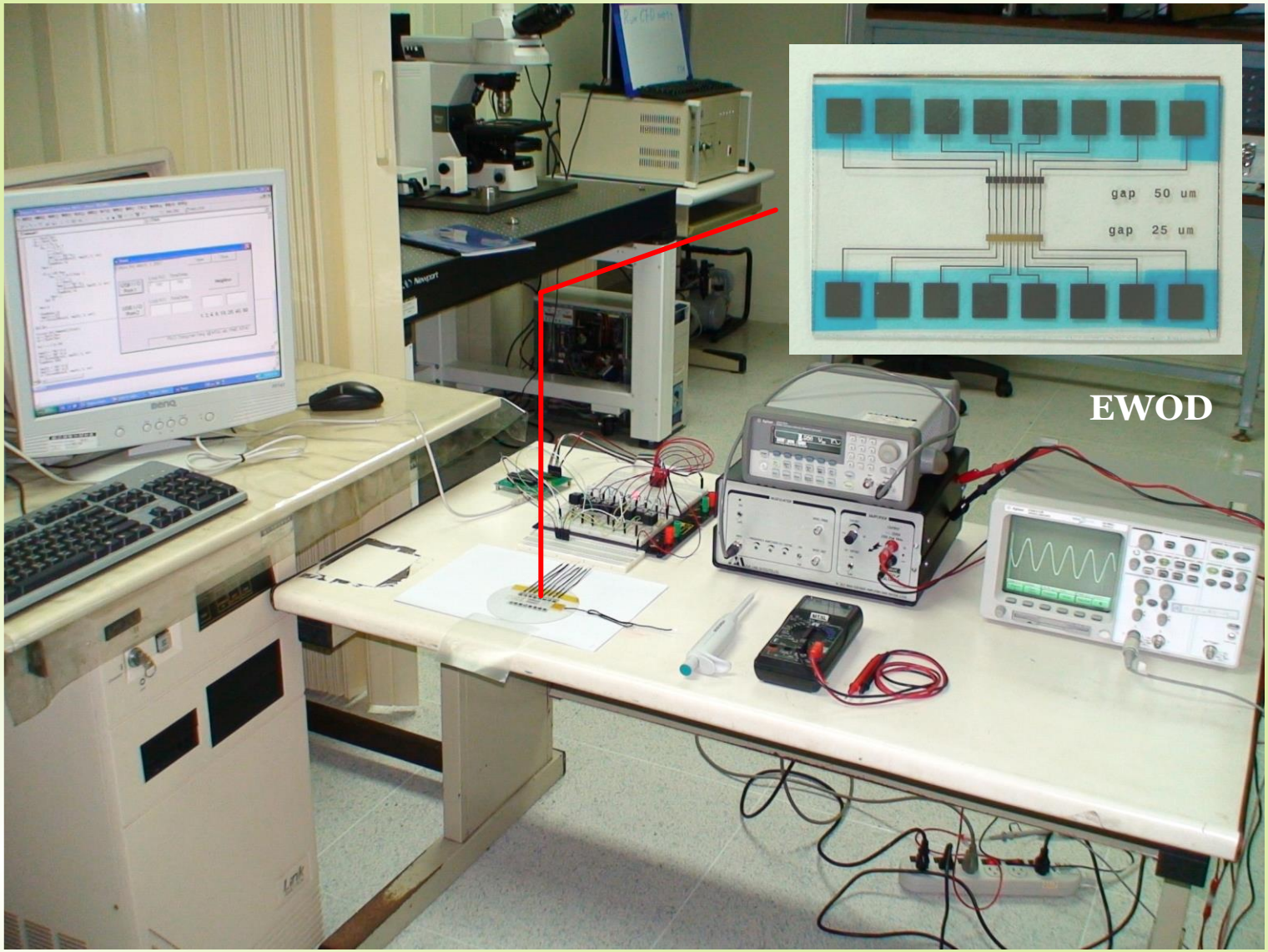
Yang et al., Highlights of JMM, 2009 (33)



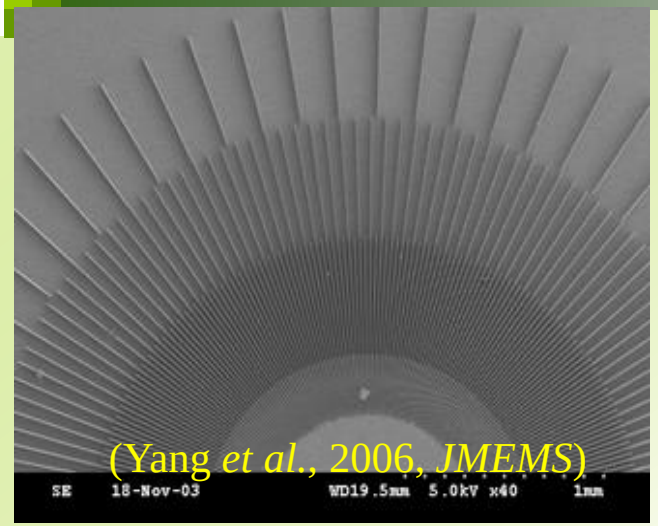
SEM, AFM, and Platform for EWOD Biochips– 2004-2008

楊鏡堂教授, 台大機械系

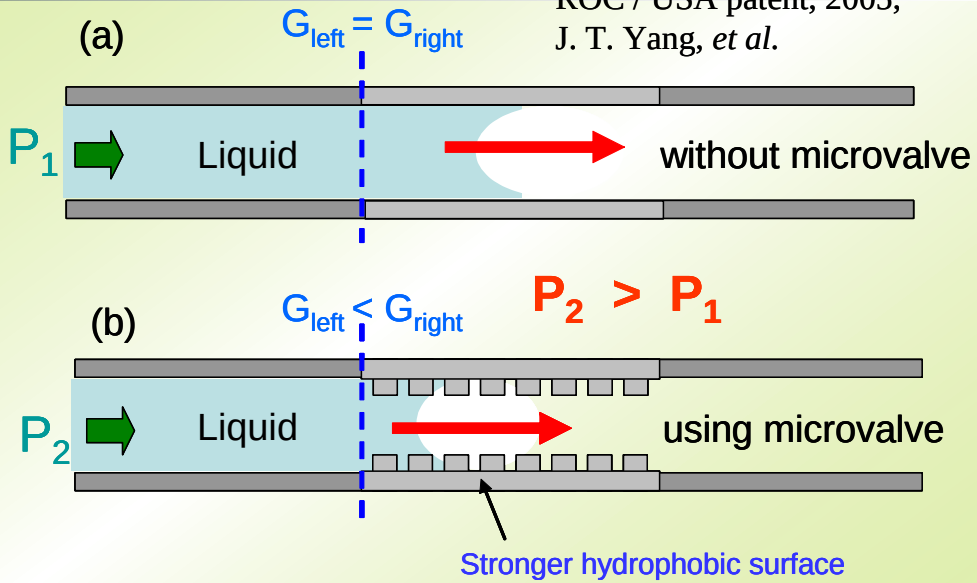
US Patent 7,189,359, 2007; cited 93

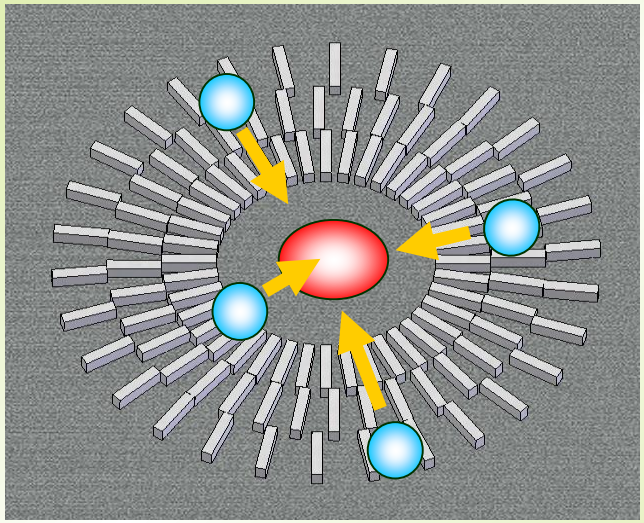


Engineering Application & Patents

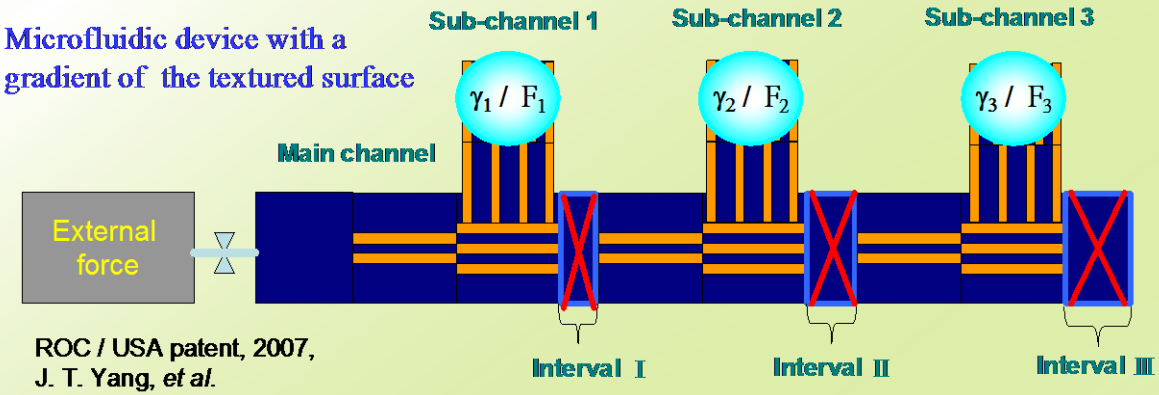


ROC / USA patent, 2005,
J. T. Yang, *et al.*





Microfluidic device with a gradient of the textured surface



ROC / USA patent, 2007,
J. T. Yang, *et al.*

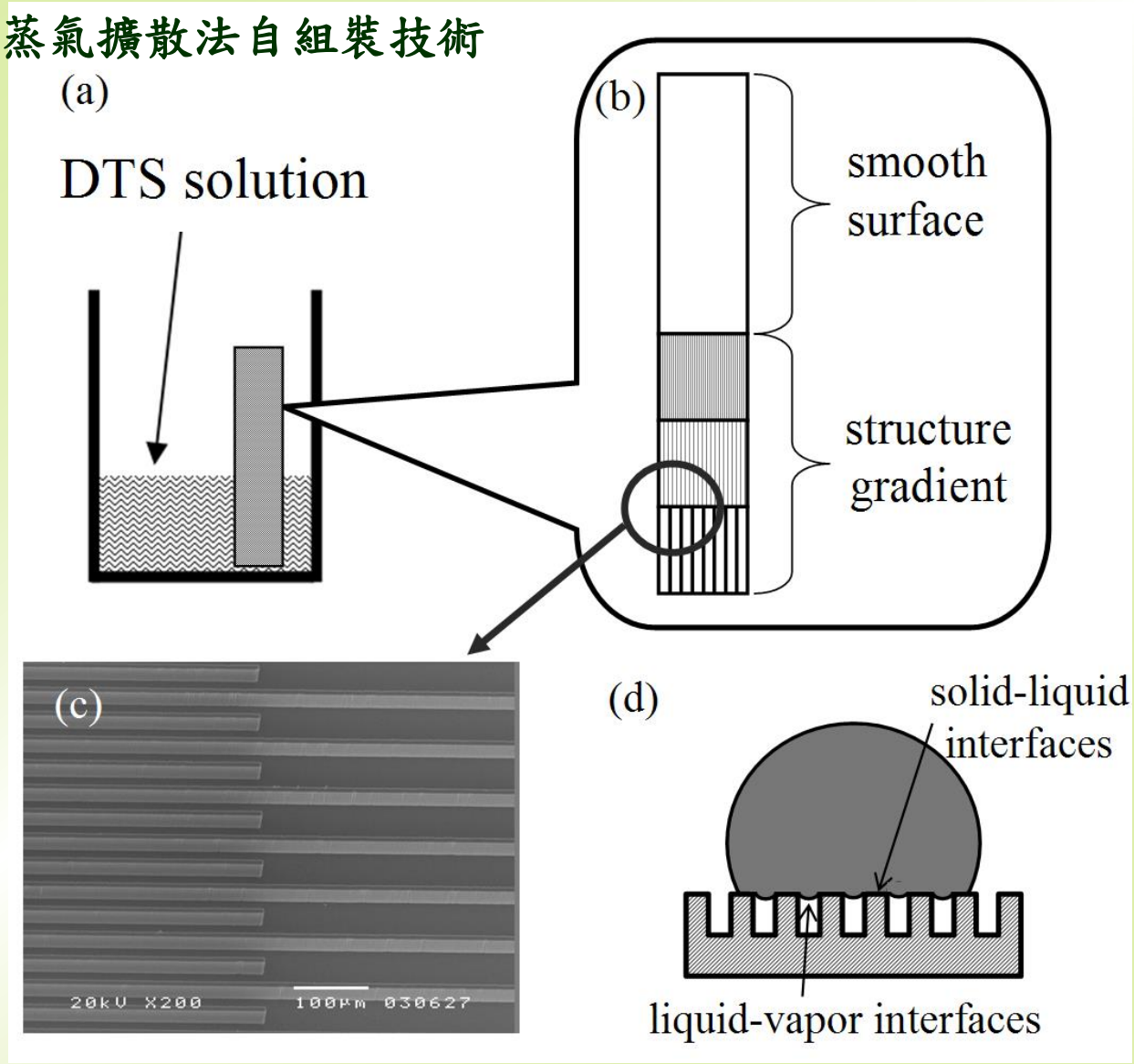
第一屆上銀碩士論文獎銅質獎, 2007
第四屆國家新創獎, 2008

(*J. MEMS*, 2006, cited 83; *Langmuir*, 2008, cites 71)

分子自組裝技術應用於表面改質

Lai *et al.*, *Lab Chip*, 2009;Yang *et al.*, ROC Patent, 2009.

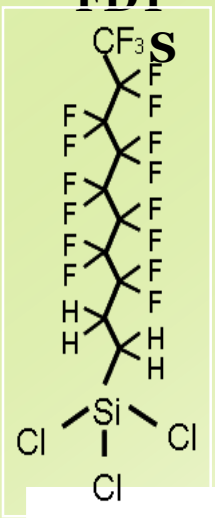
浸泡/蒸氣擴散法自組裝技術



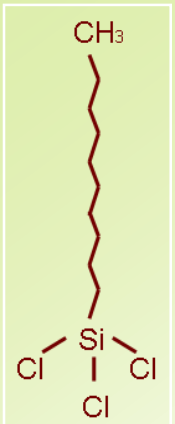
A Microchip using SAM & Gradient Surface

Lai, Yang, Shieh, *Lab Chip*, 2010a (77)

FDT

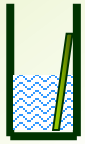


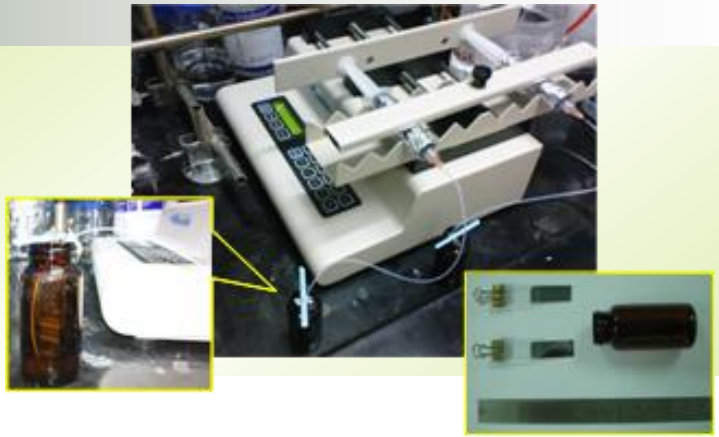
DTS

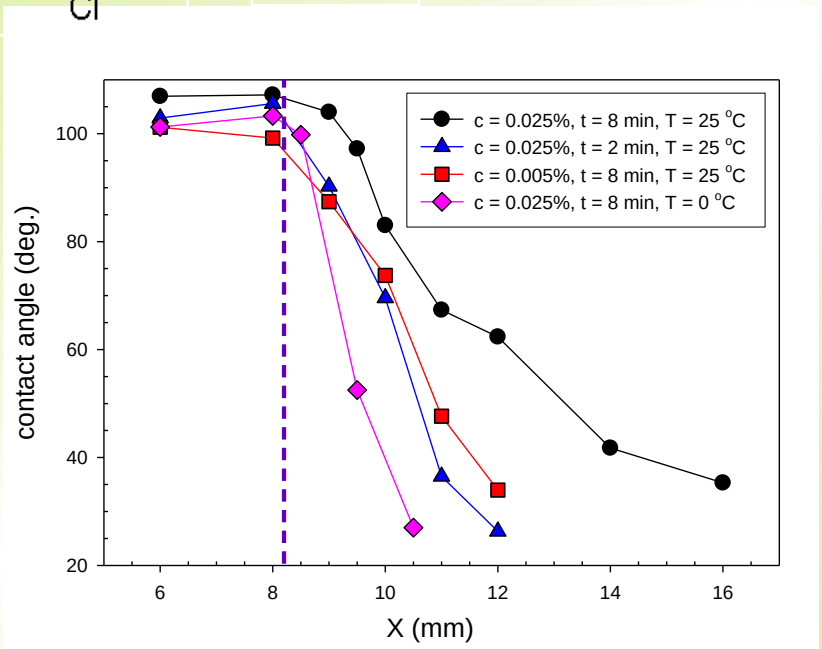


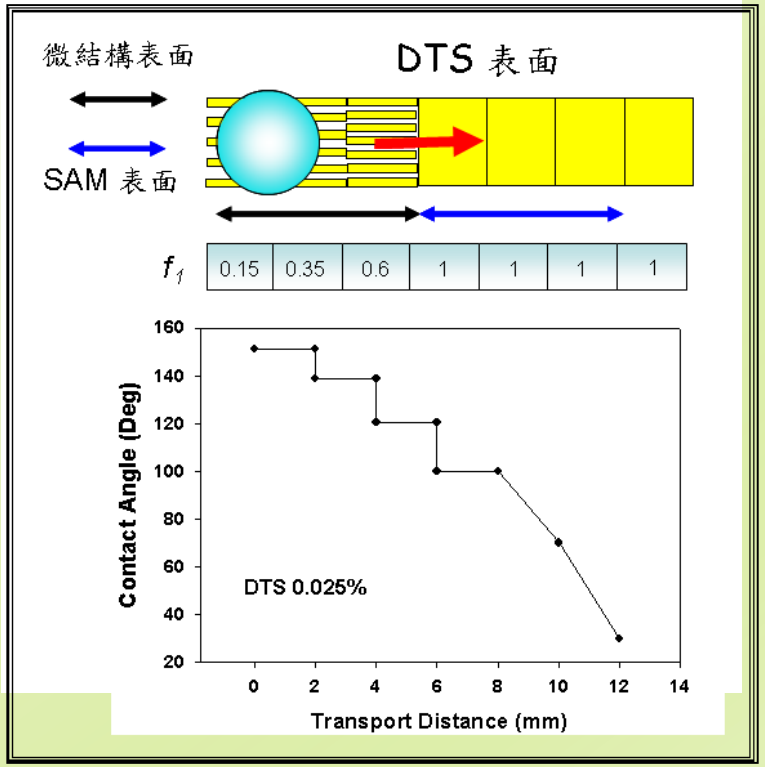
滴定法

蒸汽法





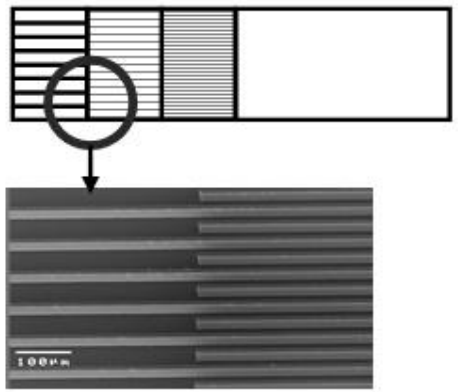




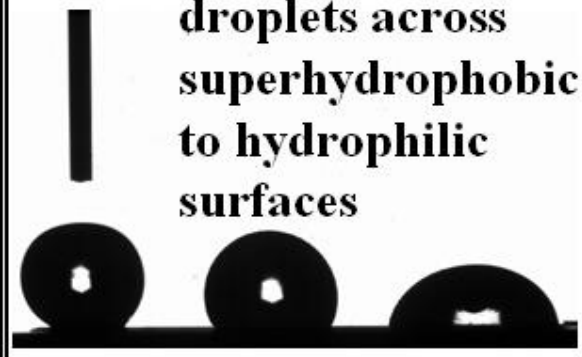
A biochemical droplet transporting across superhydrophobic to hydrophilic surfaces.

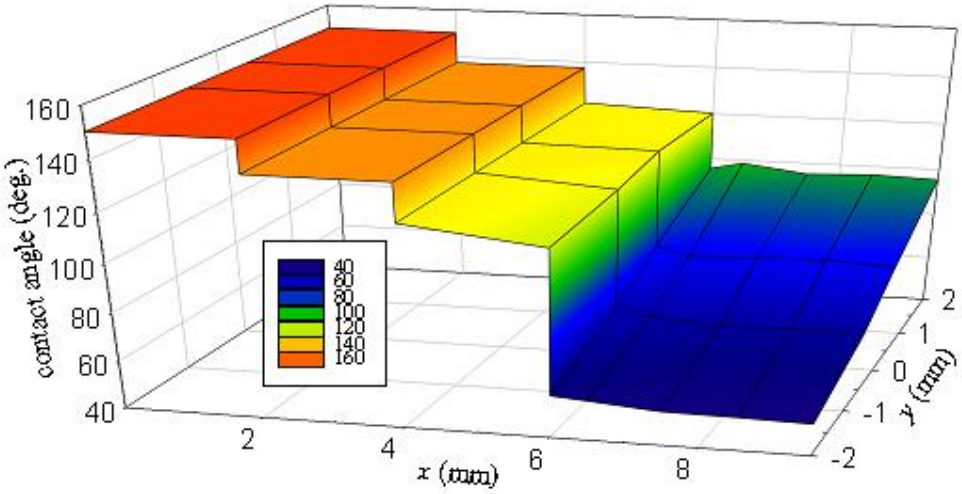
Lai, Yang,* Shieh, *Lab Chip* 2010a *(77)*

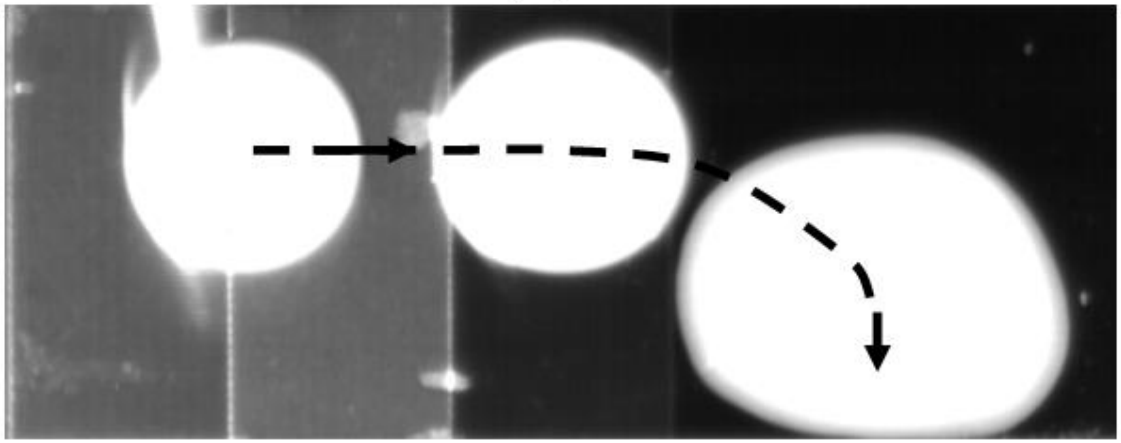
a microstructure and SAM composition gradient surface



transport of droplets across superhydrophobic to hydrophilic surfaces

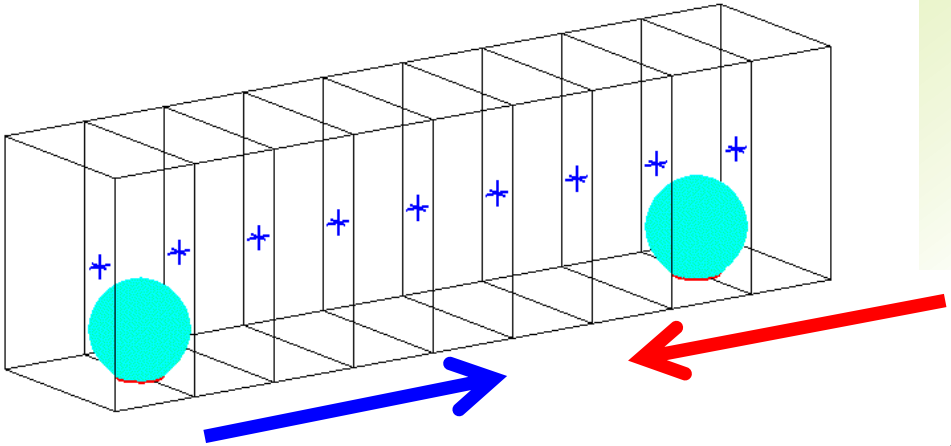


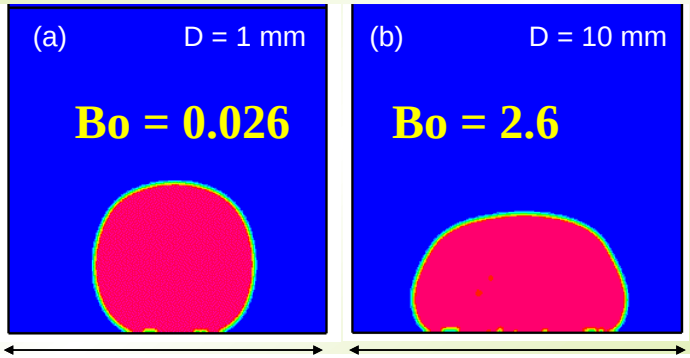


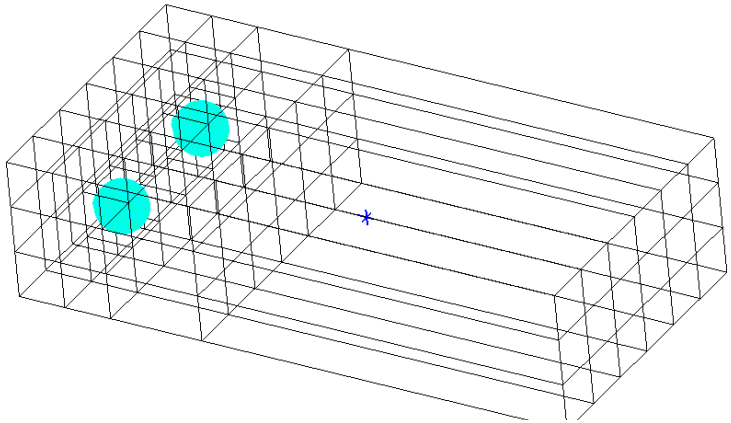


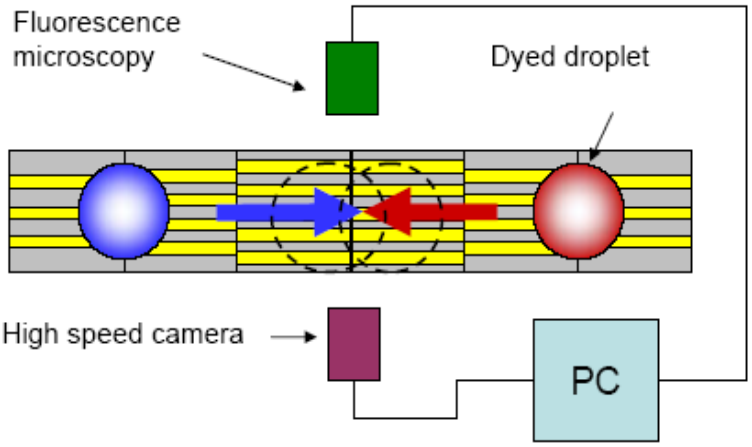
a double-direction gradient

Challenges for Numerical Simulation

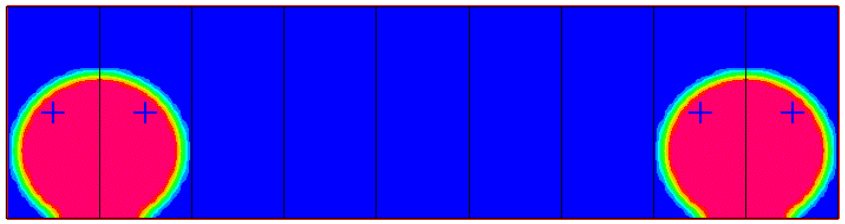








Collision and Mixing of two Droplets



Michael Jackson ?

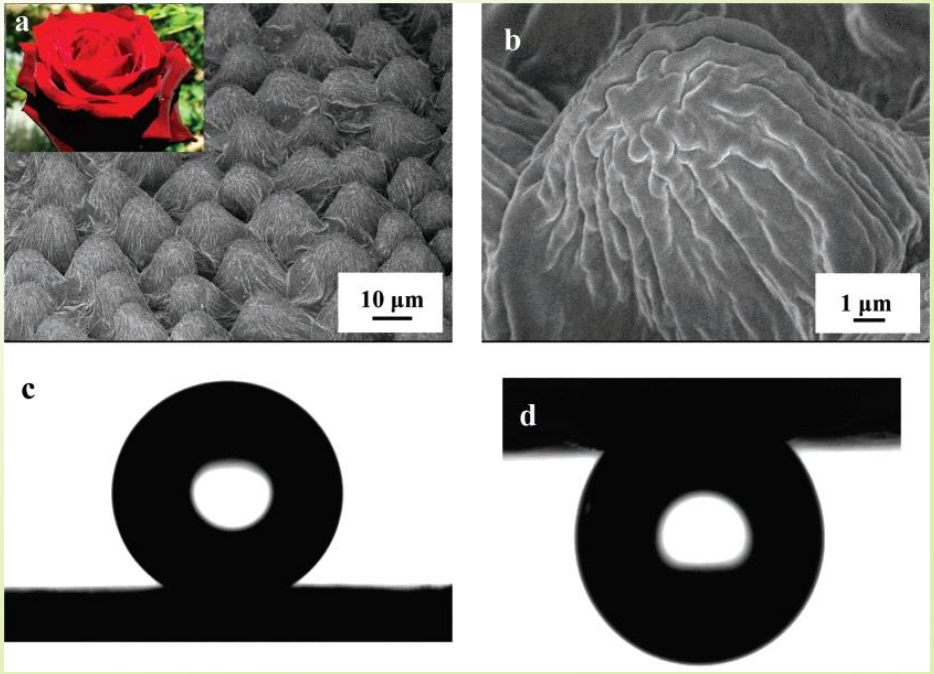
劉謙 ?

玫瑰的“花瓣效應”

-- *Rose's 'Petal Effect'*

ScienceDaily (Apr. 25, 2008)

This fascinating "petal effect" could lead to unique new adhesive materials, coatings and fabrics.



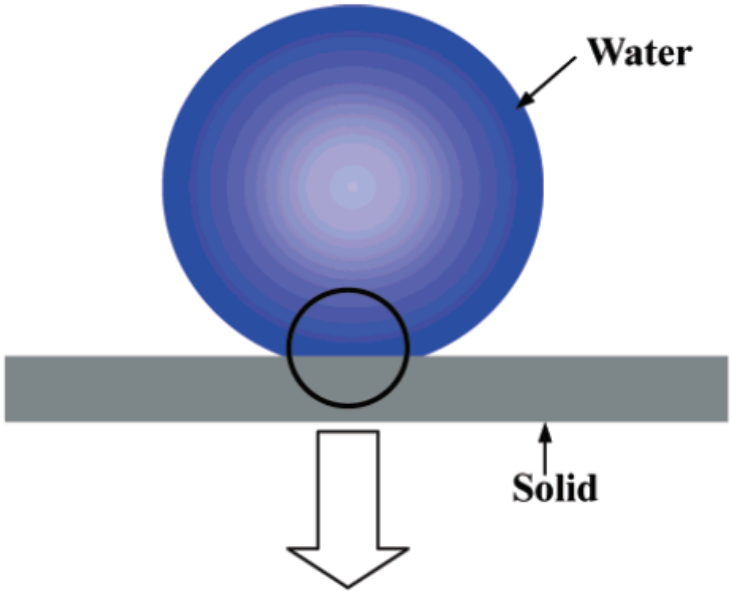
Feng et al., Langmuir, 2008.

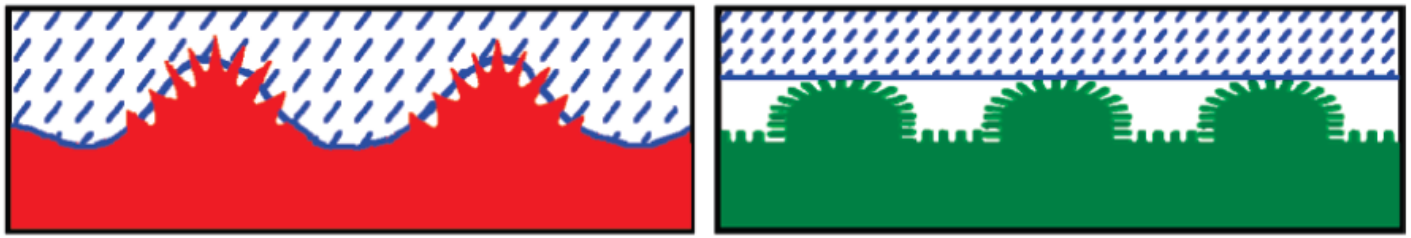
Petal Effect:

A Superhydrophobic State with High Adhesive Force

The rose's ability to grip water droplets in place, even when the flower is upside down.

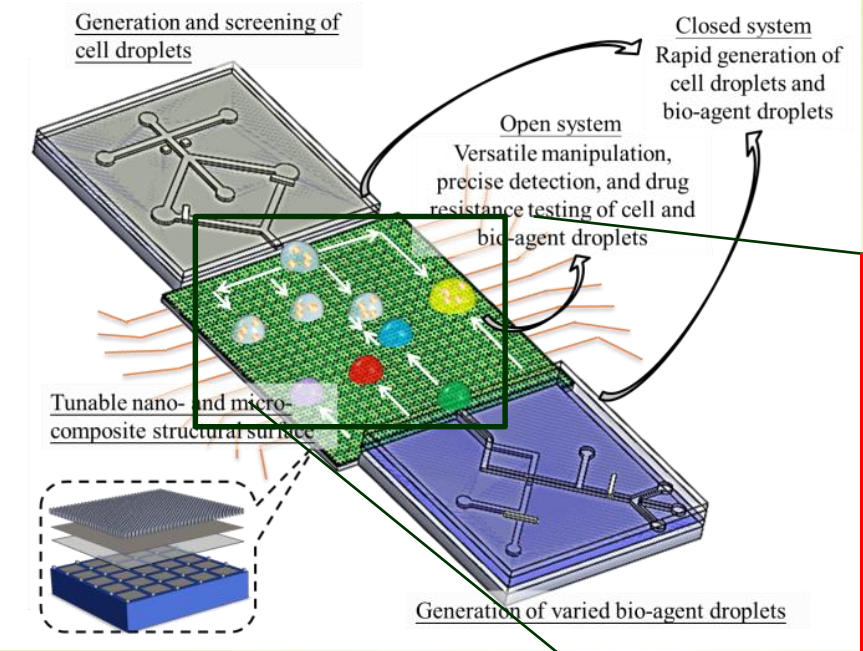
Petal Effect and Lotus Effect





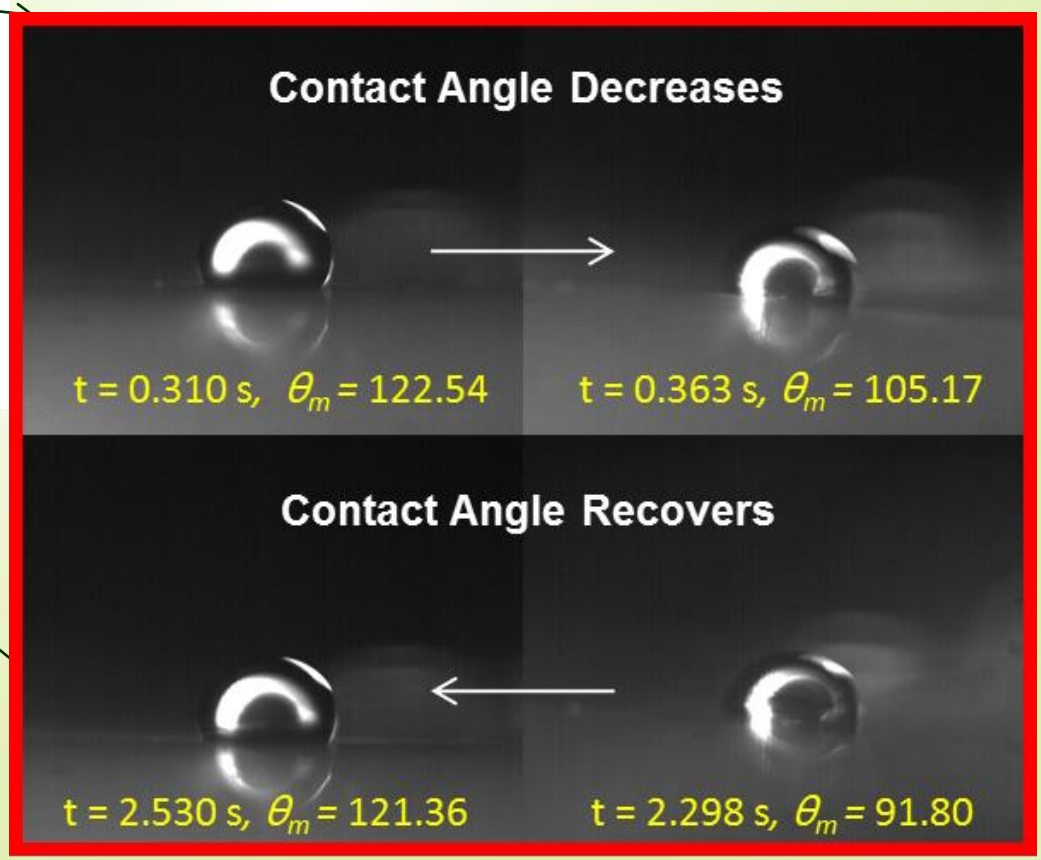
Petal (Cassie impregnating wetting state)

Lotus (Cassie's state)



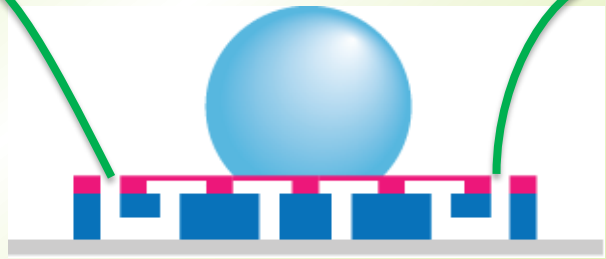
Rose + Lotus

操控液珠平台

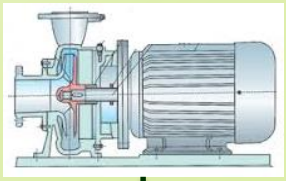


氣動操控系統架設

CCD



氣動幫浦

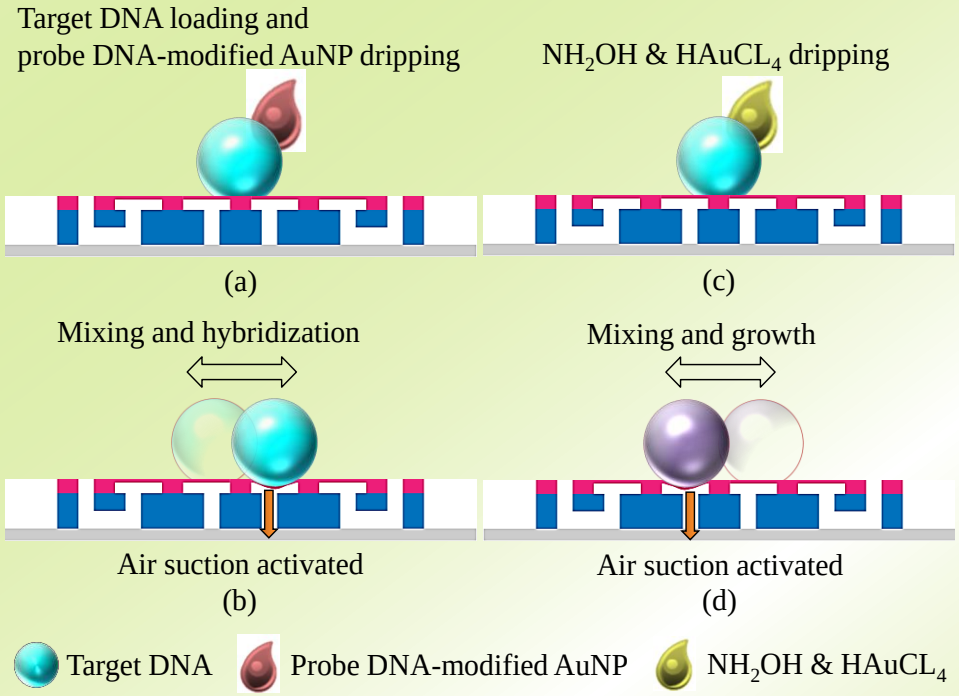


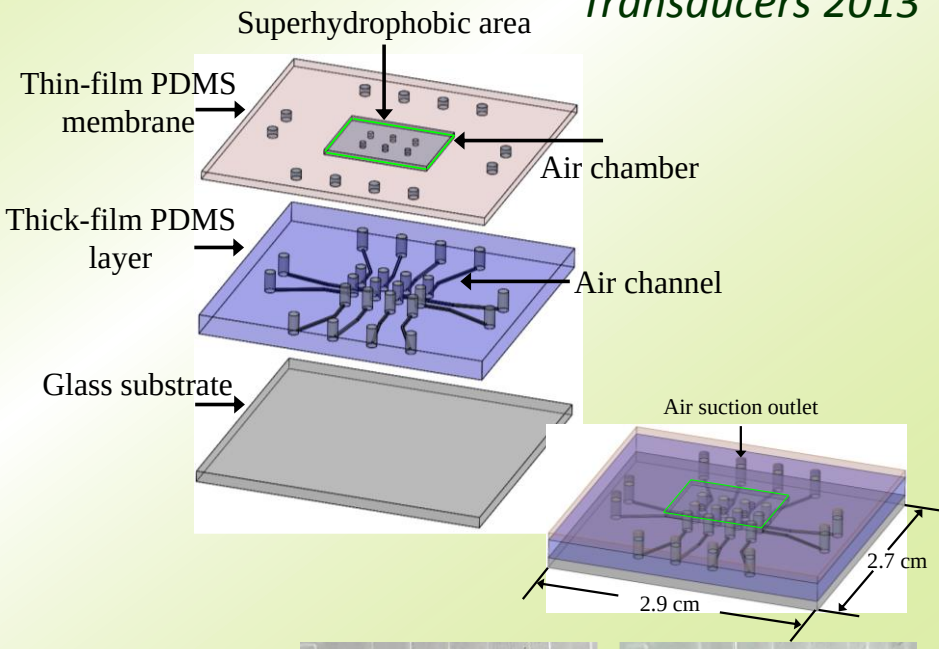
電磁閥

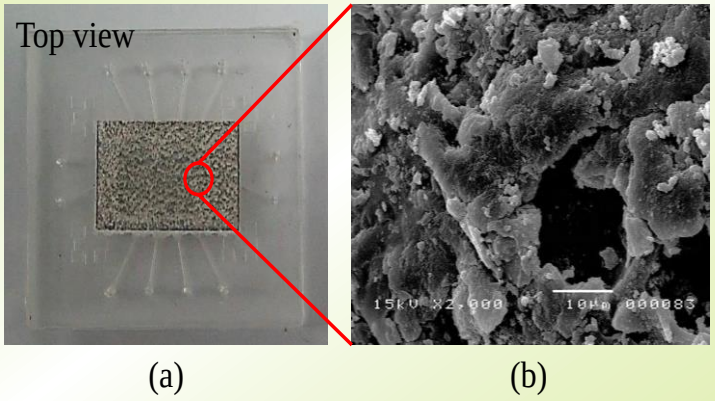
A biocompatible open-surface droplet manipulation platform for multi-nucleotide polymorphisms detection

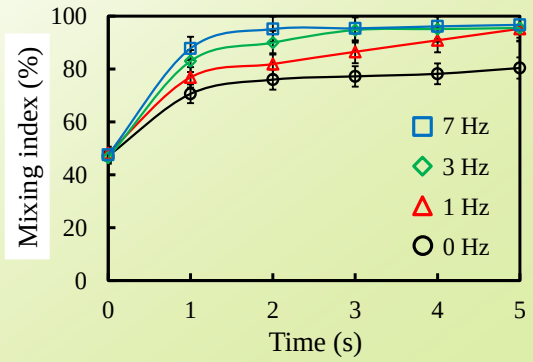
Lab on a Chip, 2014a

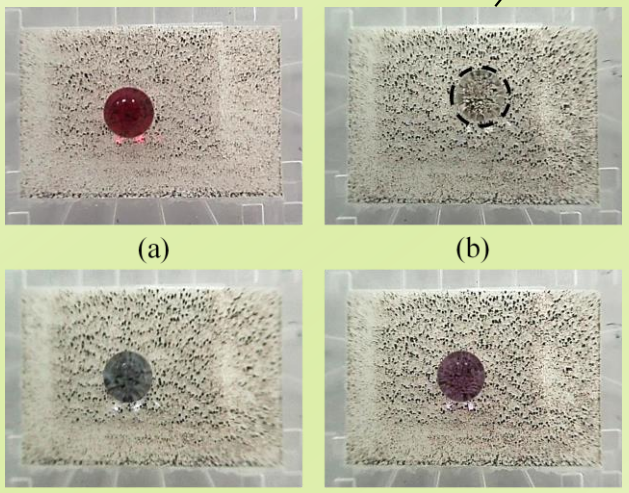
Transducers 2013





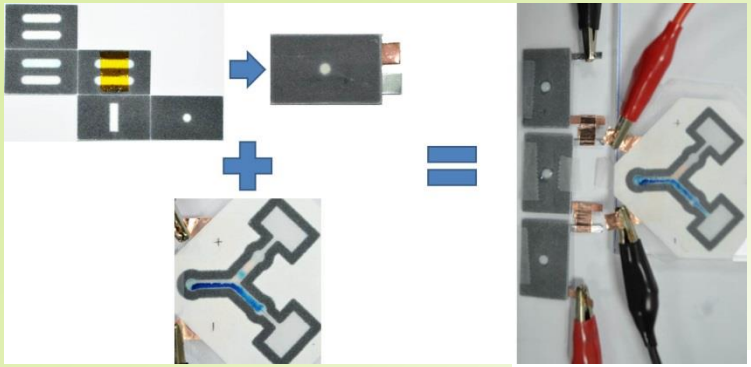


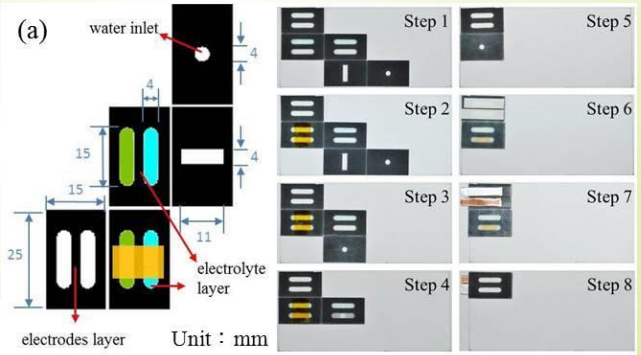


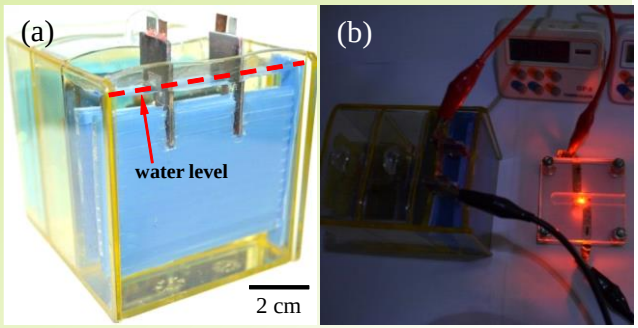


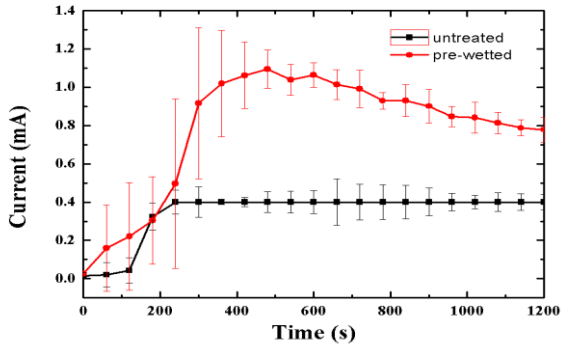
Origami Paper-Based Fluidic Batteries for Portable Electrophoretic Devices

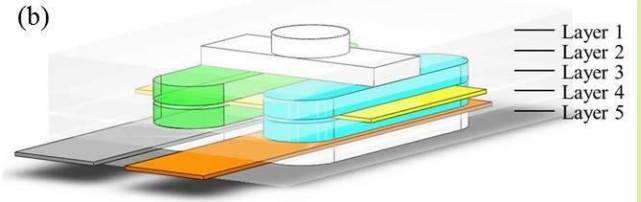
Lab on a Chip, 2014b

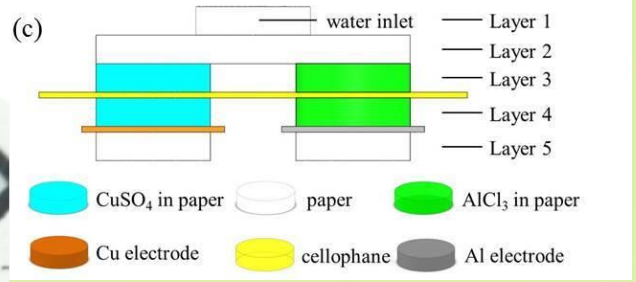


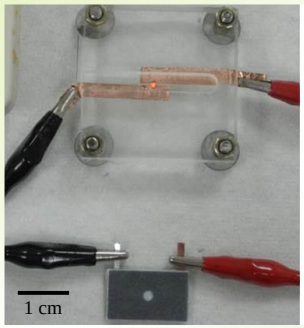


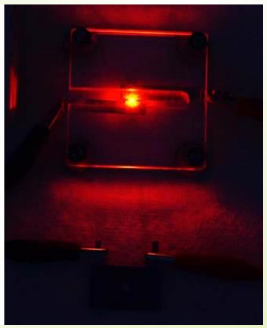


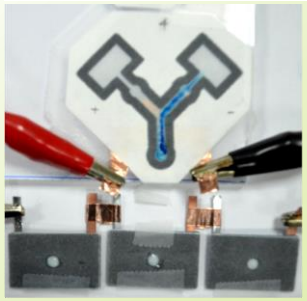


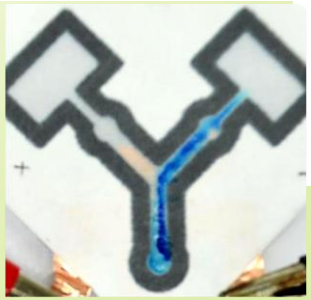








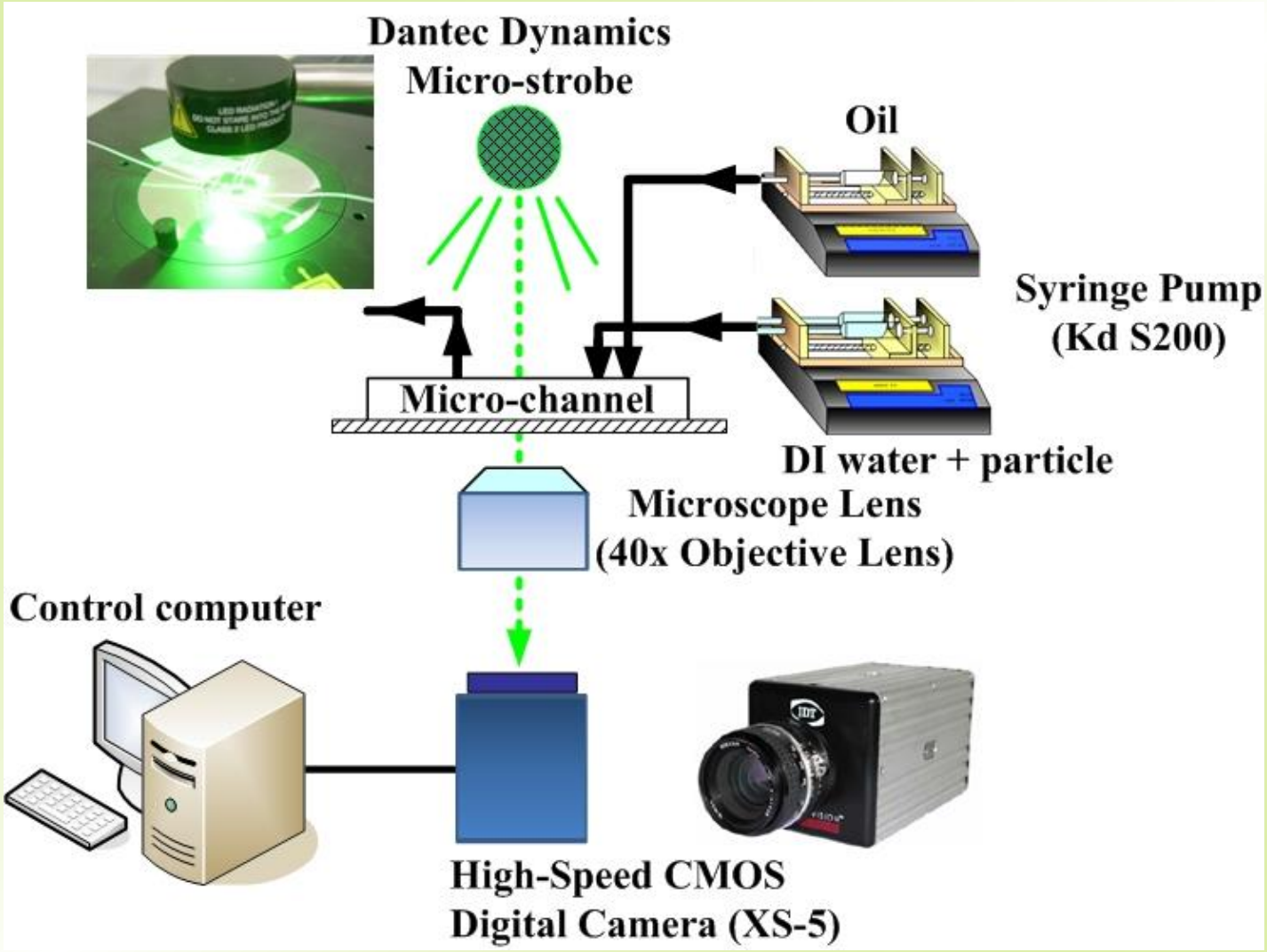


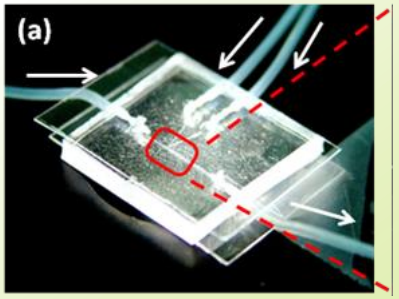


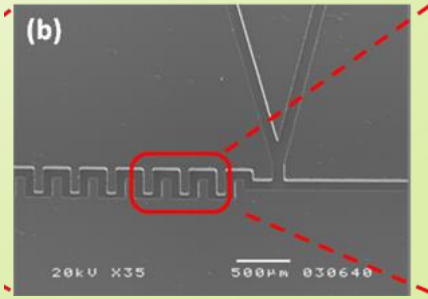
μ-TAS 2013

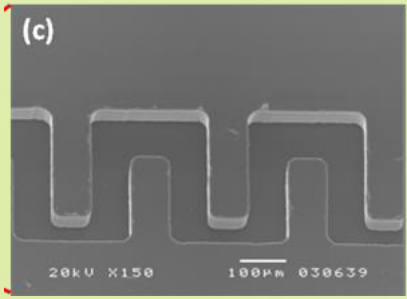
Application

Droplets Transport and Mixing



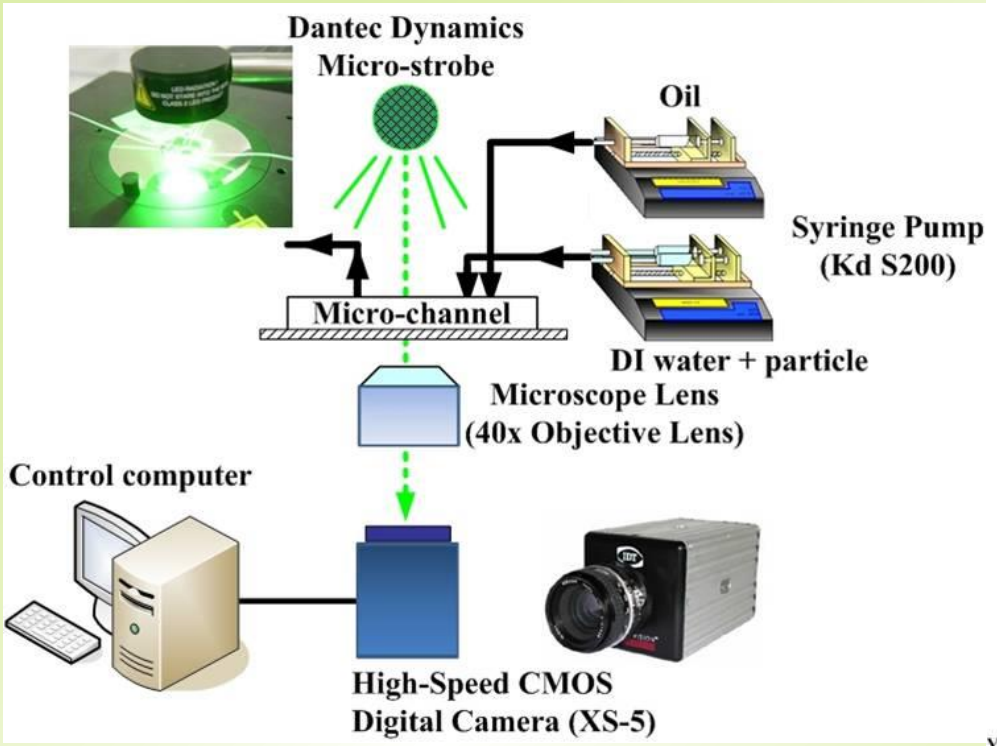


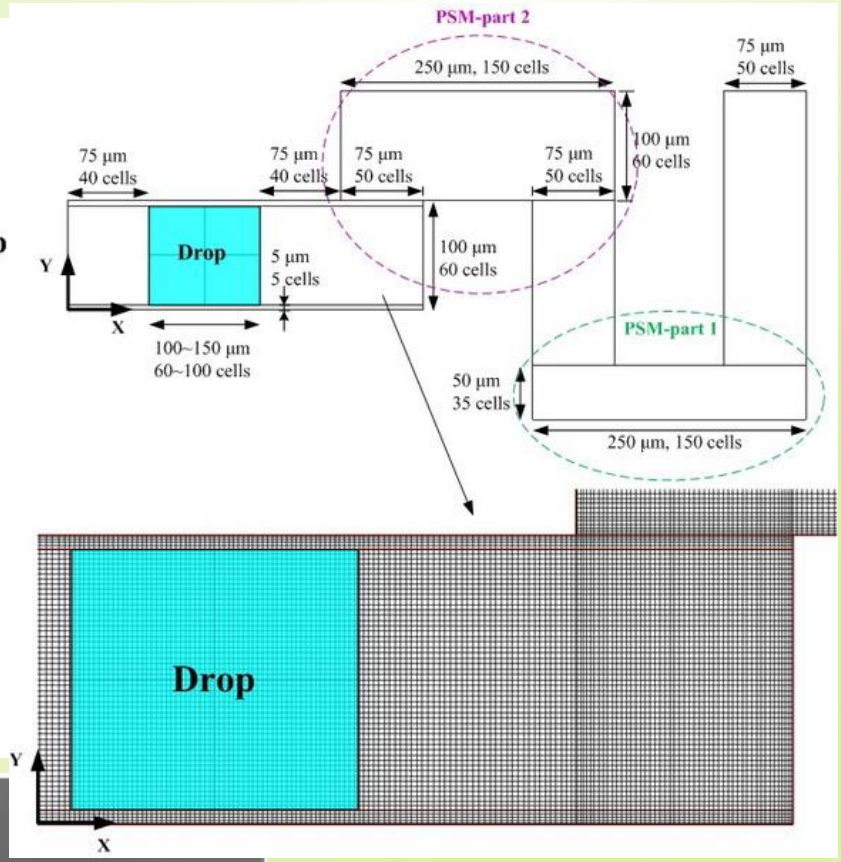


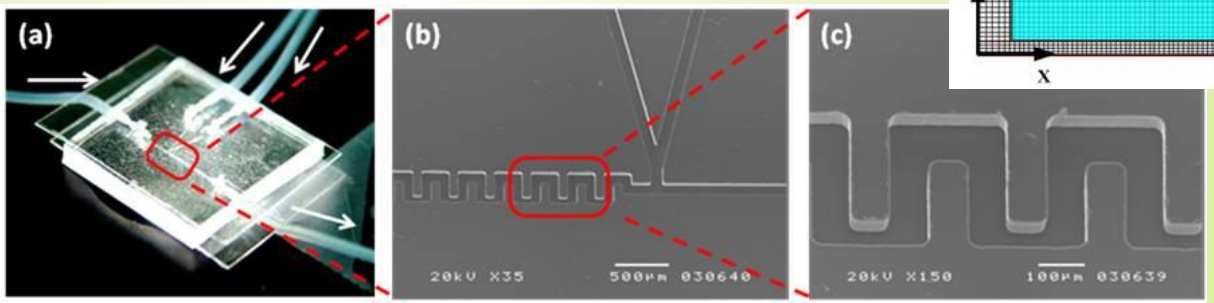


Mixing and hydrodynamic analysis of a droplet in a planar serpentine micromixer

Kai-Yang Tung, Chih-Chieh Li, and Jing-Tang Yang



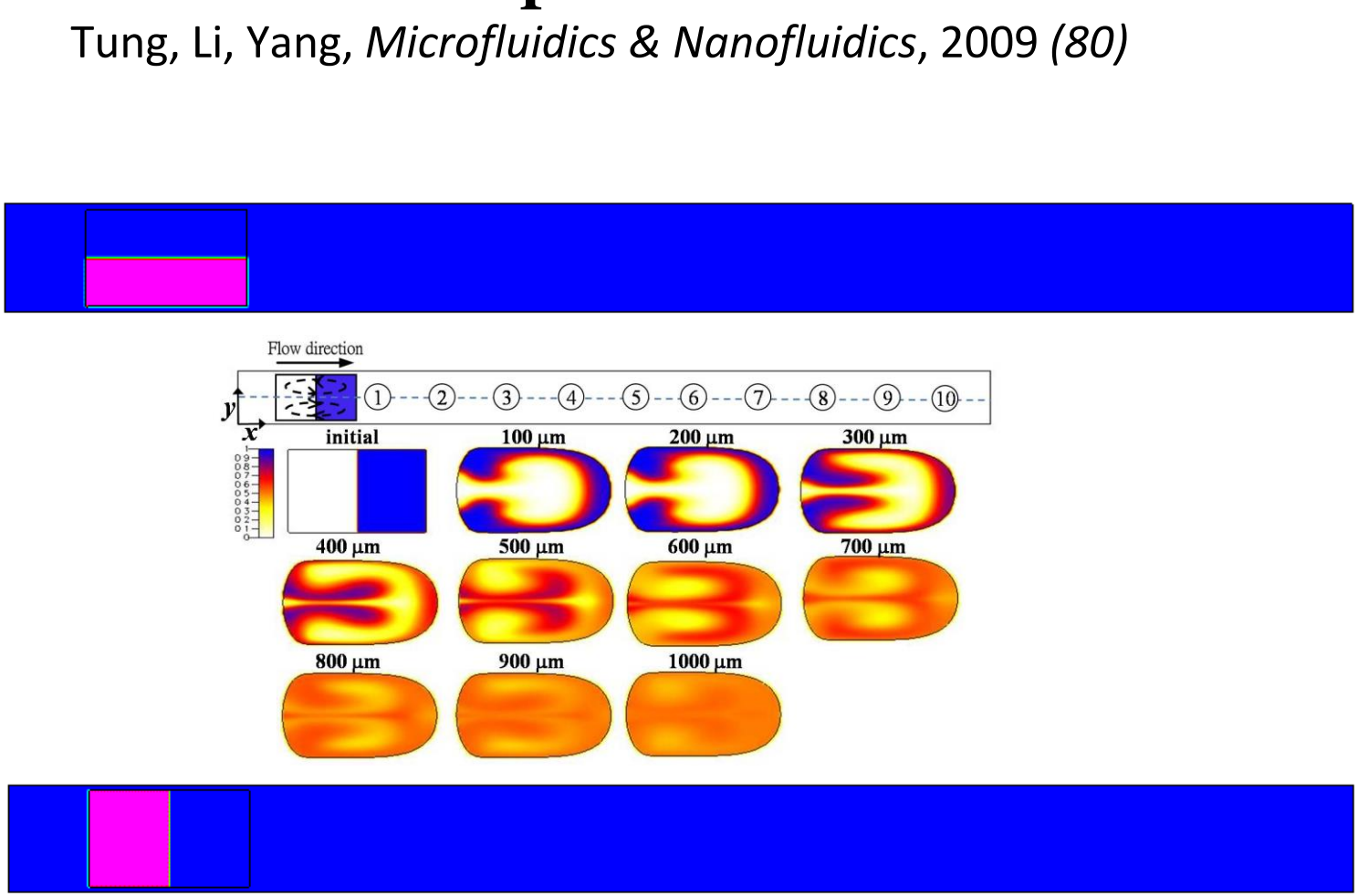




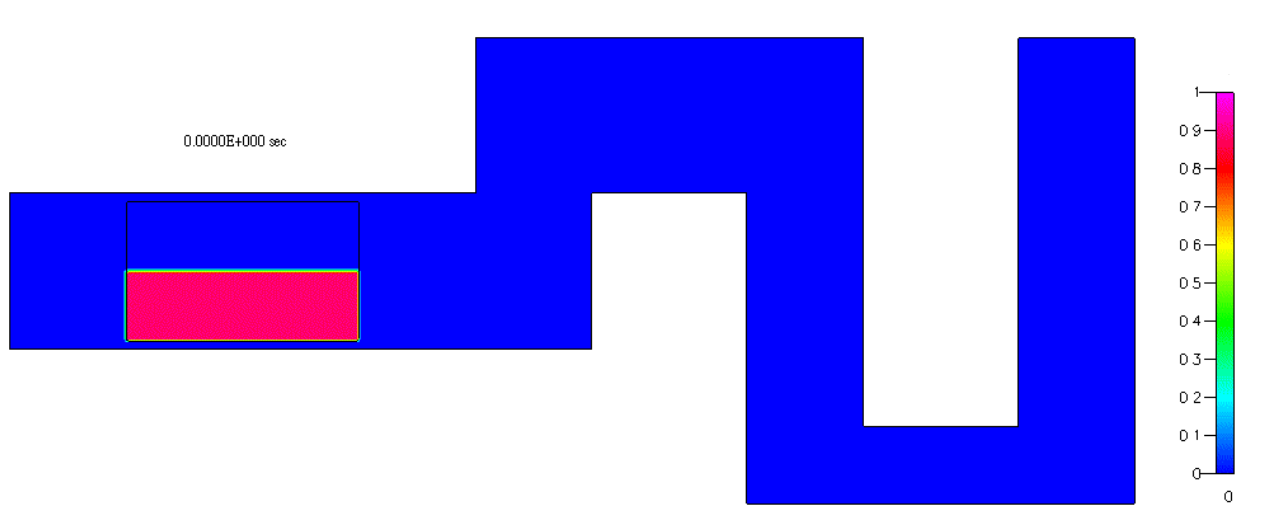
Microfluidics & Nanofluidics, 2009

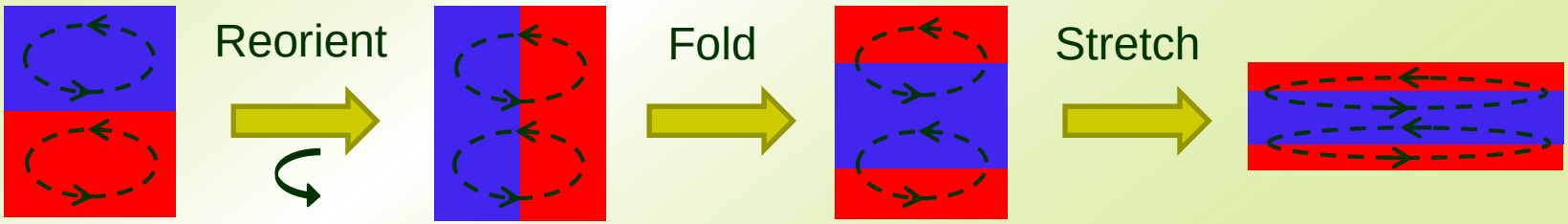
Mixing and Hydrodynamic Analysis of a Droplet in a Planar Serpentine Micromixer

Tung, Li, Yang, *Microfluidics & Nanofluidics*, 2009 *(80)*



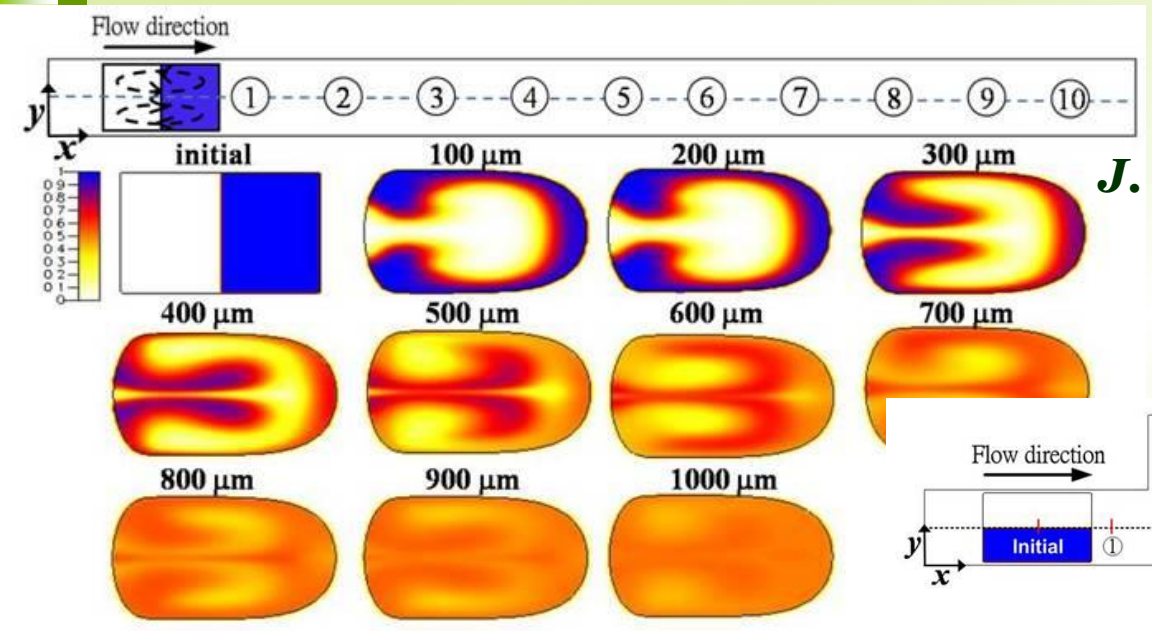
Mixing Mechanism





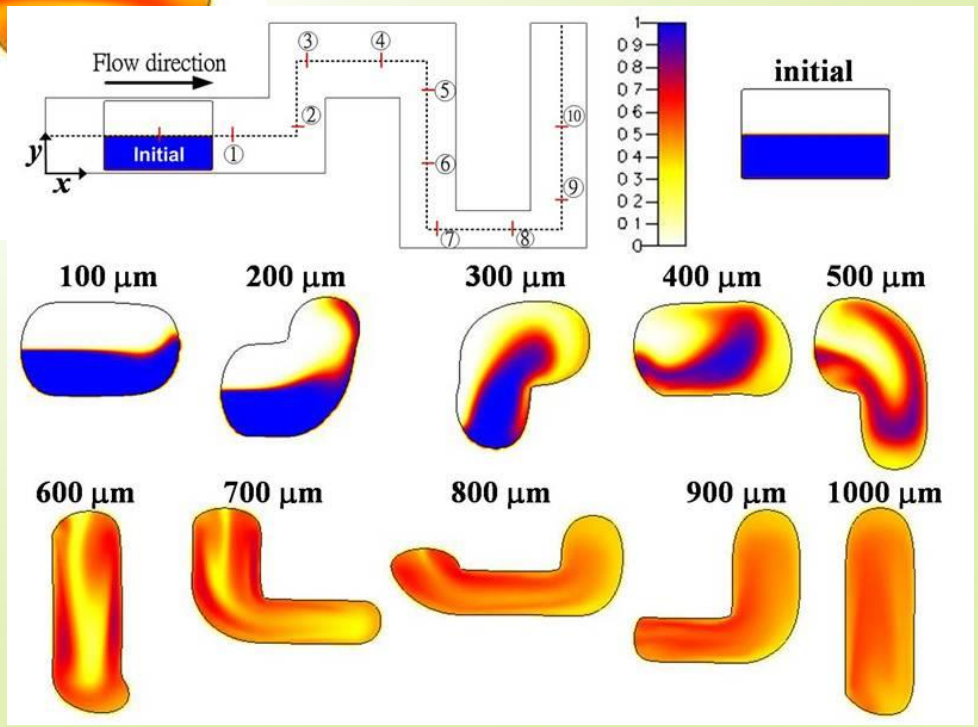
Mixing is promoted by periodic motion of the fluid. It is conducted by iterated reorientation, stretching and folding of the interface here.

Droplets Transport and Mixing (1/2)



Tung, Li, & Yang, 2009

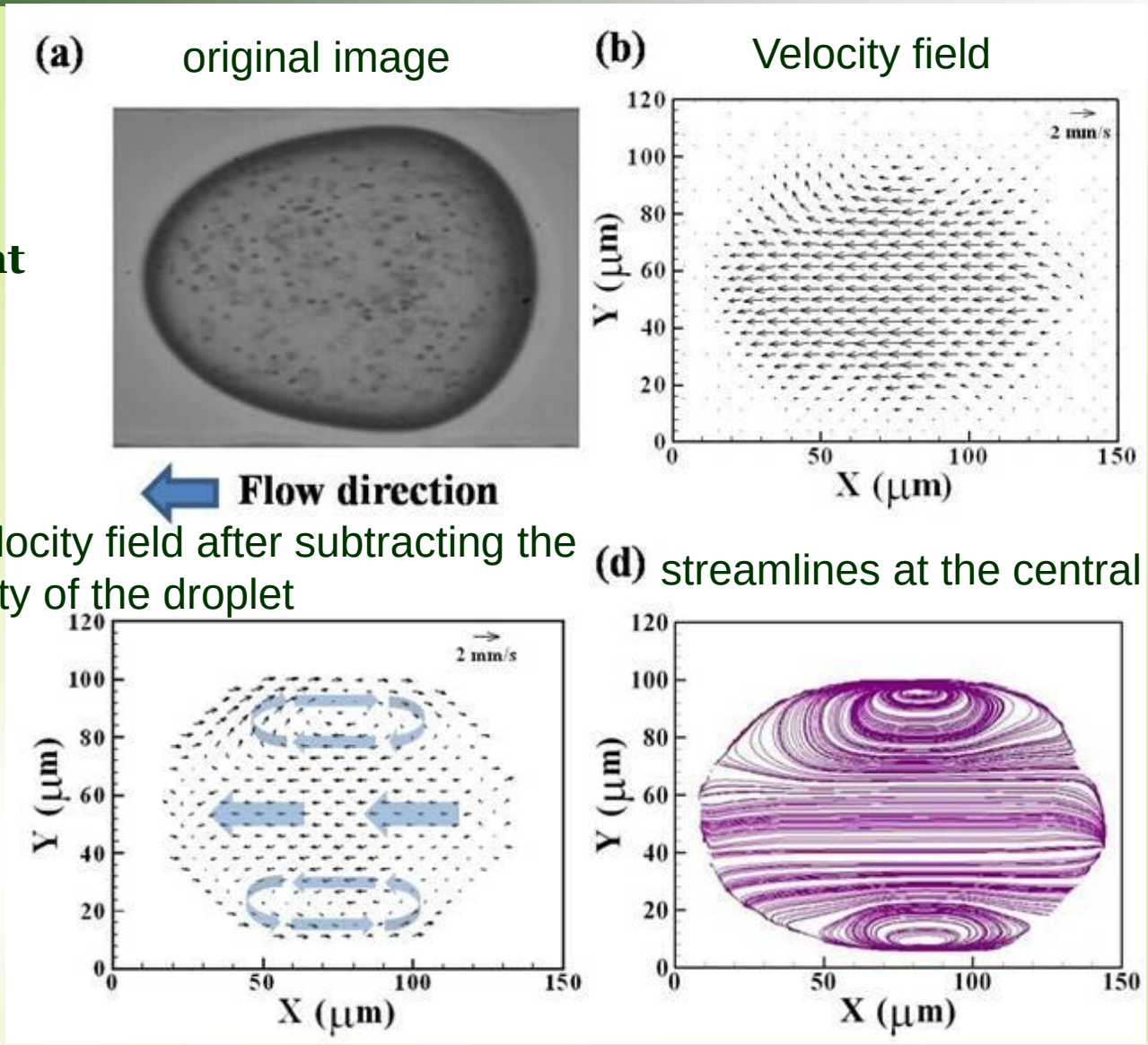
J. Microfluidics & Nanaofluidics



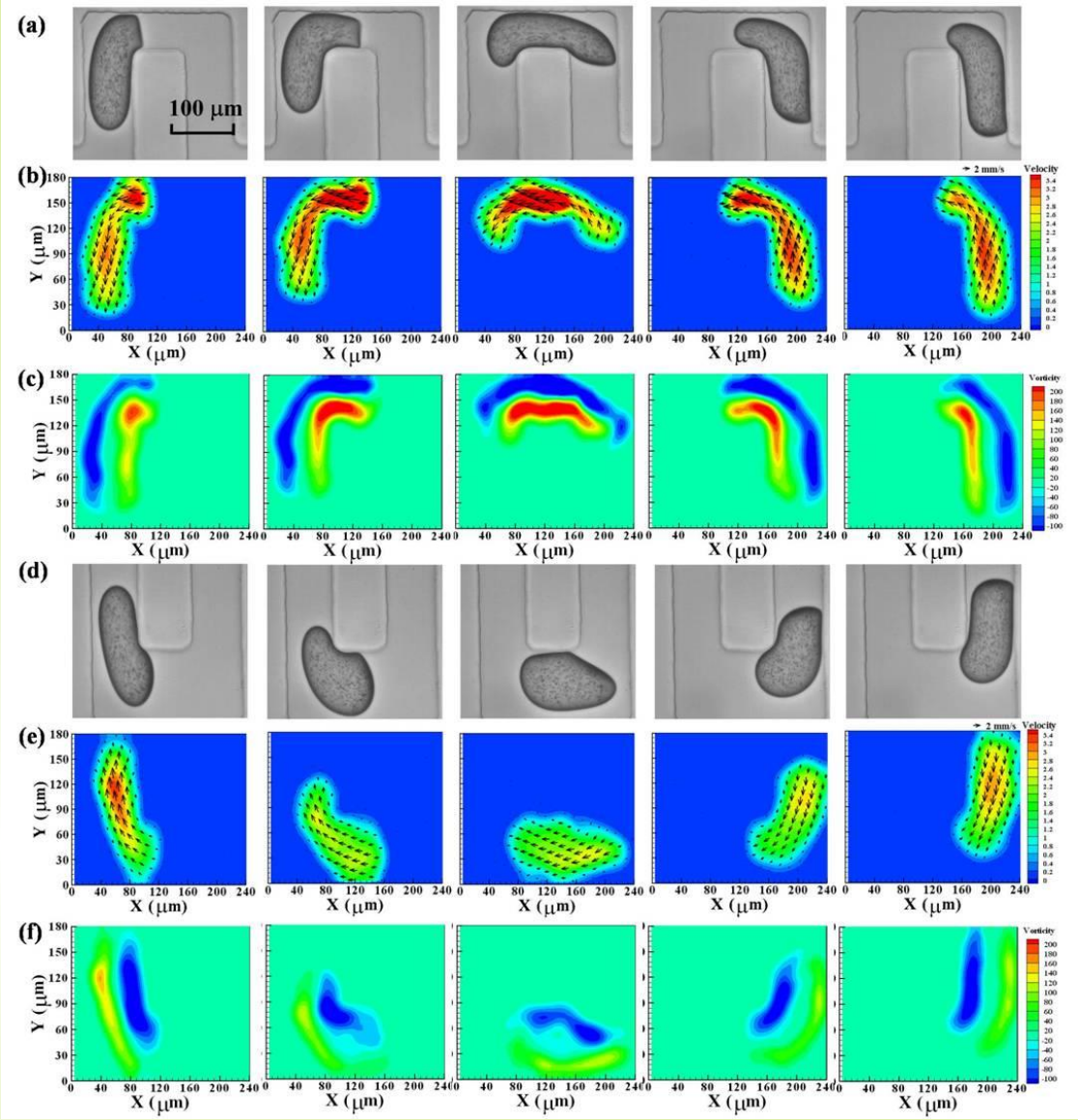
Results of numerical simulation

Droplets Transport and Mixing (2/2)

μ-PIV measurement

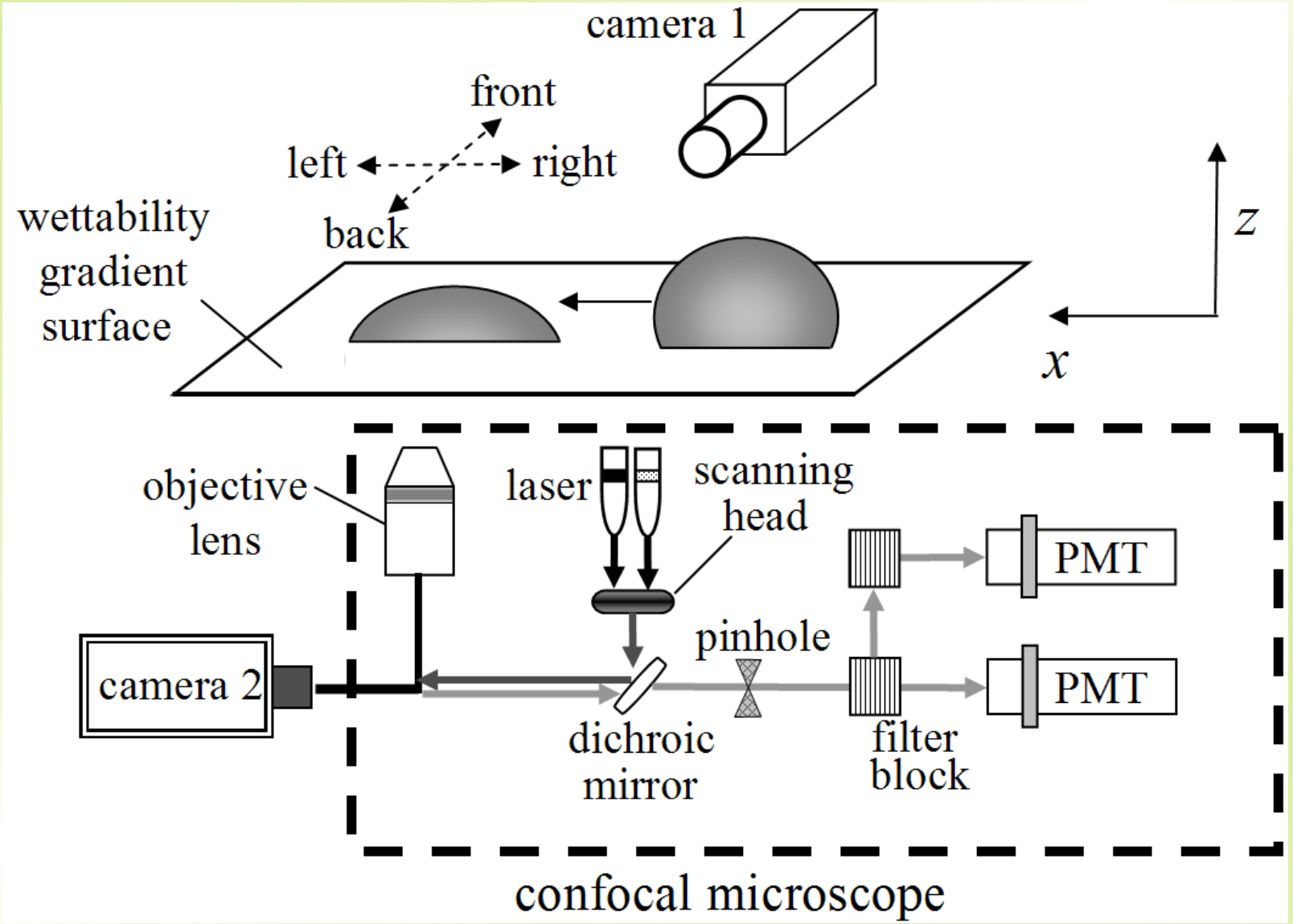


Micro-PIV measurement inside a droplet. Original droplet images along a PSM

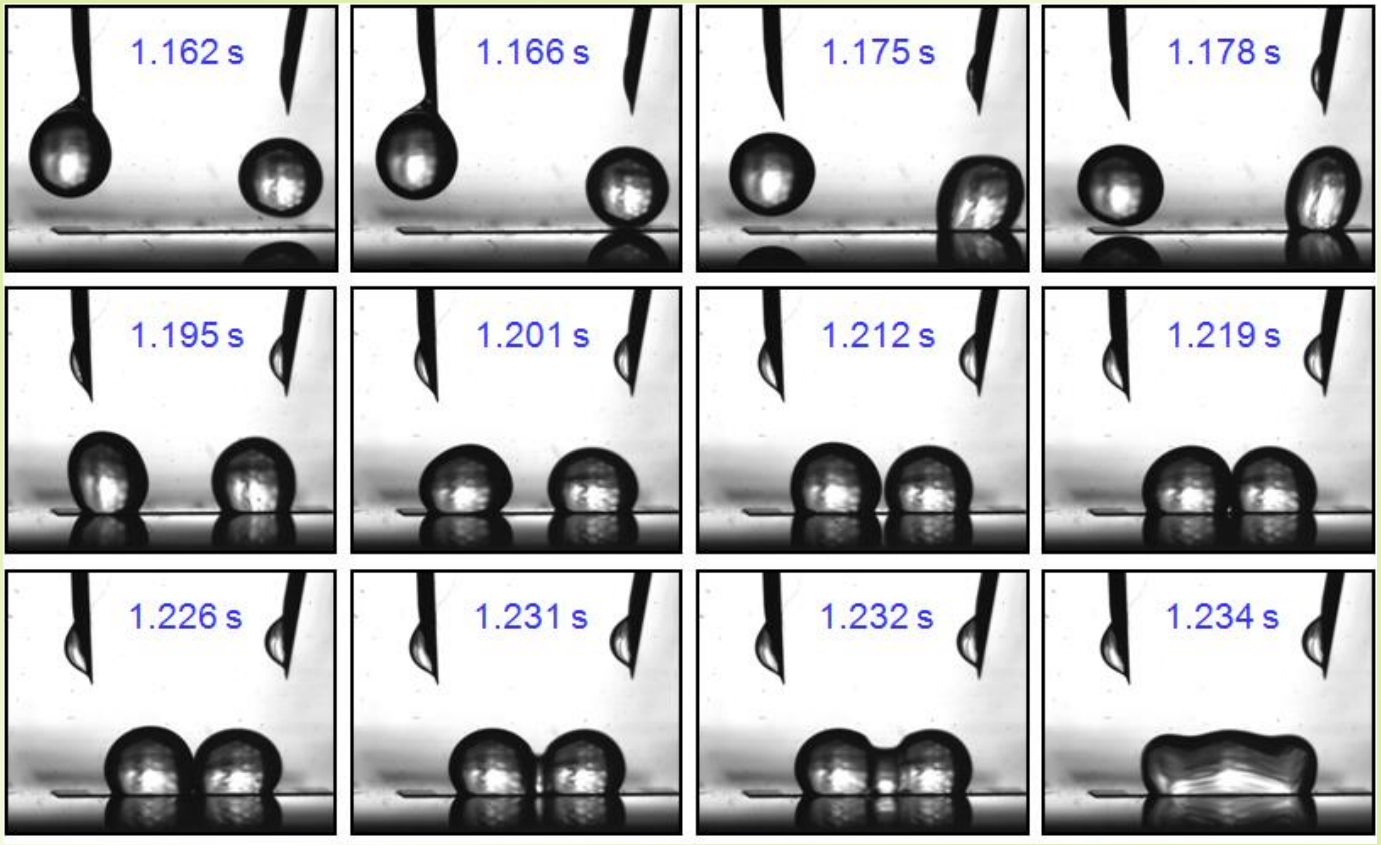


Multi-color Micro-PIV & Species Concentrations

Lai and Yang, *Lab Chip*, 2010

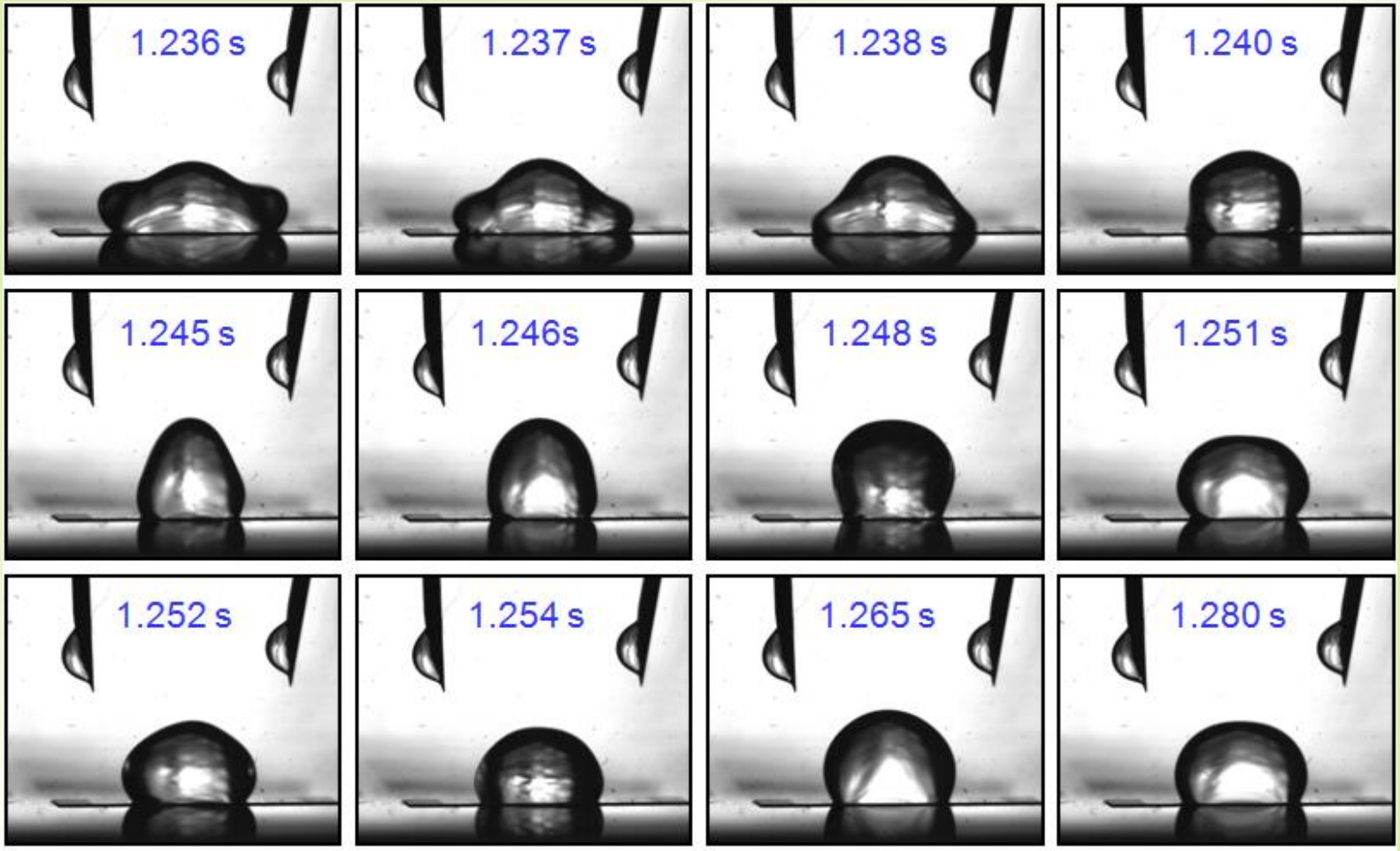


Sequence of images during two droplets collision (1)



- Each droplet of volume 5 μL (DI water).
- Transport path: 8 mm by 2 mm.
- Two average velocities of 58.14 mm/s and 54.35 mm/s .

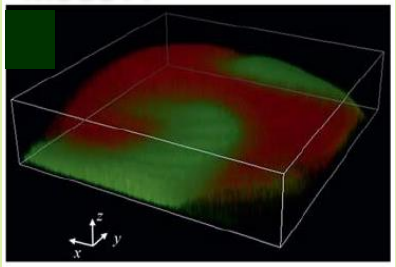
Sequence of images during two droplets collision (2)

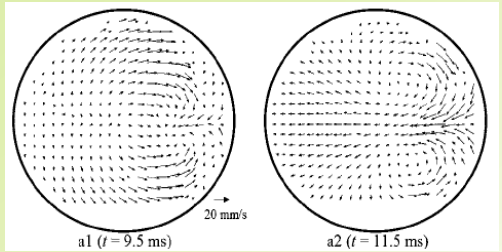


微液珠碰撞融合行為

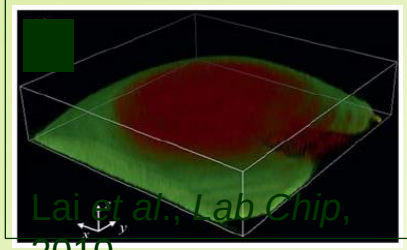
Lai, Hsu, Yang,*, *Lab Chip* 2010b *(47)*

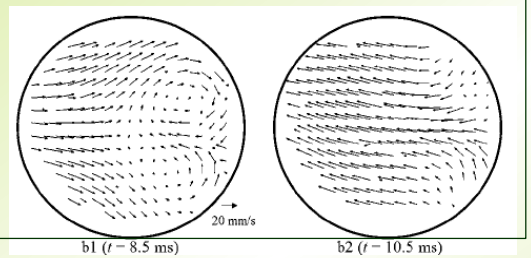
Mode A





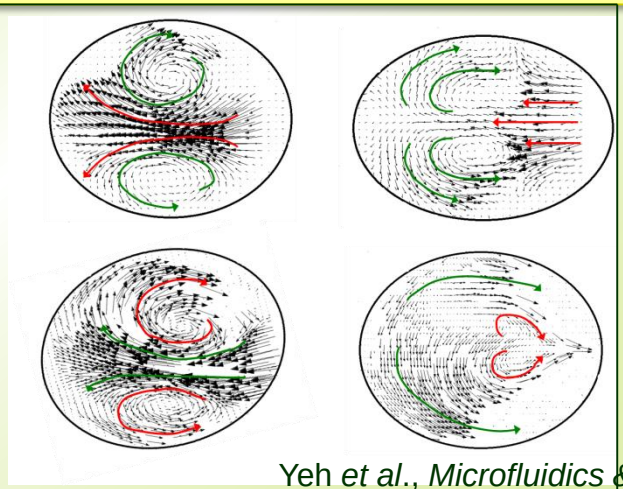
Mode B



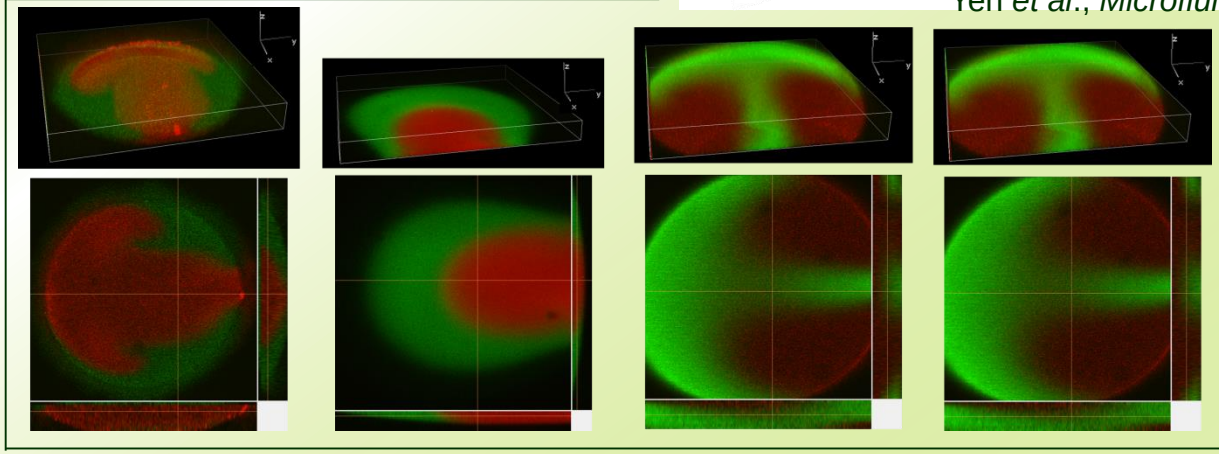


Lai *et al.*, *Lab Chip*, 2010

使用micro-PIV以及共軛焦顯微鏡進行微液珠融合過程的行為分析，結合流場與三維混合圖形探討不同流體之融合行為差異。

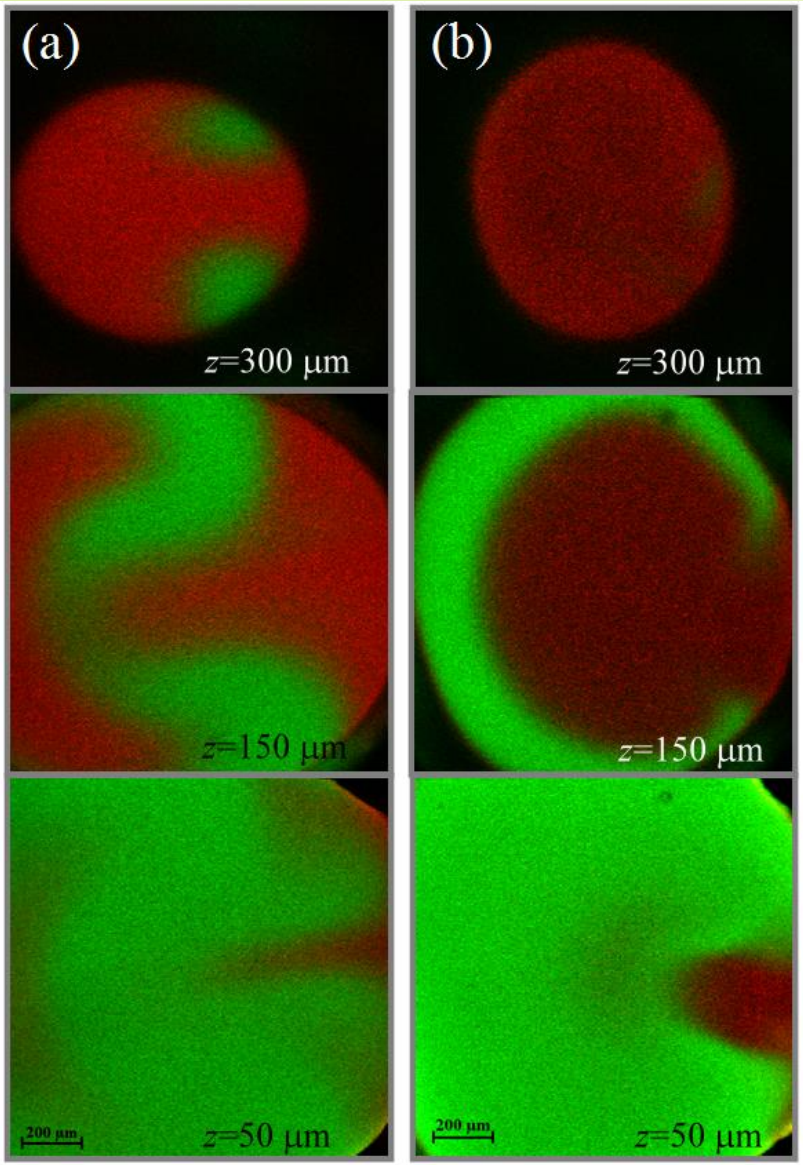


Yeh *et al.*, *Microfluidics & Nanofluidics, 2012*

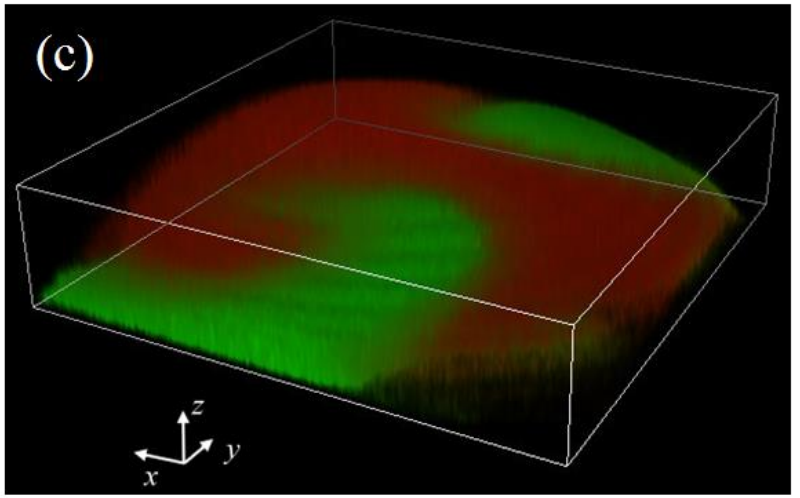


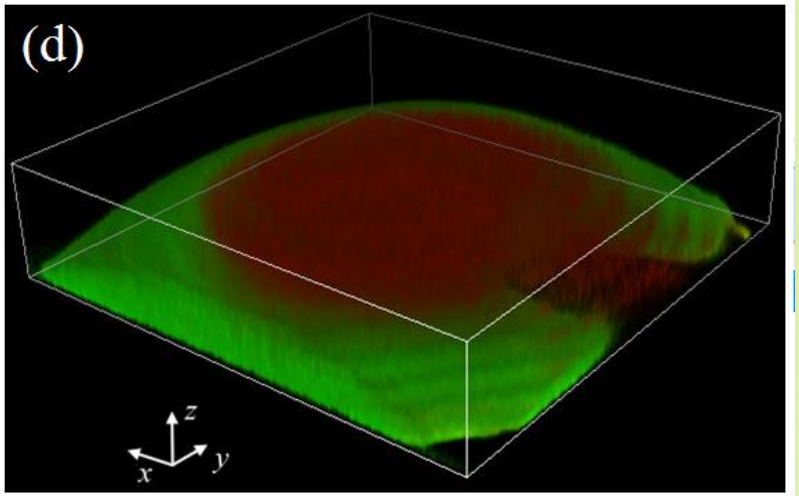
DNA hybridization in Reaction Channels

Lai, Hsu, Yang,*, *Lab Chip* 2010b *(47)*



Application and pilot-test

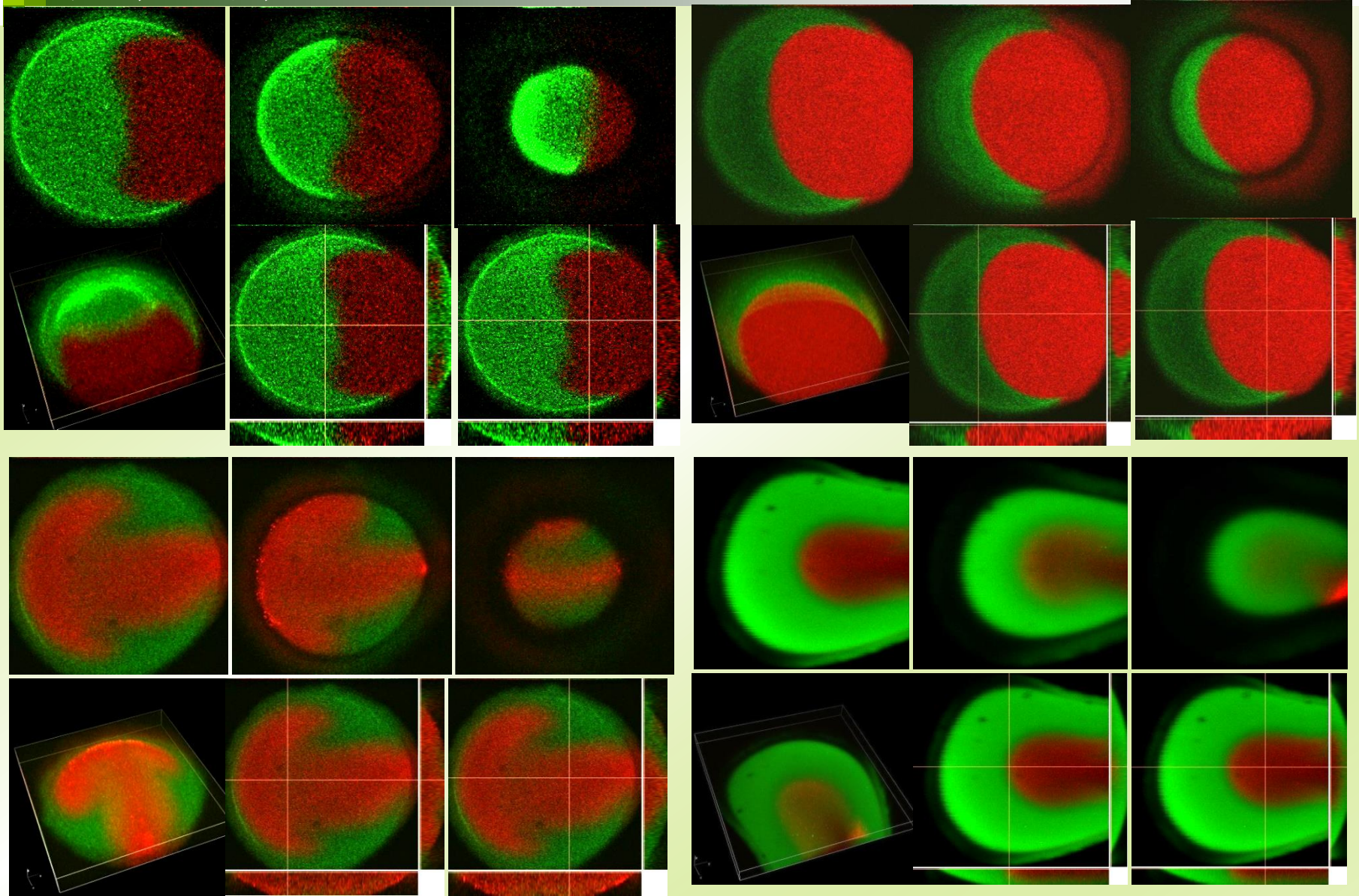




Reconstruction of Species Concentrations Interior the Colliding Droplets

楊鏡堂, 台大機械, 2011

Lai, Hsu, Yang,*, *Lab Chip* 2010b *(77)*

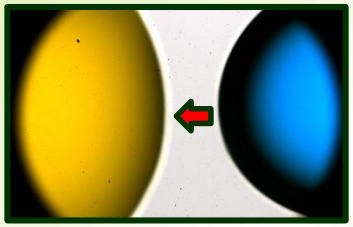


Mixing Test— food coloring & chemical reaction

Sometimes a color change is the result of a chemical reaction. Sometimes it is just the result of mixing colors.

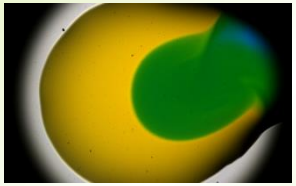
MNF, 2013

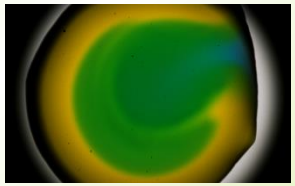
Tartrazine (stationary droplet)



Indigo Carmine (moving droplet)

Round-head shaped

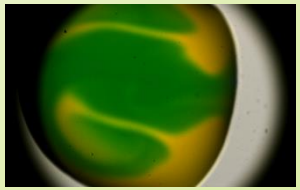




T = 0.100 92 s

T = 1.000 s

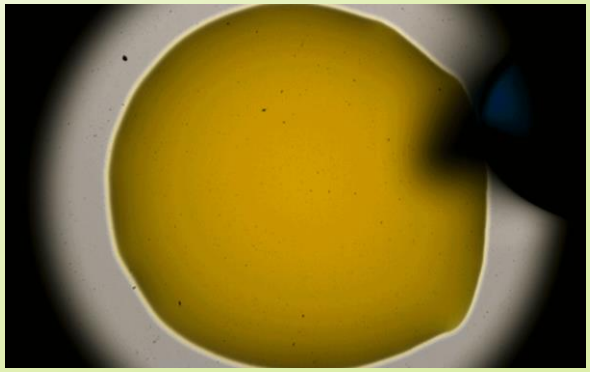
Mushroom-shaped

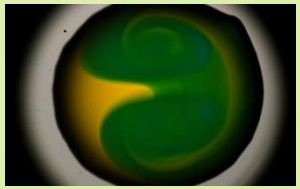


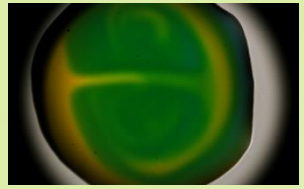
T = 0.100 s

T = 1.000 s

Heart-shaped







T = 0.100 s

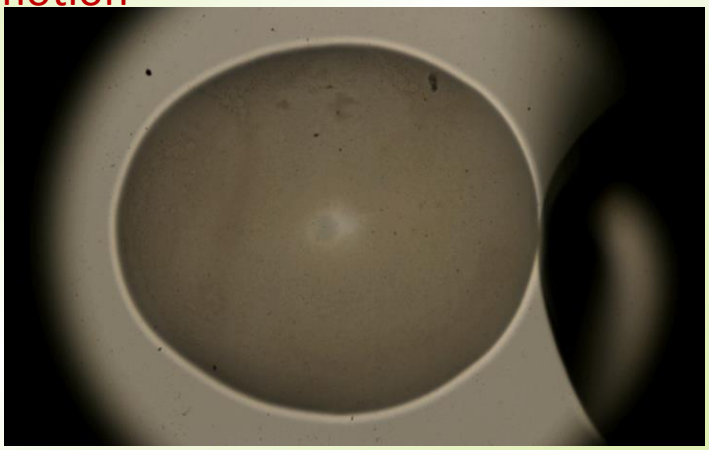
T = 1.000 s

1280 × 800 pixels, 3200 fps, 512X Slow motion

Chemical Reaction in Droplets

Mode C 1280 × 800 pixels, 3200 fps 512X Slow motion **Mode D**

MNF, 2015



T = 5 ms

T = 25 ms

T = 25 ms

T = 250 ms

T = 50 ms

T = 1.000 s

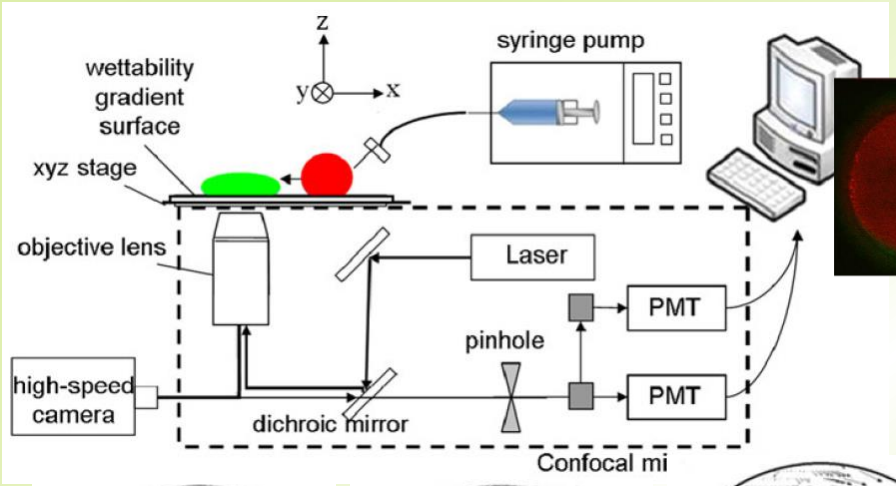
T = 1.500 s

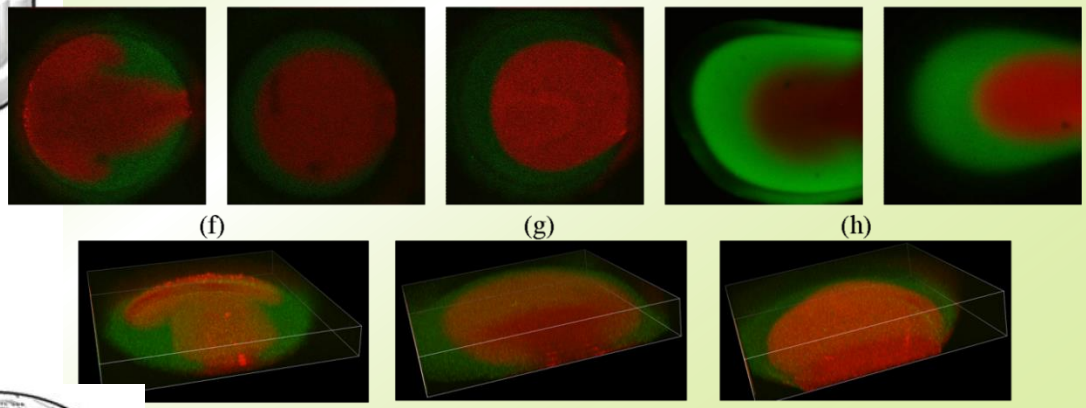
T = 2.500 s

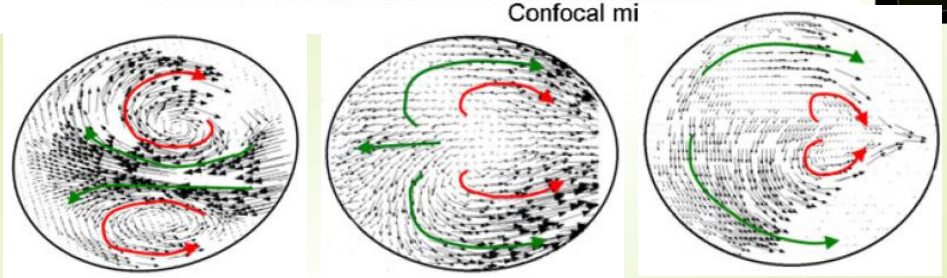
Droplets Coalescence and Mixing with Identical and Distinct Surface Tension on a Wettability-Gradient Surface

S. I. Yeh, W. F. Fang, H. J. Sheen, **J. T. Yang***

Microfluidics and Nanofluidics, doi: 10.1007/s10404-012-1096-2, 2013

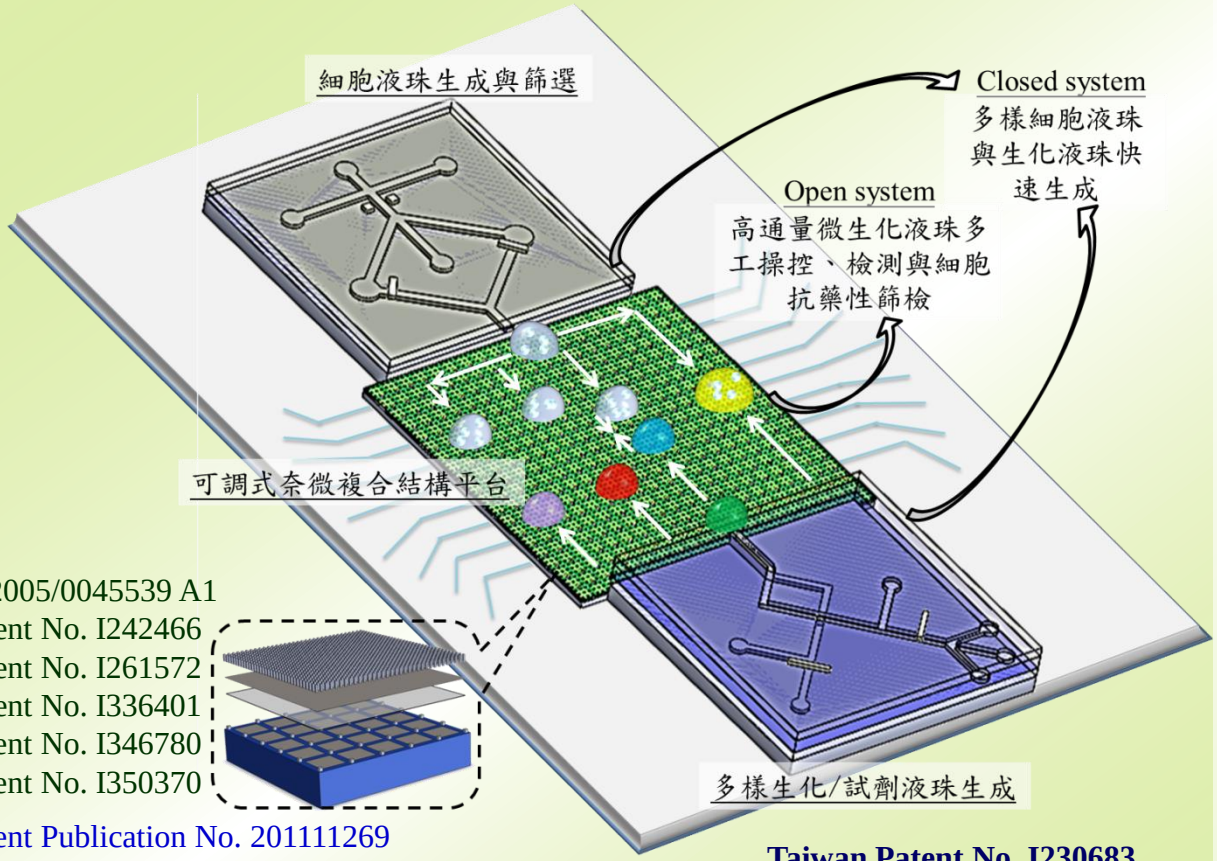






This study investigates the influence of different viscosities and surface tensions on droplet coalescence and mixing processes after a head-on collision between a moving droplet and a stationary droplet by micro-PIV and micro-LIF technique.

計畫構想（平台系統）



US Patent 2005/0045539 A1
Taiwan Patent No. I242466
Taiwan Patent No. I261572
Taiwan Patent No. I336401
Taiwan Patent No. I346780
Taiwan Patent No. I350370

Taiwan Patent Publication No. 201111269
Taiwan Patent Publication No. 201113524
Taiwan Patent Publication No. 201038465
Taiwan Patent Publication No. 201038635
Taiwan Patent Publication No. 201111272
JMM Highlights, 2009
Institute of Physics IOP Select, 2009

Taiwan Patent No. I230683
JMM Highlights, 2006

film

系統特點

- ✓具**高通量**之微液珠生成，可自動化且**同步多功操控**微液珠進行**平行化處理，縮短試驗時程**
- ✓包覆細胞或試劑(候選藥物)的微液珠可被**有效地篩選、分類與運用，避免細胞與試劑浪費**
- ✓可操控之微液珠體積範圍廣(pL~μL)，且**體積小於傳統檢測所需體積的數十倍以上**
- ✓此系統對**周邊的相容性高**，取樣方便，利於後端的處理與檢驗分析。可**推廣至其他細胞相關之基礎研究與分析**

An overlapping crisscross micromixer using chaotic mixing principles

Lilin Wang and Jing-Tang Yang

Highlights of J. Micromech. Microeng. 16 (2006) 2684–2691

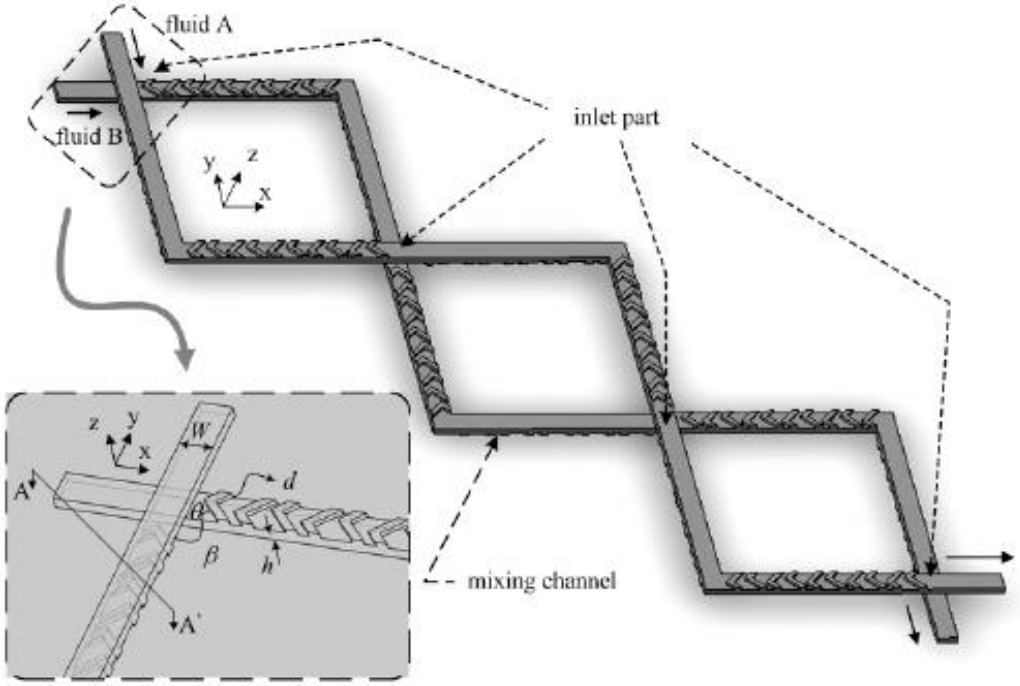
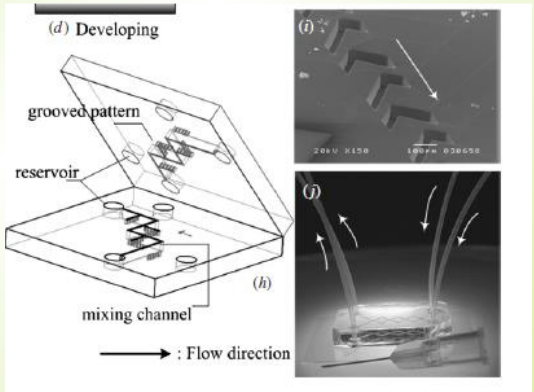


Figure 1. Schematic diagram of a staggered overlapping crisscross micromixer.



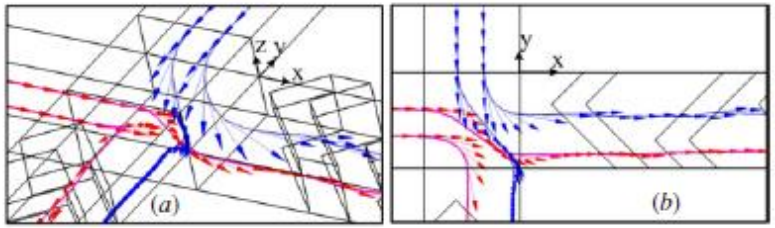


Figure 3. Lagrangian trajectories of the SOC μ-mixer from (*a*) a vertical view and (*b*) a front view near the crisscross junction.

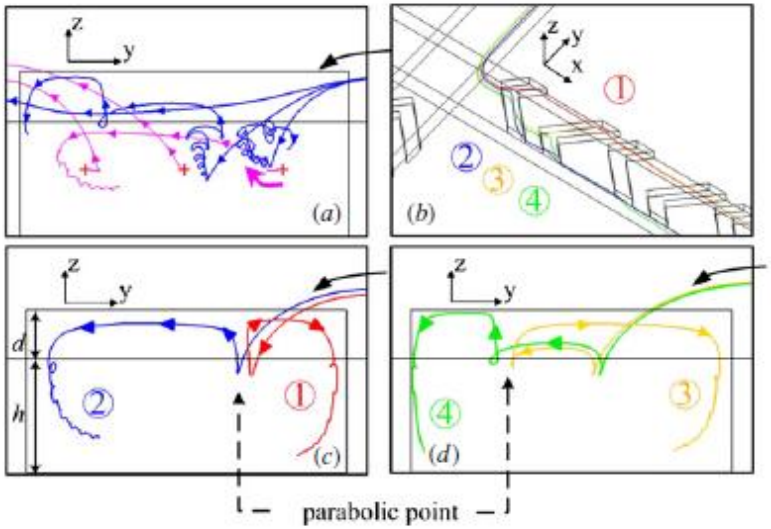
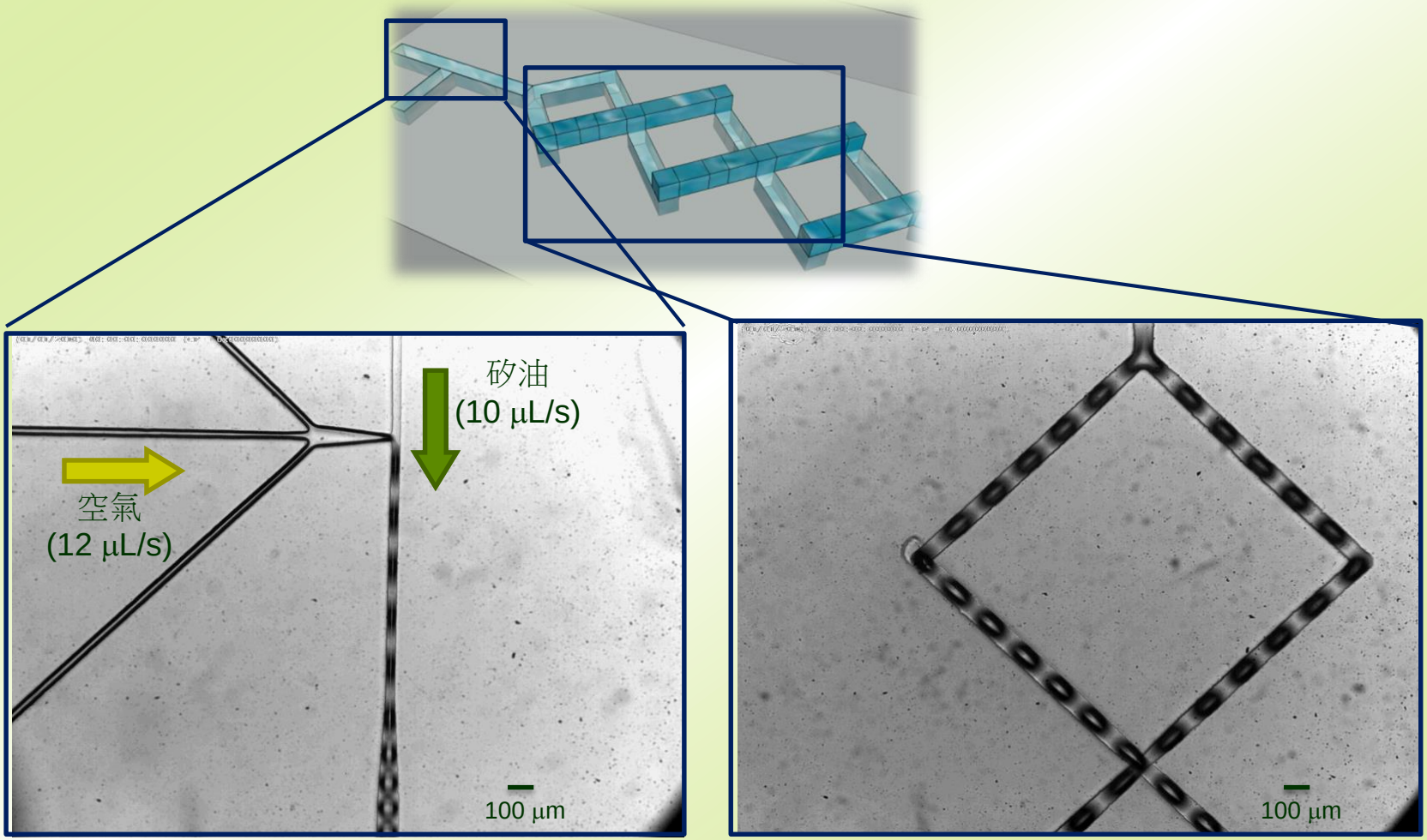


Figure 4. Lagrangian trajectories of the SOC μ-mixer displayed from (*a*), (*c*)–(*d*) end views through the *x*-direction mixing channel, and (*b*) a vertical view.

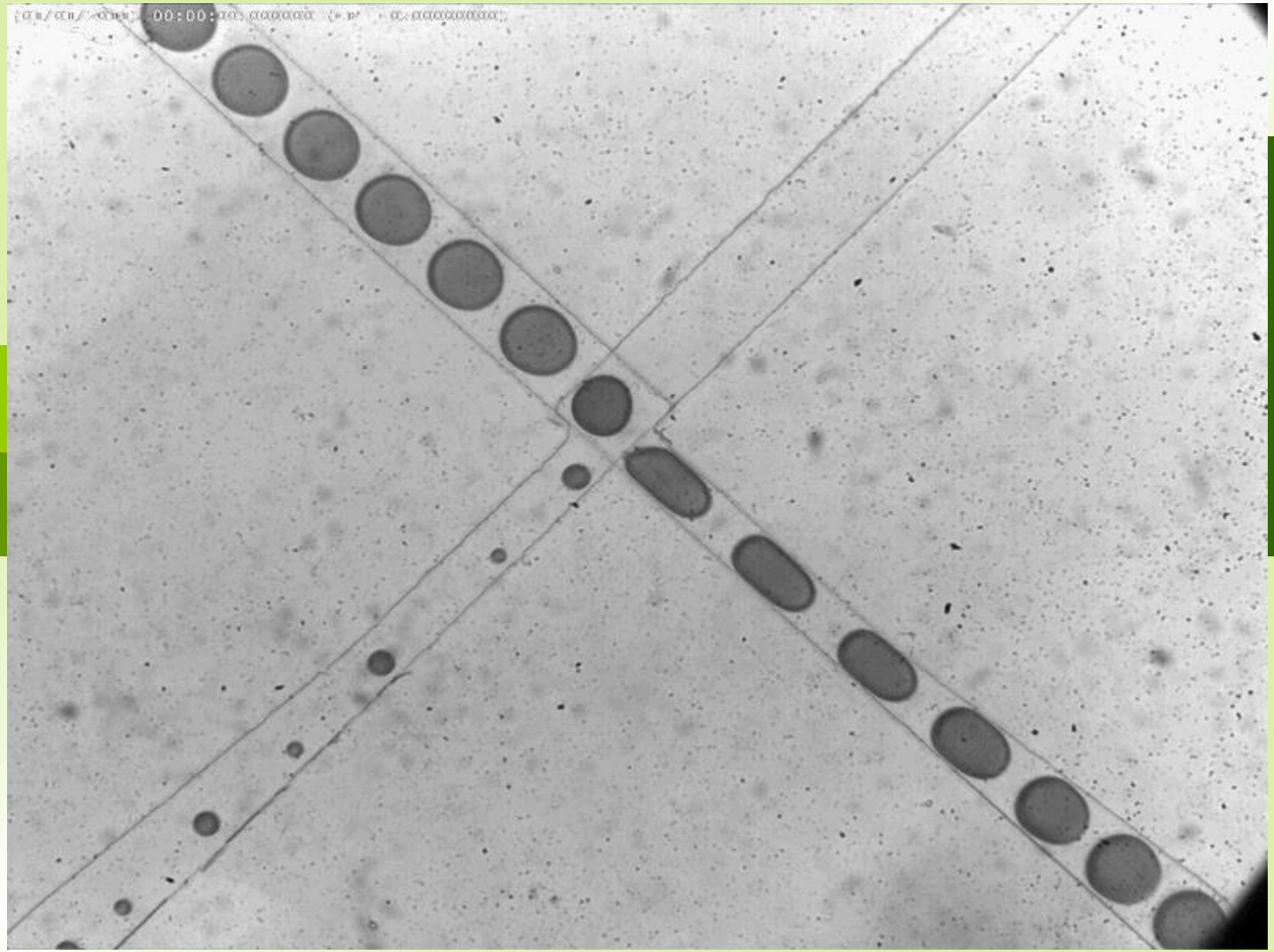
Preliminary Tests

Yang *et al.*, *Microfluidics & Nanofluidics*, 2011

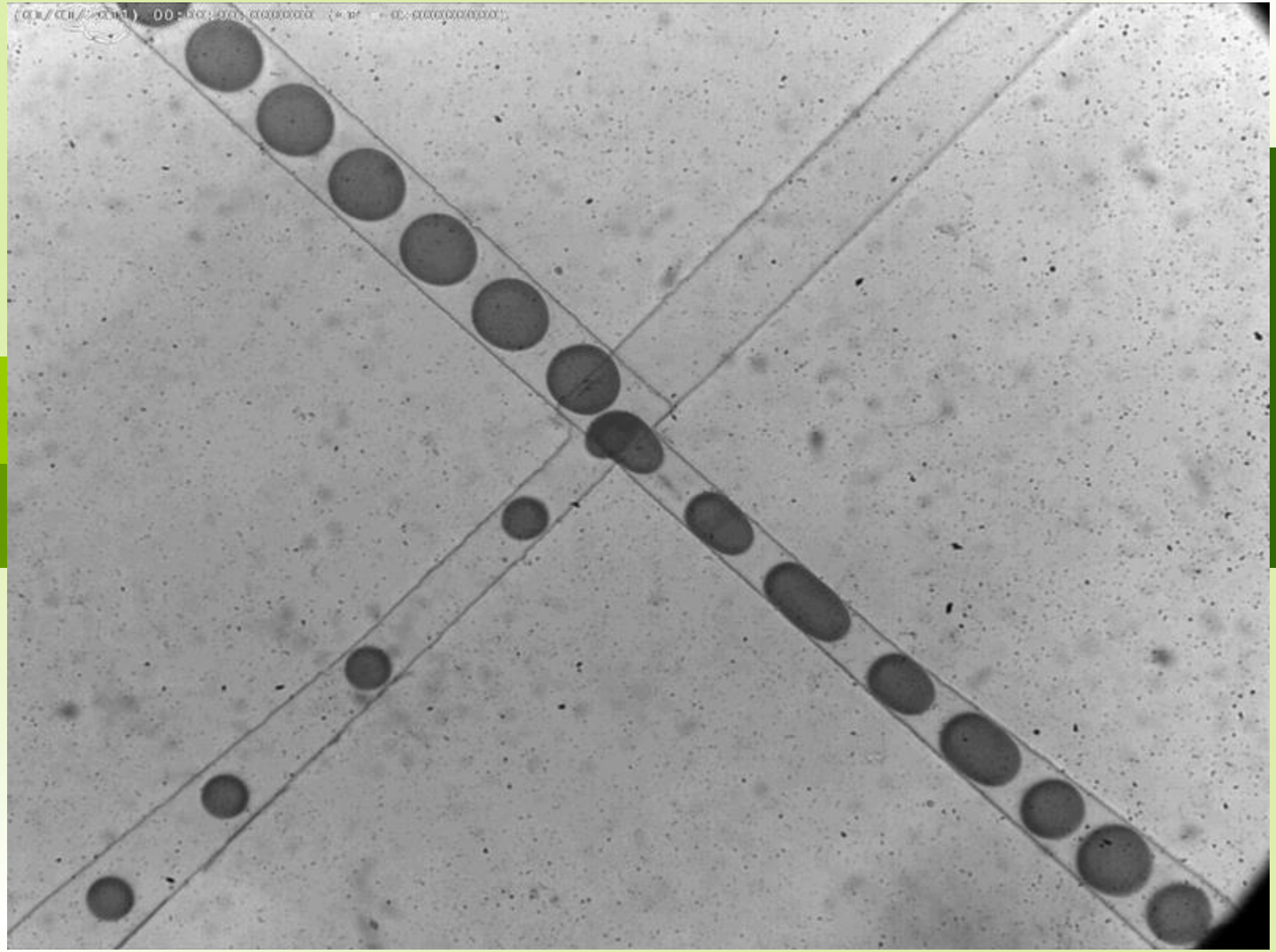


張偉軍碩士論文, 2011

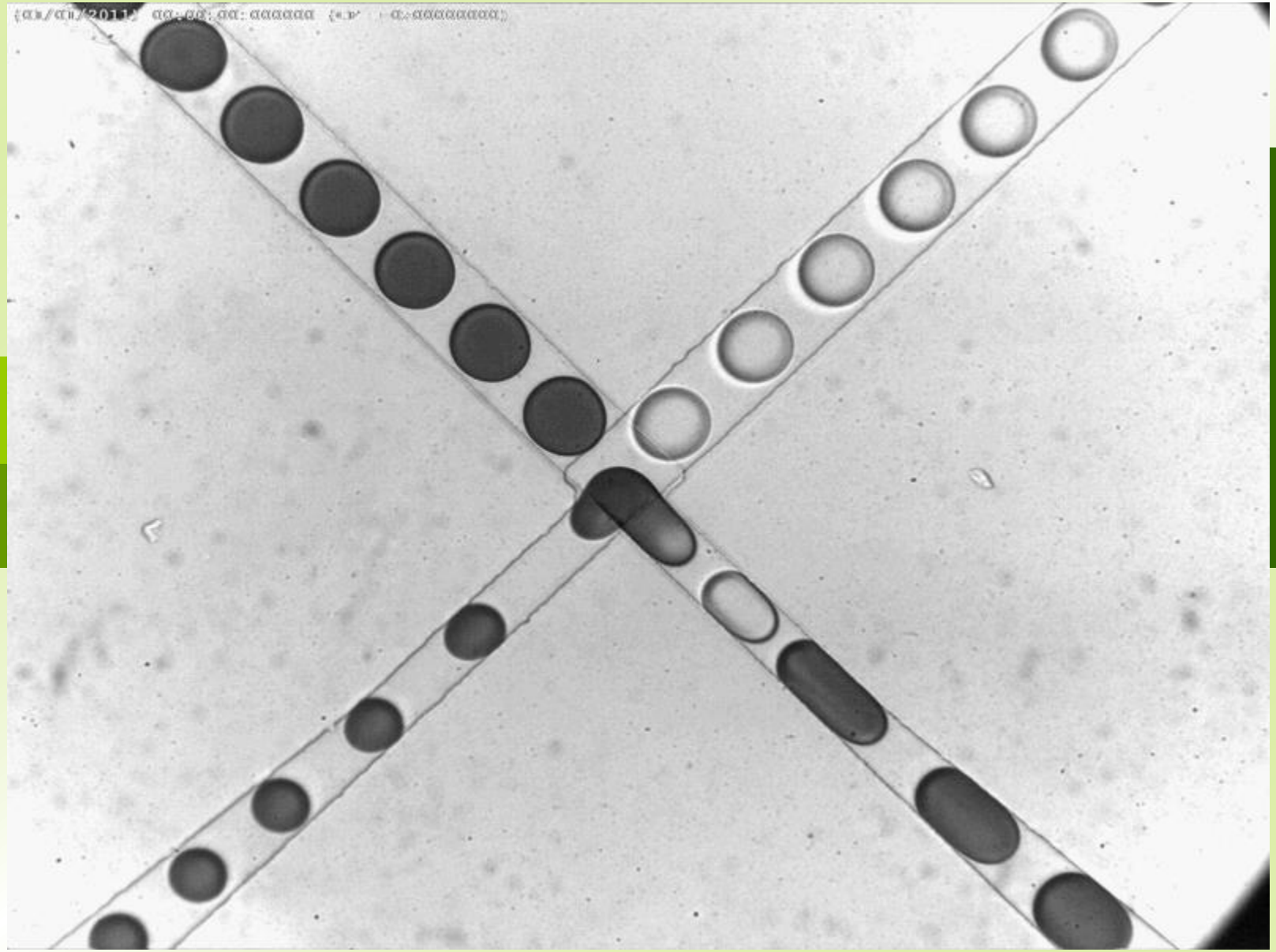
Droplet Fission (1)



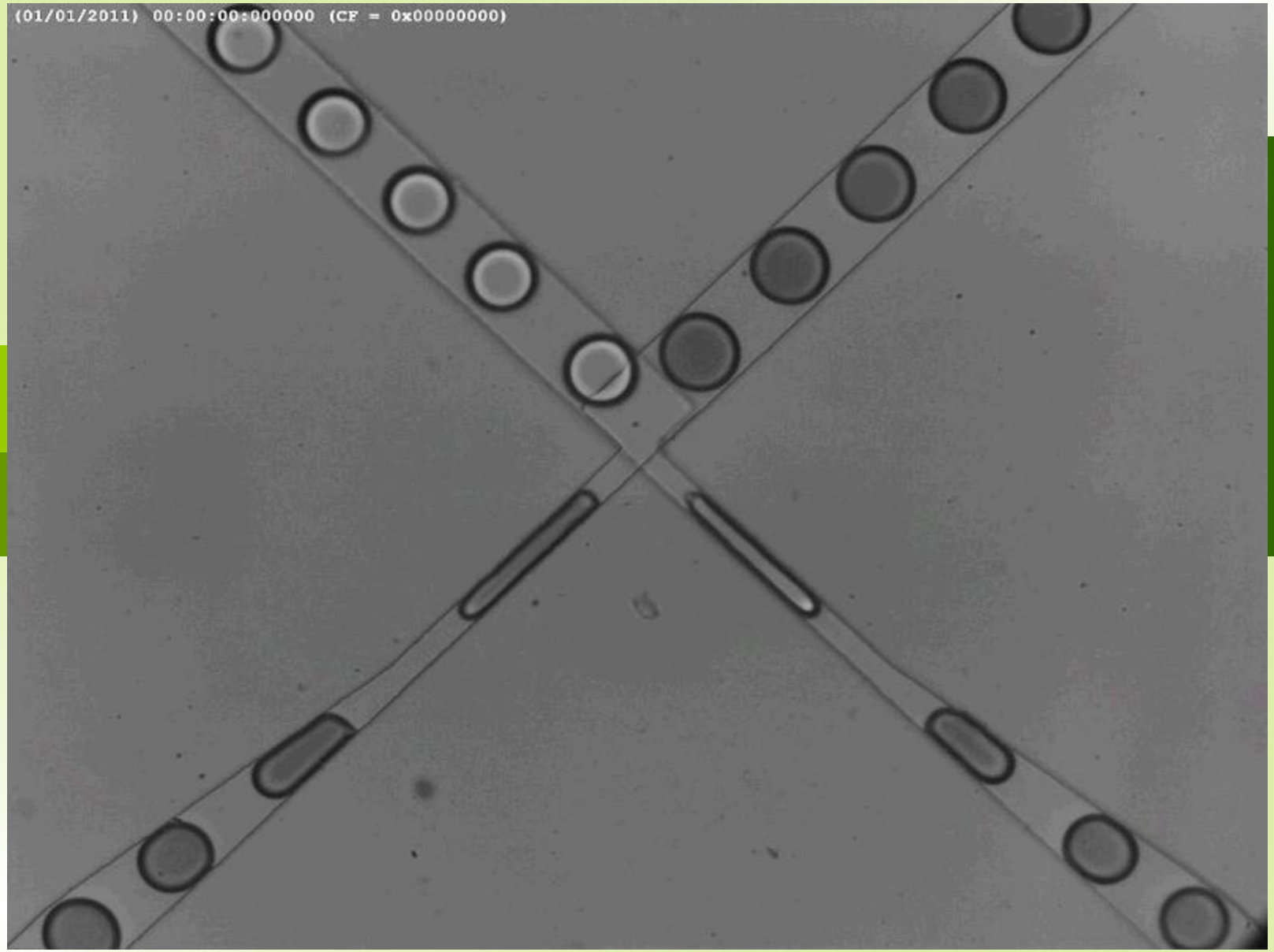
Droplet Fission (2)



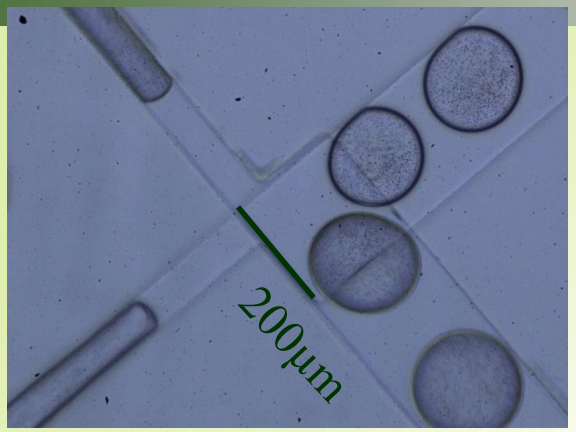
Droplet Fusion (1)



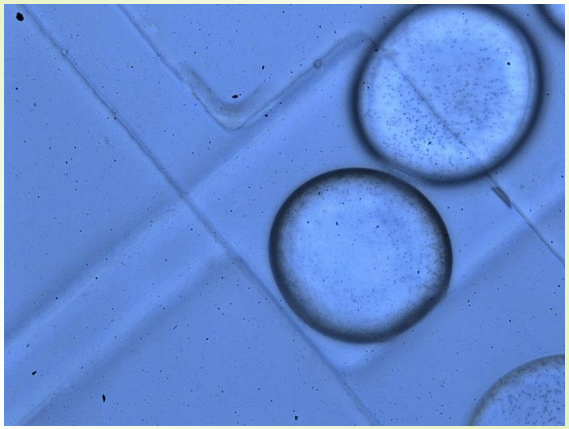
Droplet Fusion (2)



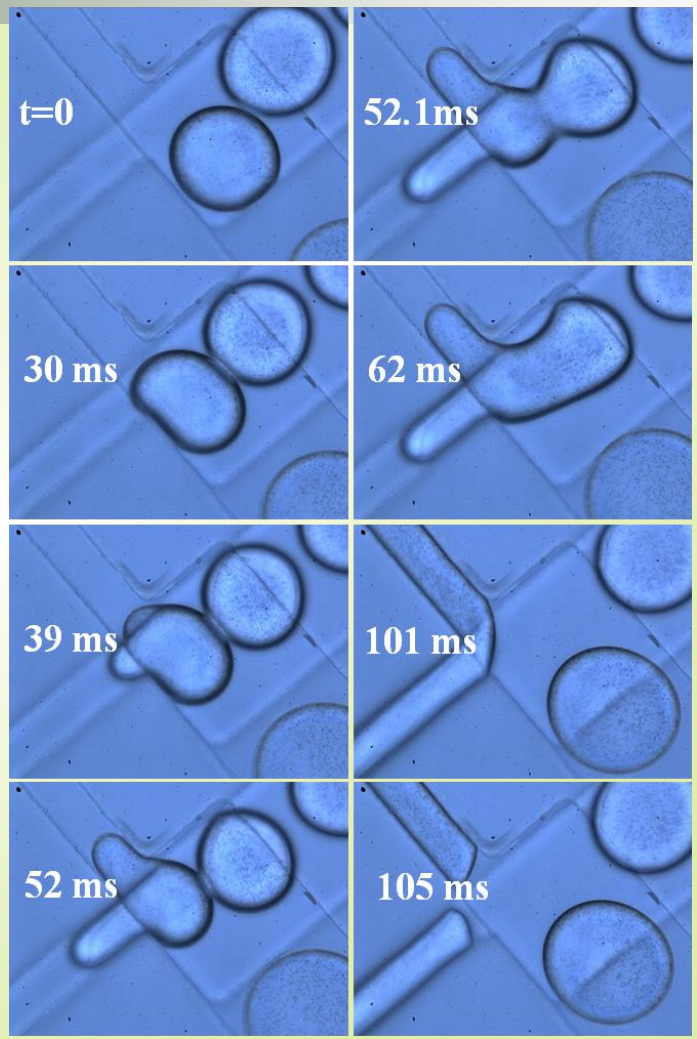
Visualization of Droplets Fusion and Fission



Frame rate：1000 fps
Spatial resolution：63.9 μm/pixel



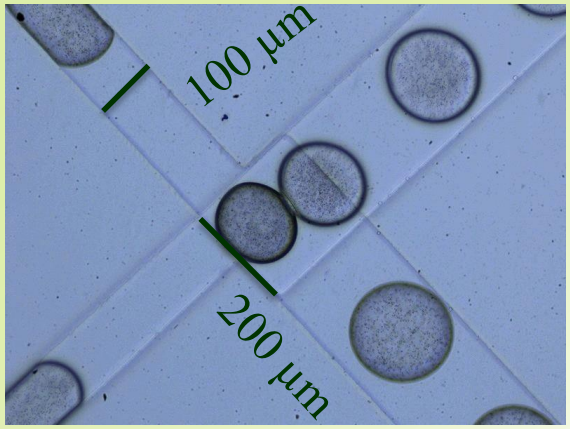
Frame rate：6000 fps
Spatial resolution：2.13 μm/pixels



Phantom V310
high-speed CMOS camera
Observation zone：800 x 600 pixels

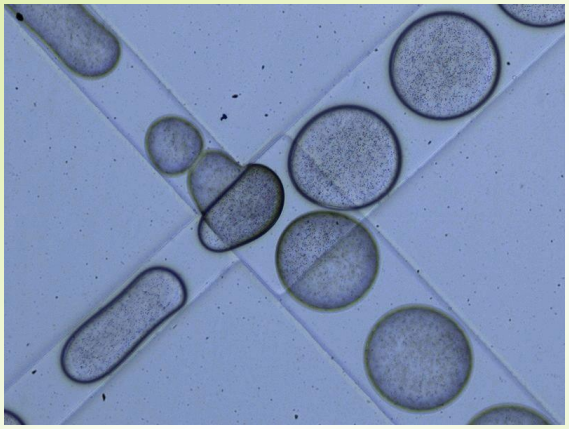
Mechanism
Droplets Fusion, Fission, and Distribution

(a.) fusion and fission



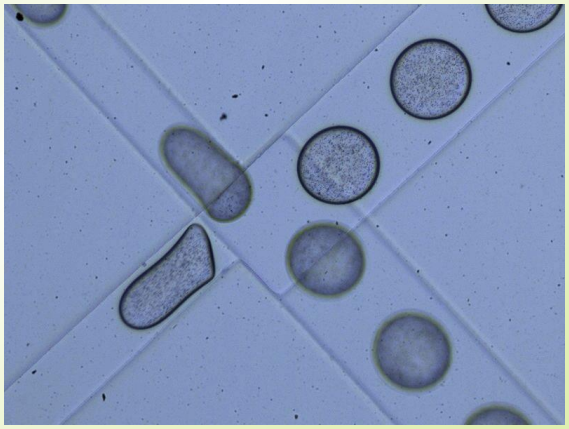
Deep of single layer: 51 µm
DI water: 0.5 µl/min
Silicone oil: 1 µl/min
Re: 0.031 ; Ca: 0.0006

(b.) fission and distribution

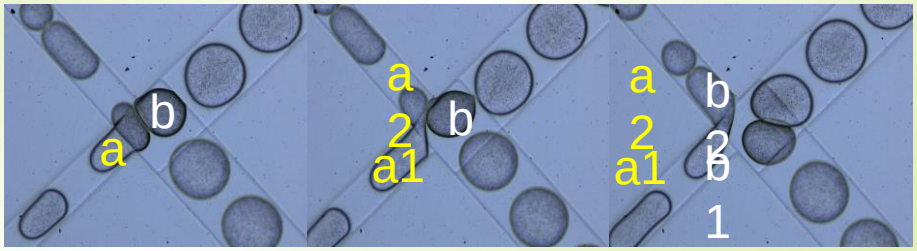


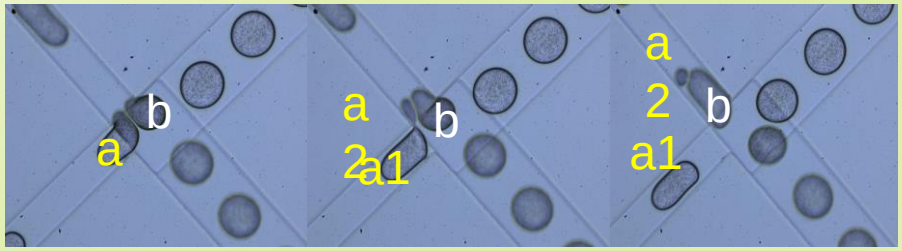
Deep of single layer: 51 µm
DI water: 2 µl/min
Silicone oil: 2 µl/min
Re:0.083 ; Ca: 0.0016

(c.) fission and distribution

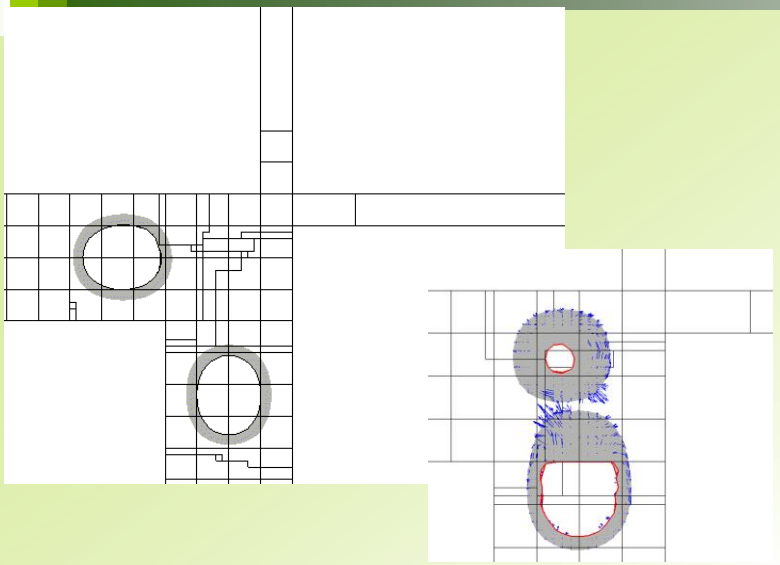


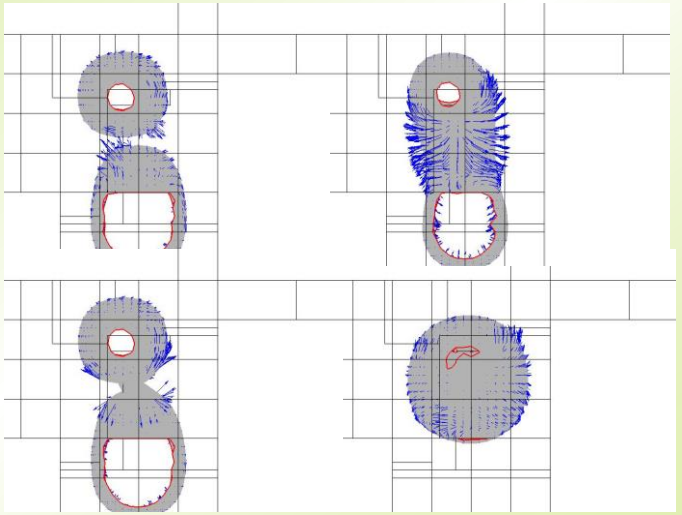
Deep of single layer: 51 µm
DI water: 2 µl/min
Silicone oil: 5 µl/min
Re: 0.145 ; Ca: 0.0028

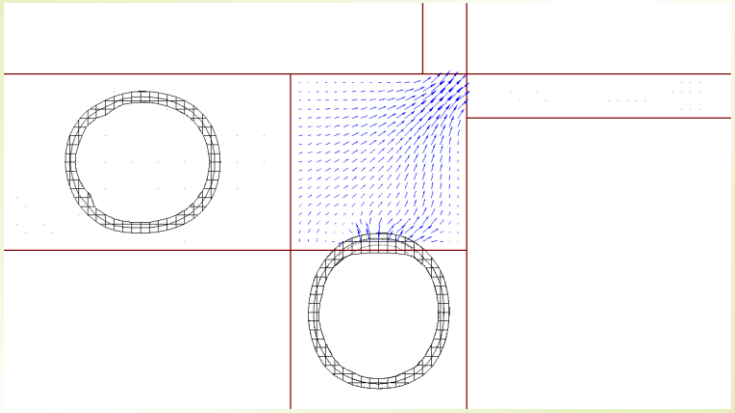


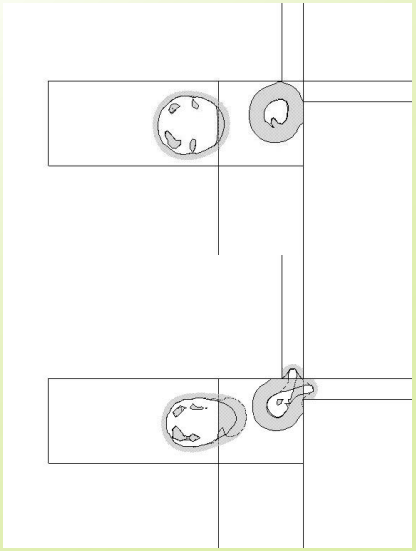


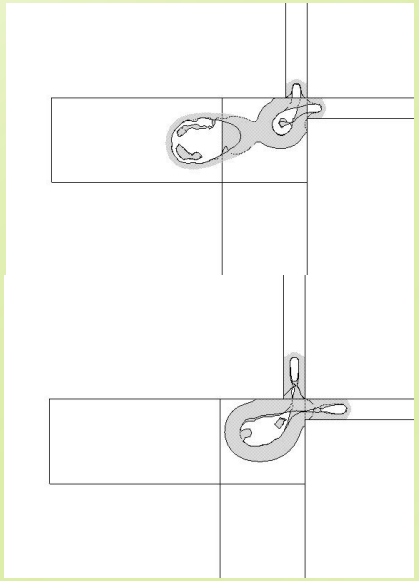
Droplets Simulation











台大的實驗室的幾項技術發展

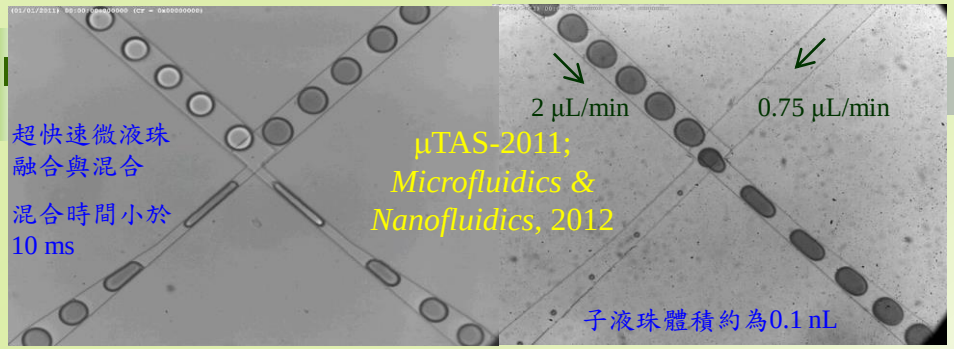
(2008-2016)

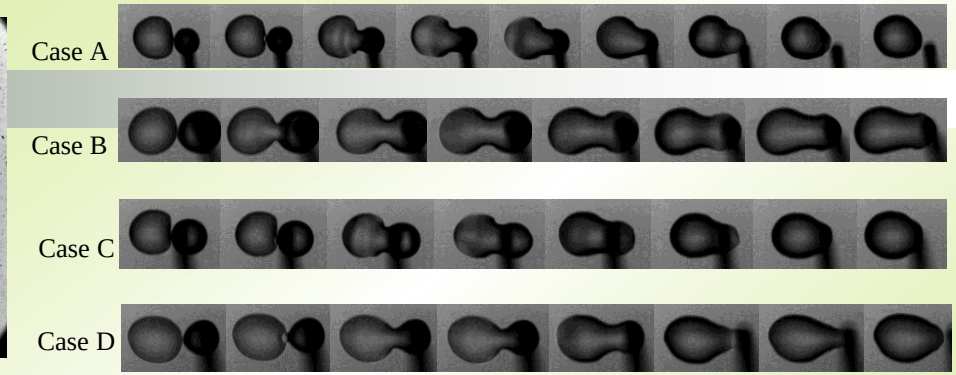
A. 液珠碰撞反應之平台與分析技術
B. 基因變異之液珠型目視檢測平台
C. 生質柴油製程之毫米級系統
D. 胰島素目視檢測平台
E. 番茄與蘭花之病毒檢測技術 (王子明博士)
F. PLGA製藥技術 (葉思沂教授)

簡報大綱

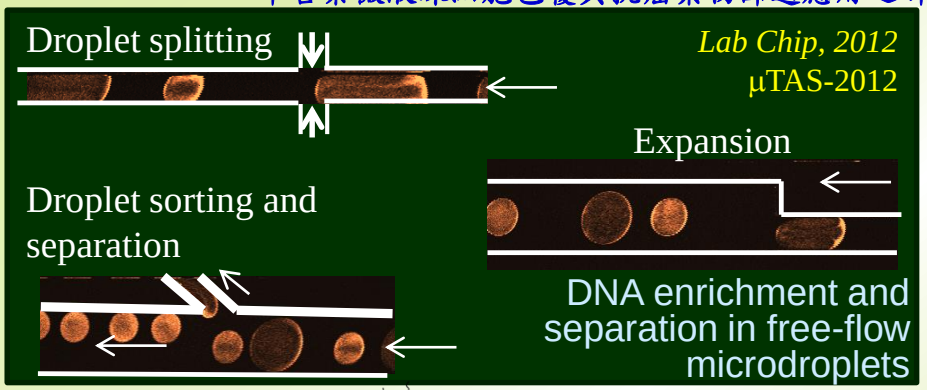
1. 奈微流體技術與系統之優劣
2. 簡介連續式微流體系統與液珠型微流體技術

Progress of droplet-based microfluidics

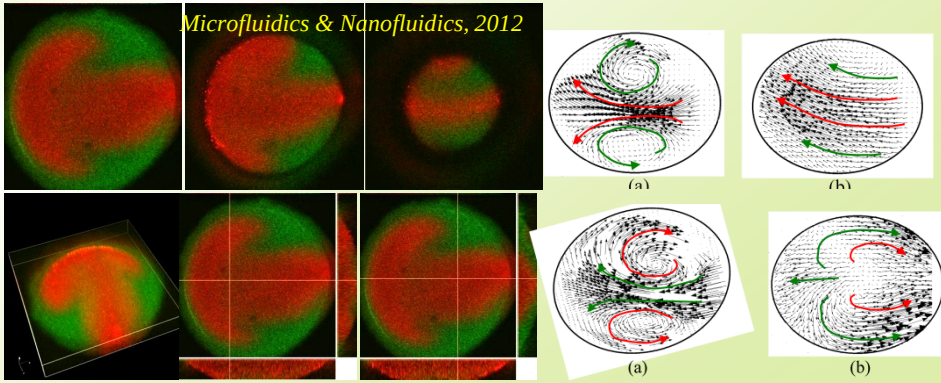


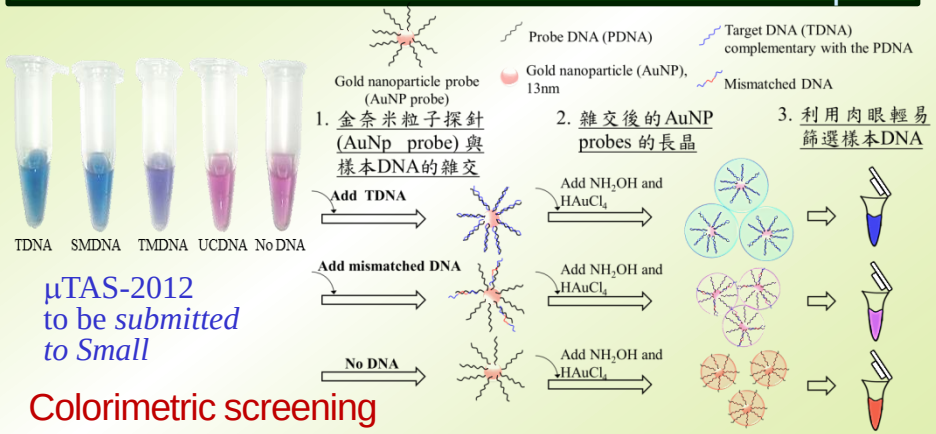


Fusion and fission of droplets → 研發糖尿病新藥篩檢的平台奈微液珠細胞包覆與抗癌藥物篩選應用之研究



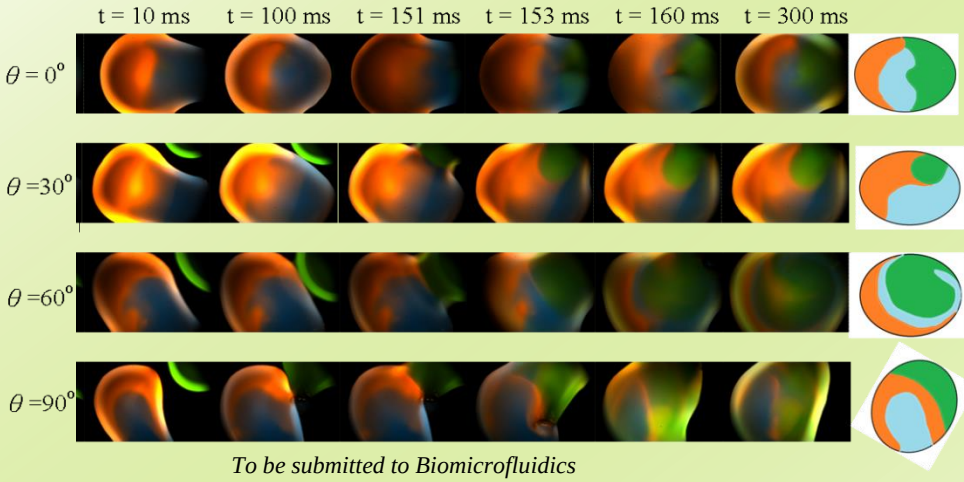
Coalescence and Mixing of Colliding Droplets





μTAS-2012
to be *submitted to Small*

Colorimetric screening of DNA using hybridization-mediated AuNP probes



To be submitted to Biomicrofluidics

- New Progress…

Bio-Microfluidics & Lab-on-a-Chip

- **Continuous flow**
  - Microreactor
    - DNA detection
    - Carbohydrate synthesis
    - Protein analysis
    - Cell manipulation (trapping, separation, tec.)
- **Droplets flow**
  - Open system
    - Multi-nucleotide polymorphisms detection
    - Islet screening
  - Microchannel
    - PLGA synthesis (drug release)
    - DNA concentration
    - Biodiesel synthesis
    - Precision medicine (concentration gradient of drug)

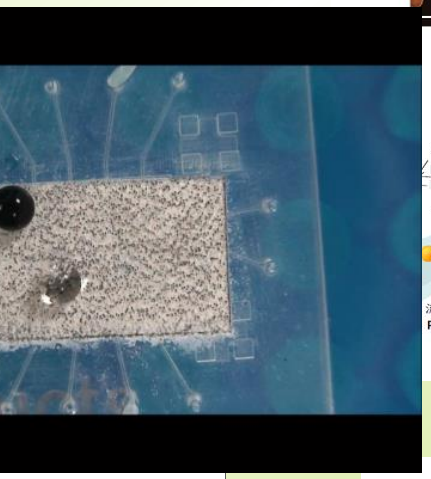
個人醫檢新紀元：可視化液珠式基因快篩技術

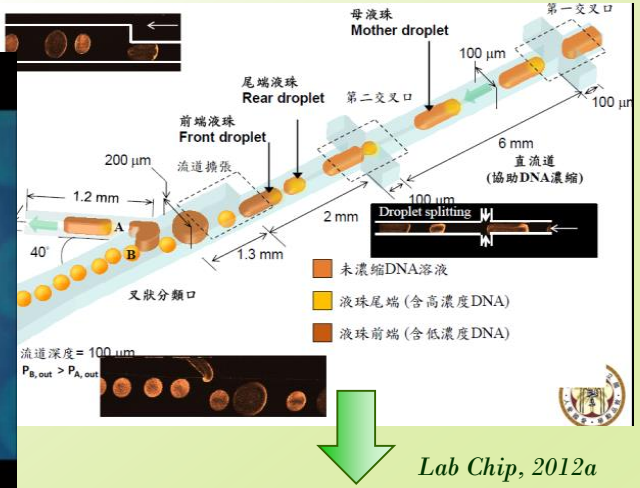
Personalized Diagnostics at Sight: Droplet-based Gene Screening

Point-of-care model

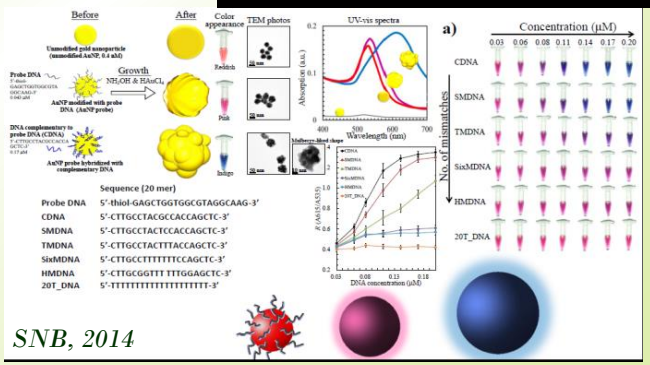
第11屆國家新創獎- 2014

一種新的檢測技術和晶片系統，不需要昂貴的設備及複雜的步驟，即可自動化進行基因型診斷，檢測結果能用肉眼直接觀察得知，並具有可攜帶、微量藥品試劑消耗及快速篩選等優點，減少醫療資源浪費、發揮藥物的最佳藥效、針對每個人不同的體質，打造專屬個人的治療方式。本技術核心包含三大項目: (1) 發展一種利用金奈米粒子探針結合長晶方法，(2) 可攜式的液珠操控平台，(3) 被動式DNA濃縮技術。

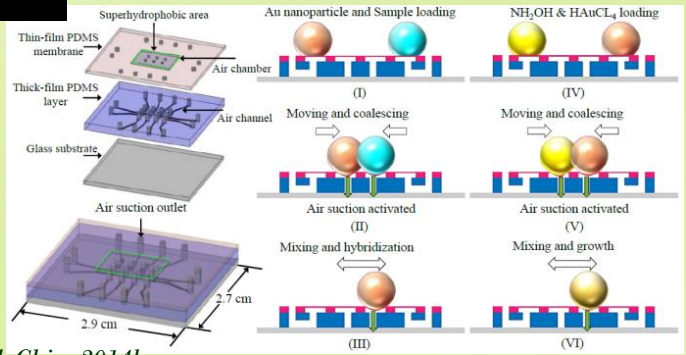




Lab Chip, 2012a



SNB, 2014

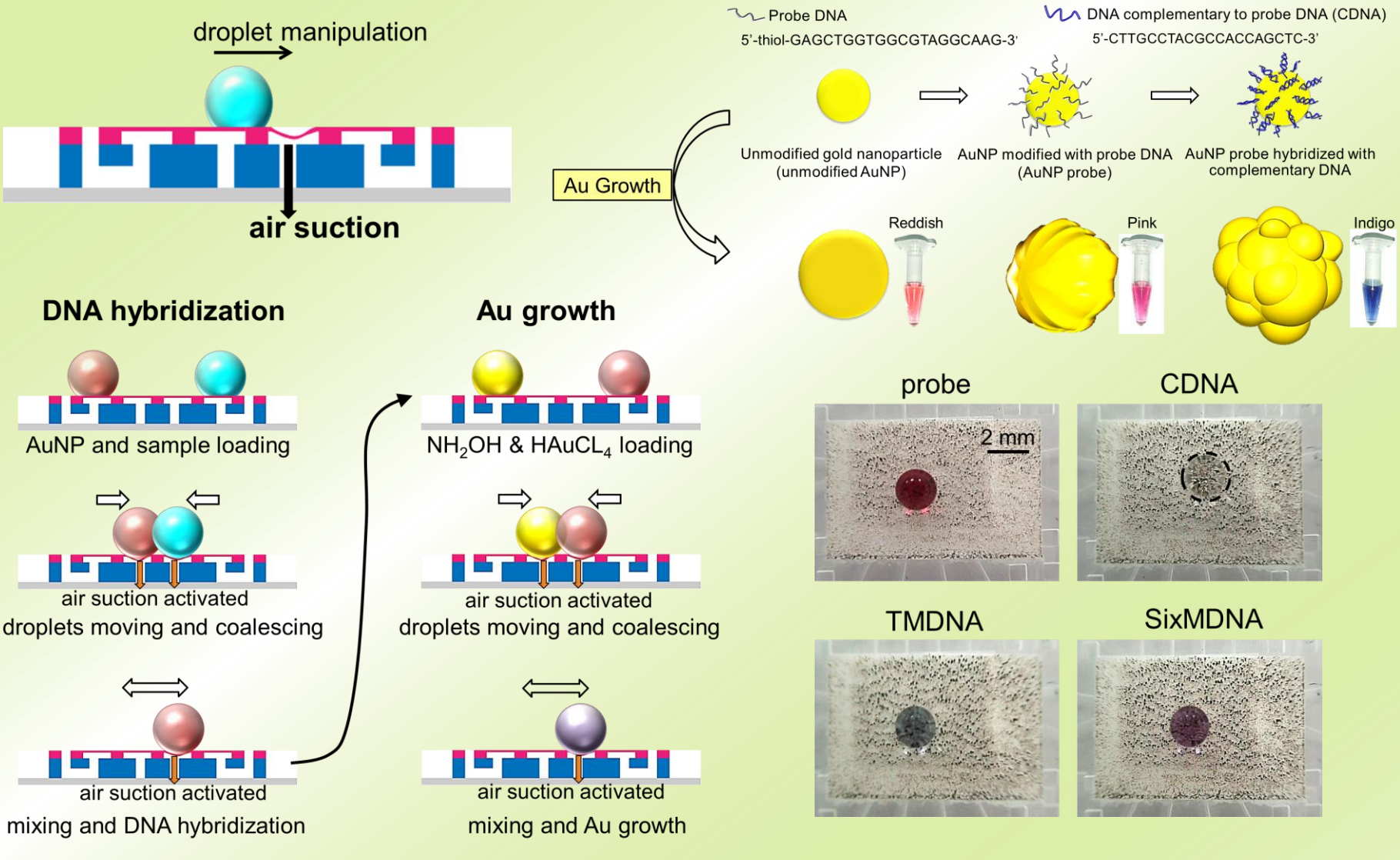


Lab Chip, 2014b

A Biocompatible Open-surface Droplet Manipulation Platform for Multi-nucleotide Polymorphisms Detection

C. J. Huang, W. F. Fang, M. S. Ko, H. Y. E. Chou, and **J. T. Yang***

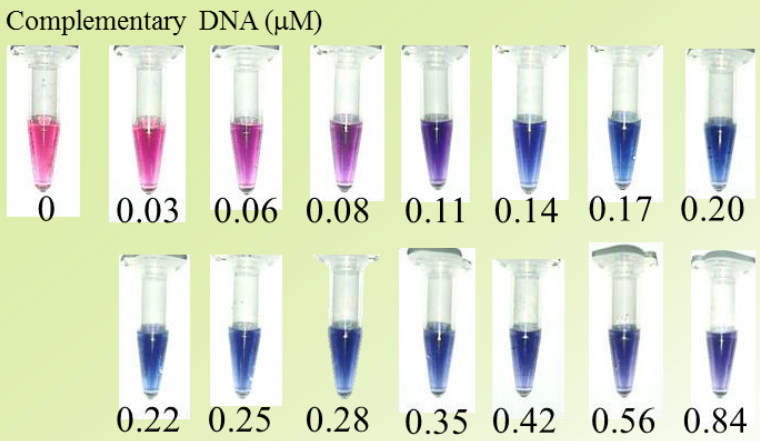
Lab on a Chip, Vol. 14, pp. 2057-2062, 2014

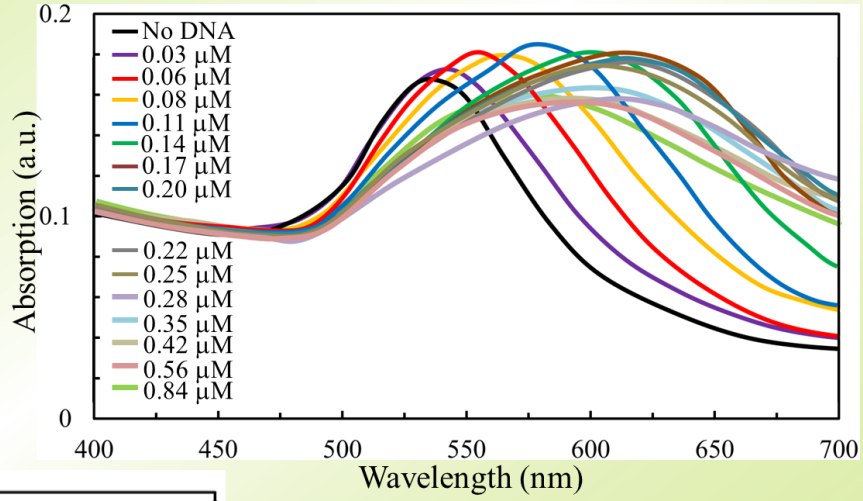


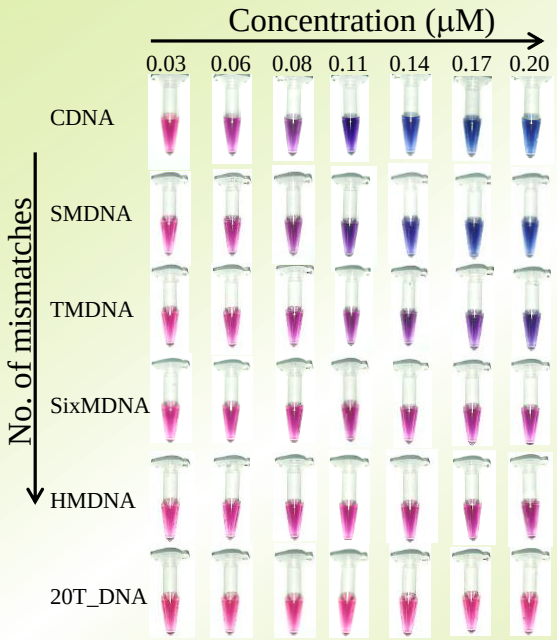
Colorimetric Determination of DNA Concentration and Mismatches using Hybridization-mediated Growth of Gold Nanoparticle Probes

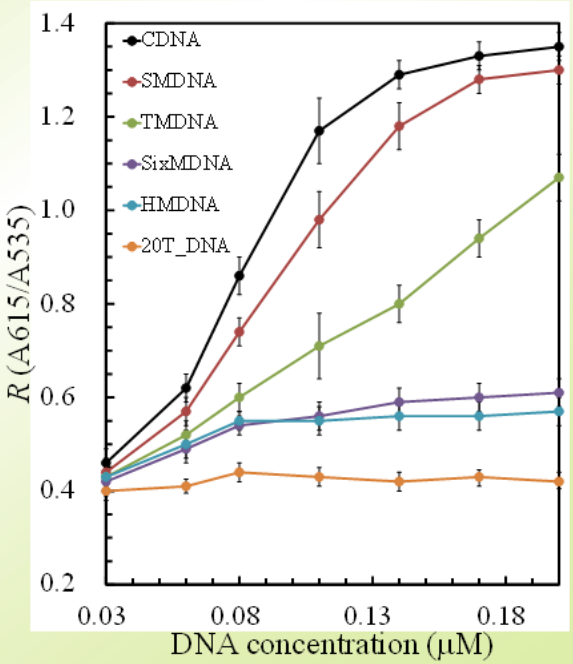
W. F. Fang, W. J. Chen, and **J. T. Yang***

Sensors and Actuators B, Vol. 192, pp. 77-82, 2014







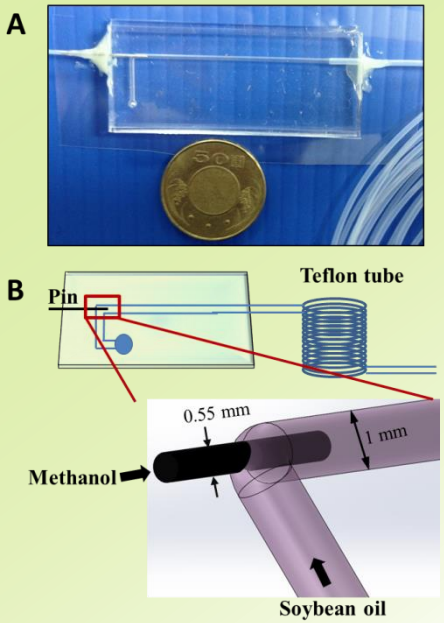


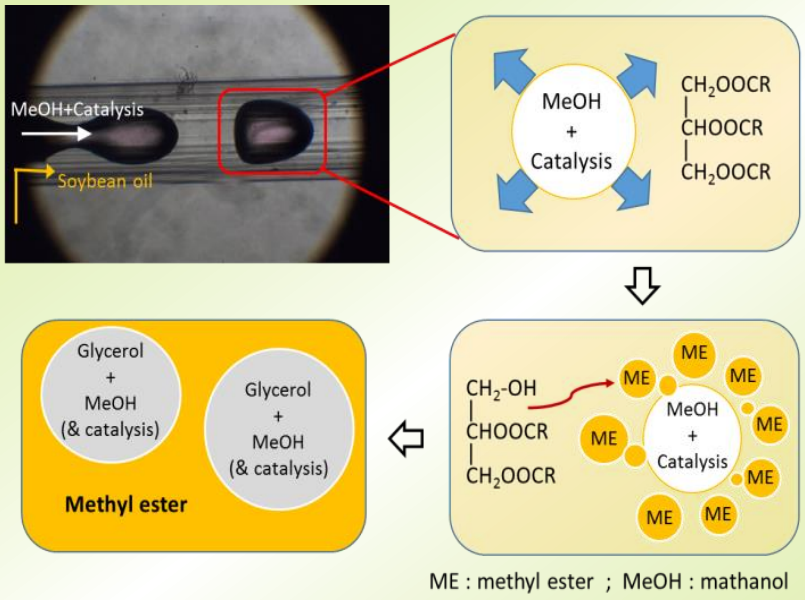
This method can be employed not only in semi-quantitative analysis of the given DNA but also in the identification of base-pair mismatches (SNP & MNP)of DNA samples

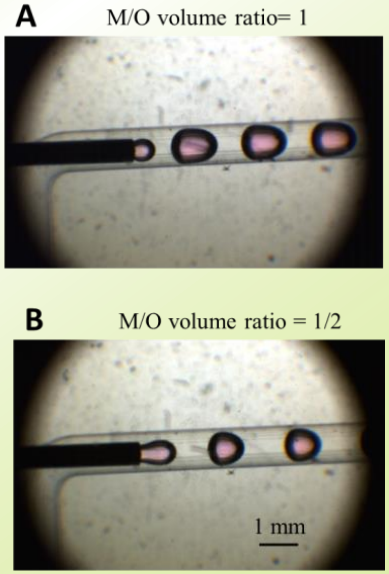
High-throughput Biodiesel Transesterification Device using the Droplet-based Co-axial Fluidic System

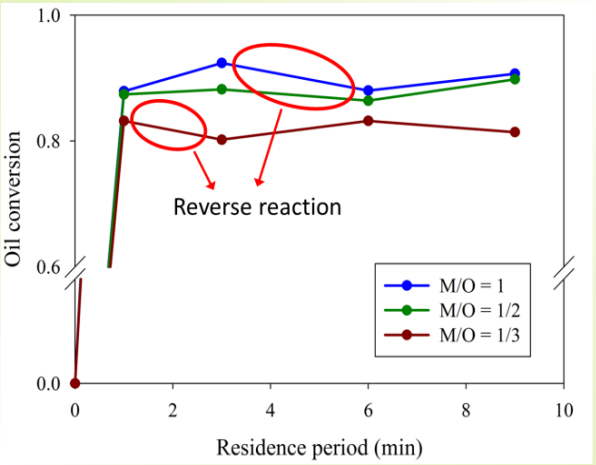
S. I. Yeh, Y. C. Huang, C. H. Cheng, C. M. Cheng, and **J. T. Yang***

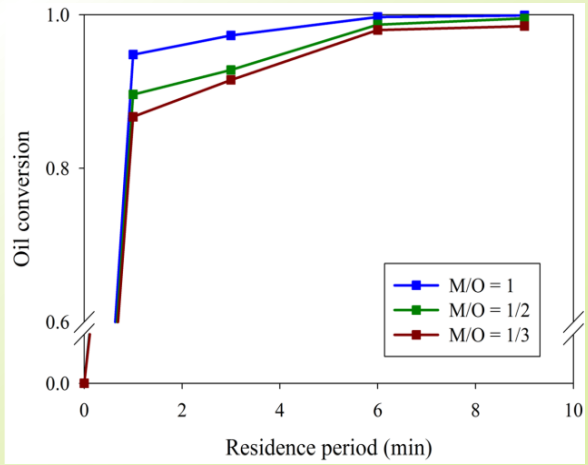
μTAS-2014, San Antonio, USA, October, 2014 *(submitted);* 第12屆國家新創獎- 2015

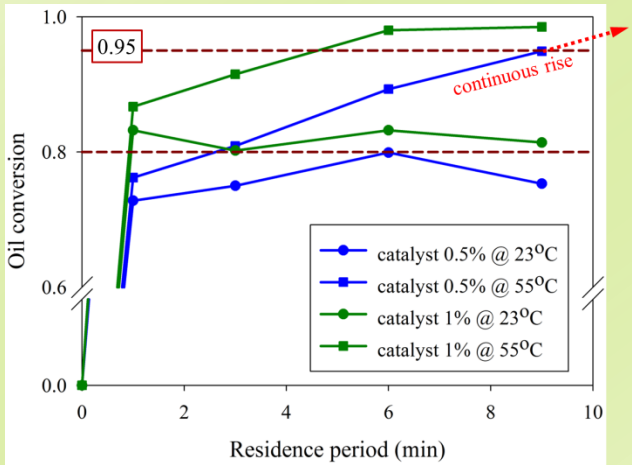










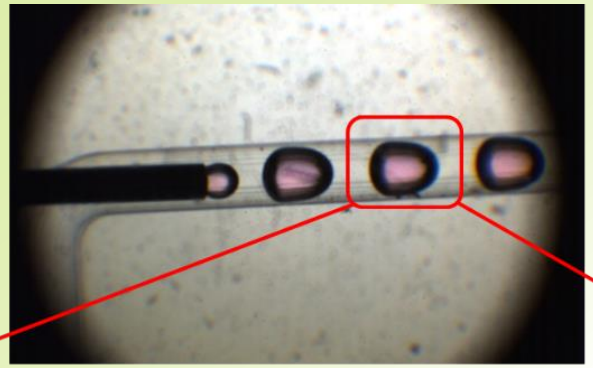


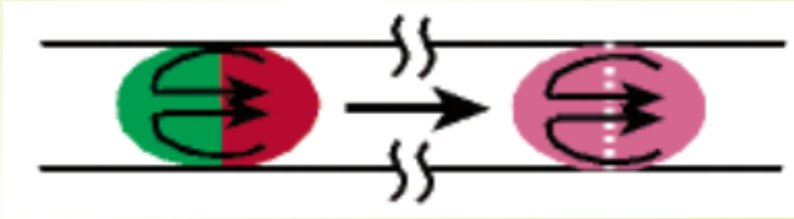
Separation and Purification of Biodiesel by a Millifluidic System

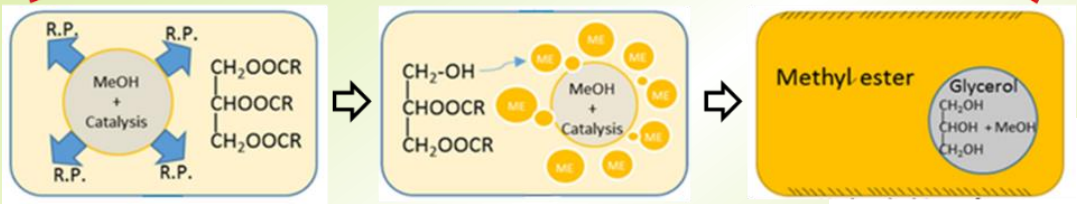
(in progress)

Key Techniques

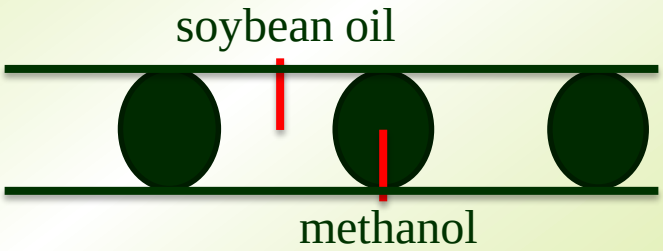
1. Droplet-based rapid reaction device

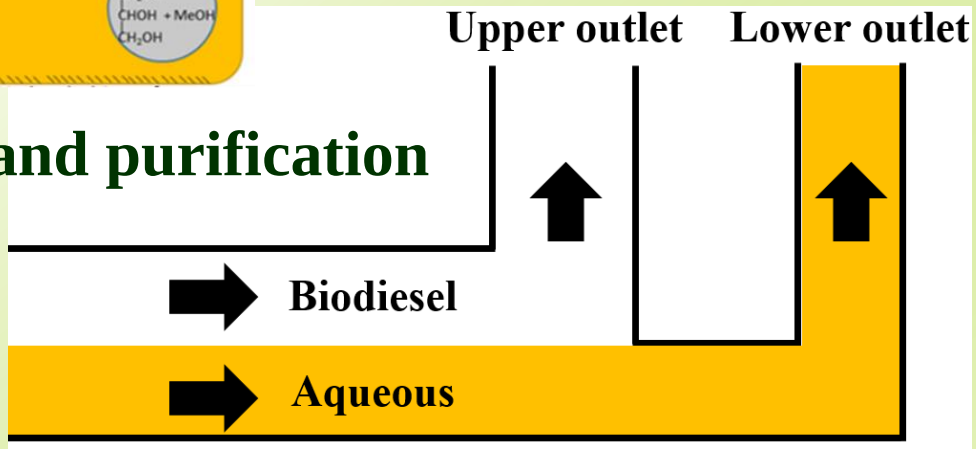






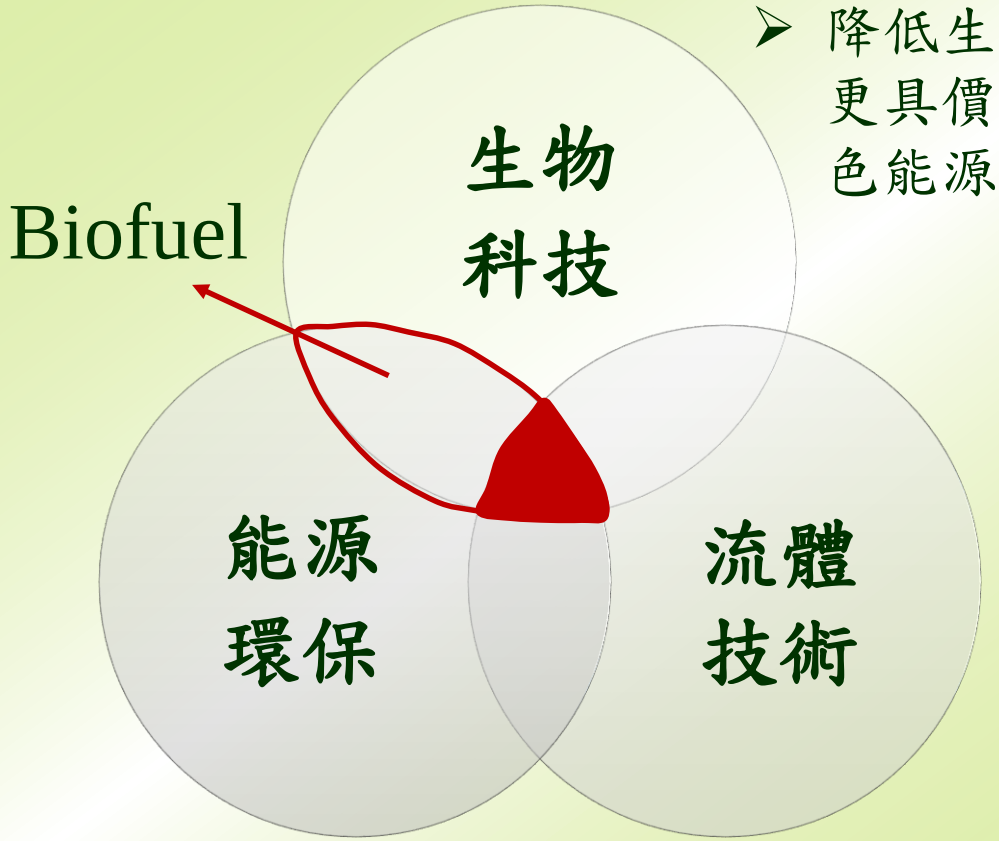
2. Passive device for separation and purification





重要創新與突破

創新的液珠式生質柴油產製系統



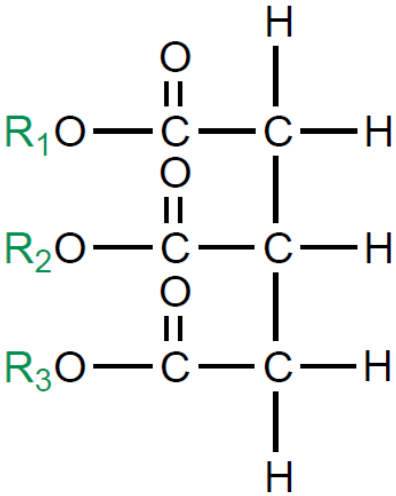
- 降低生質燃料產製成本，使其更具價格競爭力，突破目前綠色能源發展的主要瓶頸

- ☑ 液珠式流體反應元件，具有高面積與體積比之反應優勢
- ☑ 液珠具有易操控之特性可進行後續分離與純化
- ☑ 本系統可在常溫/中溫下高速率進行生質柴油產製

Biodiesel

◆ Biodegradable

Transesterification

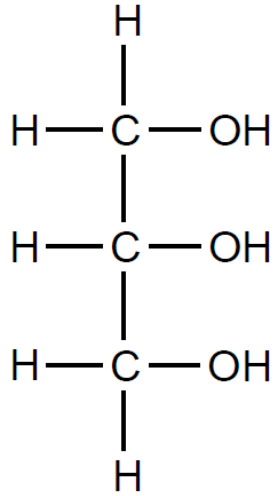


Triglyceride
(Soybean oil)

Traditional industrial methods for biodiesel production

- Need continuous stirring
- High temperature and pressure
- High energy consumption
- Take several days

3 3 3 +



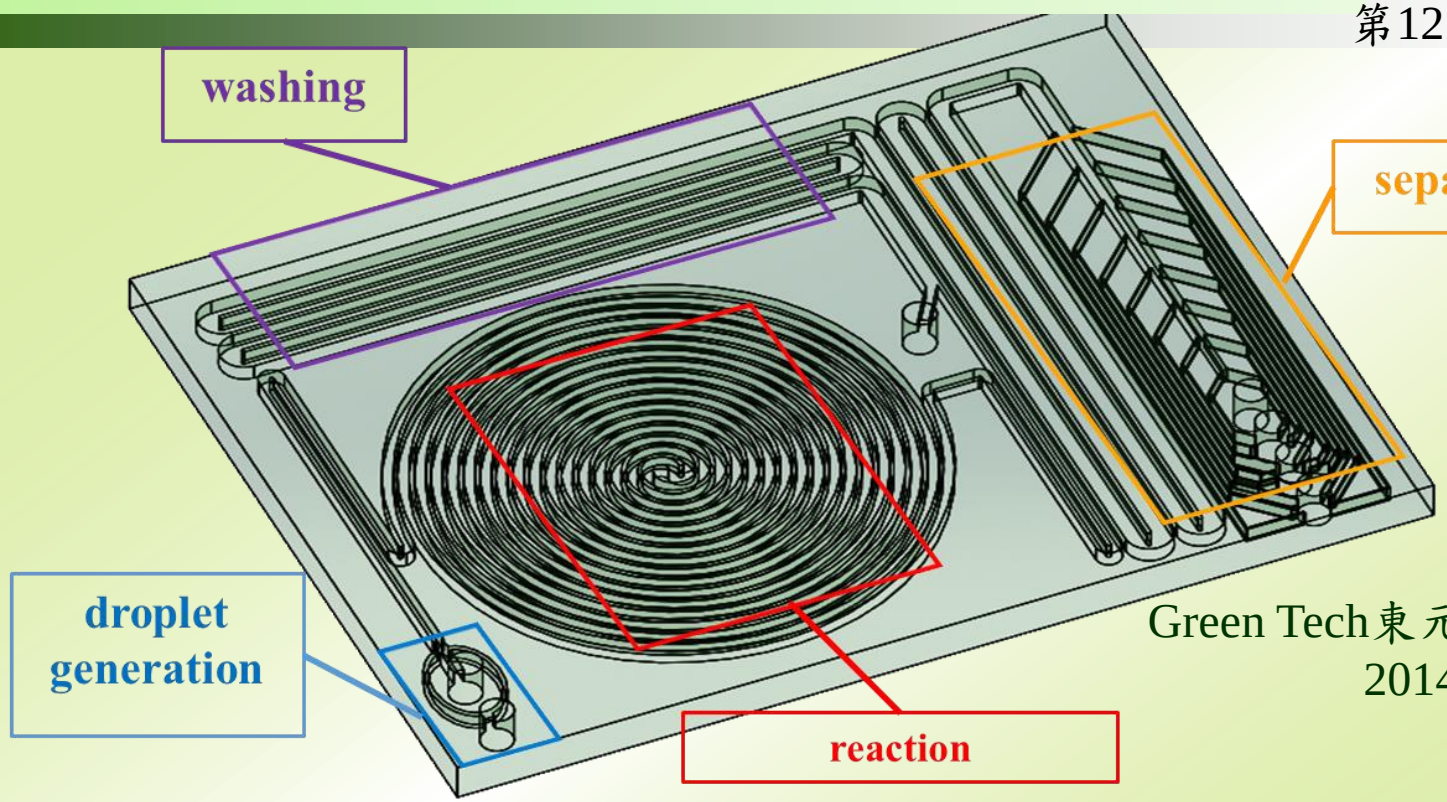
Methanol

Biodiesel
(880 kg/m^3)

Glycerol
(1260 kg/m^3)

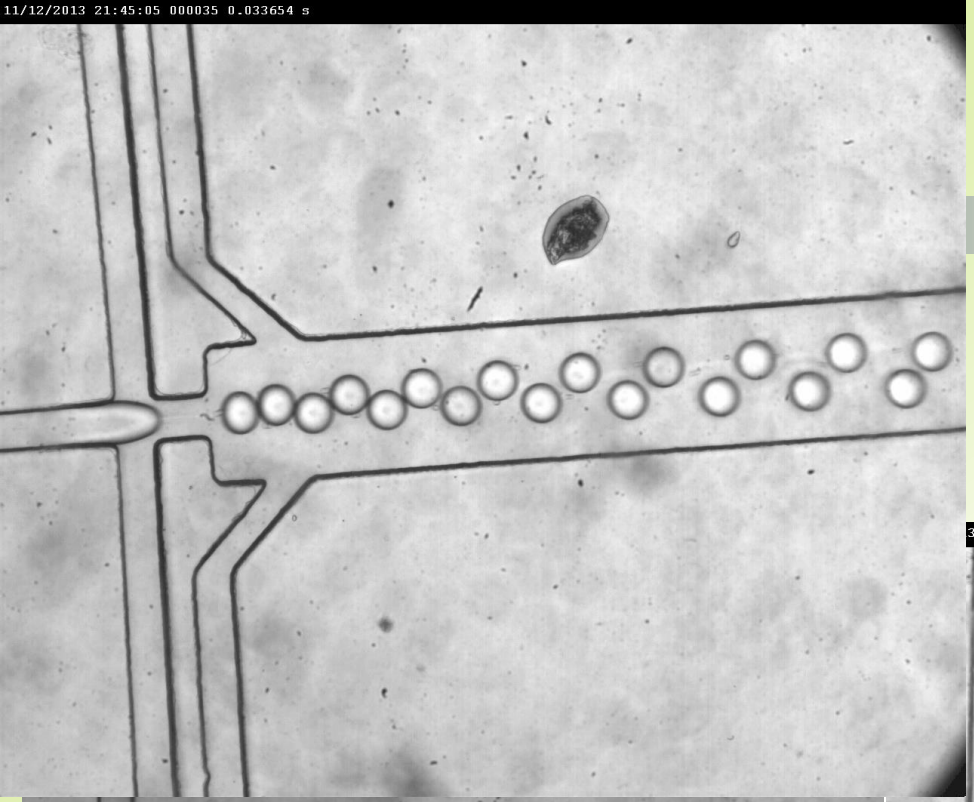
Biodiesel Producion Chip

第12屆國家新創獎



Green Tech東元科技創意競賽
2014 亞軍、人氣獎

- **Faster reaction characteristic**
- **Inputs of raw materials, outputs of available products**
- **Low energy consumption and easy operation**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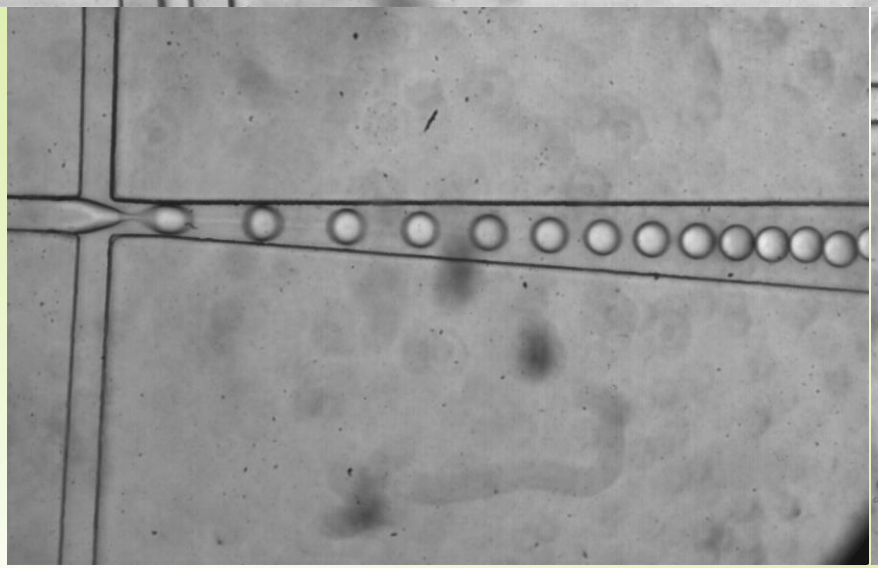

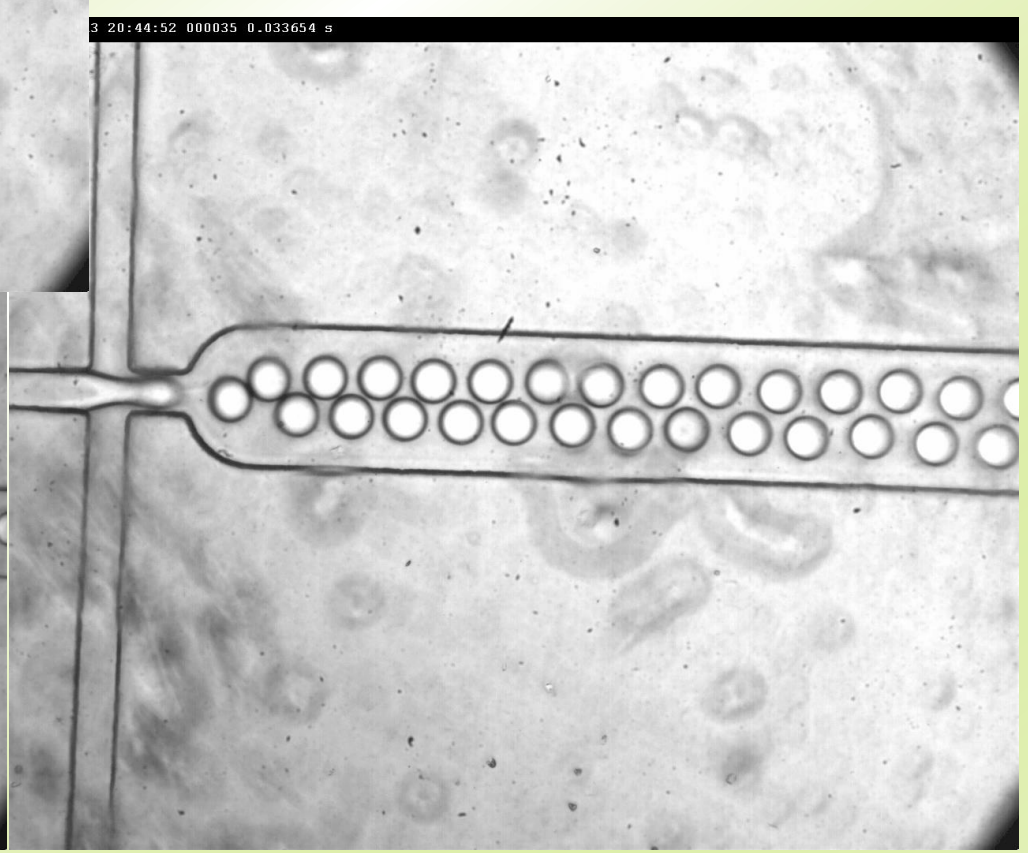
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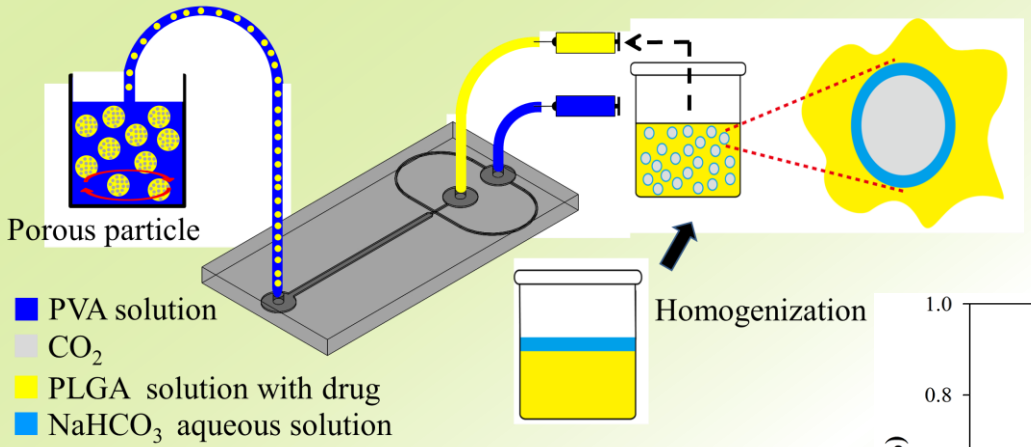
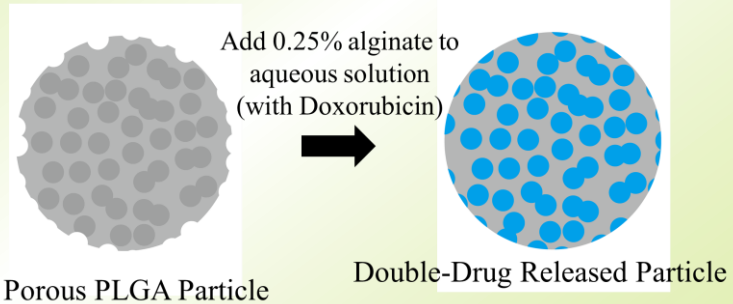
Microencapsulation of Dual-release PLGA Microparticle for Curcumin and Doxorubicin Released in Stages

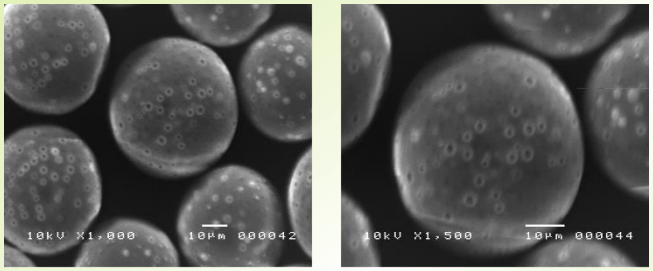
S. I Yeh, K. H. Yang, and **J. T. Yang***

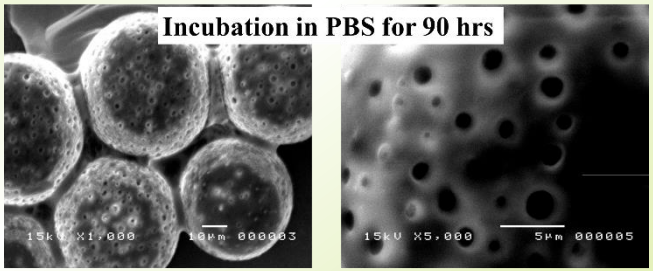
※Cooperating with NHRI

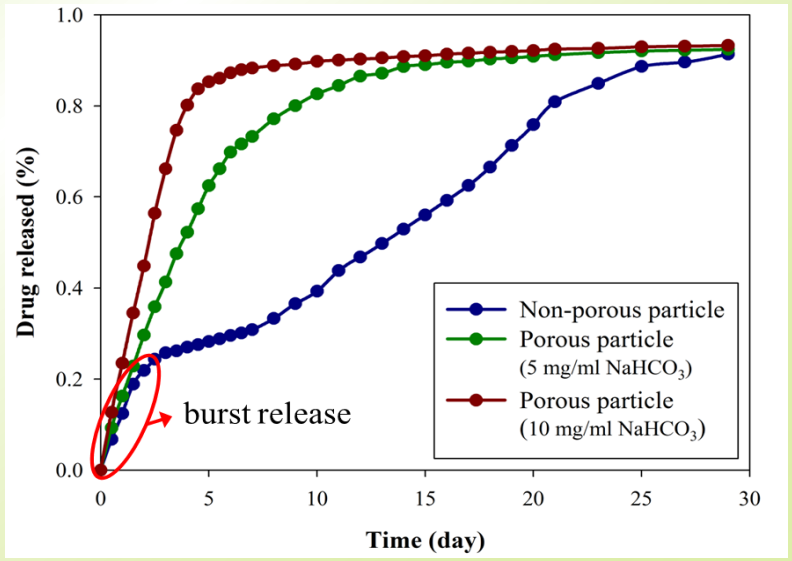
μTAS-2015, Gyeongju, Korea, October, 2015











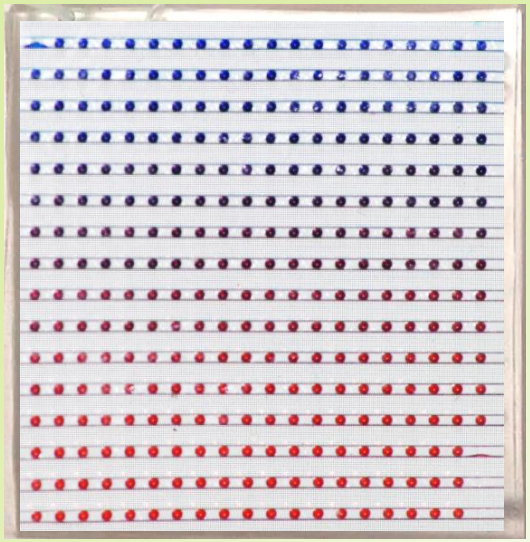
The dual-release of curcumin and doxorubicin would decrease the cardiotoxicity of chemotherapy drugs which is highly serviceable in cancer therapeutics and the clinical management of intractable diseases.

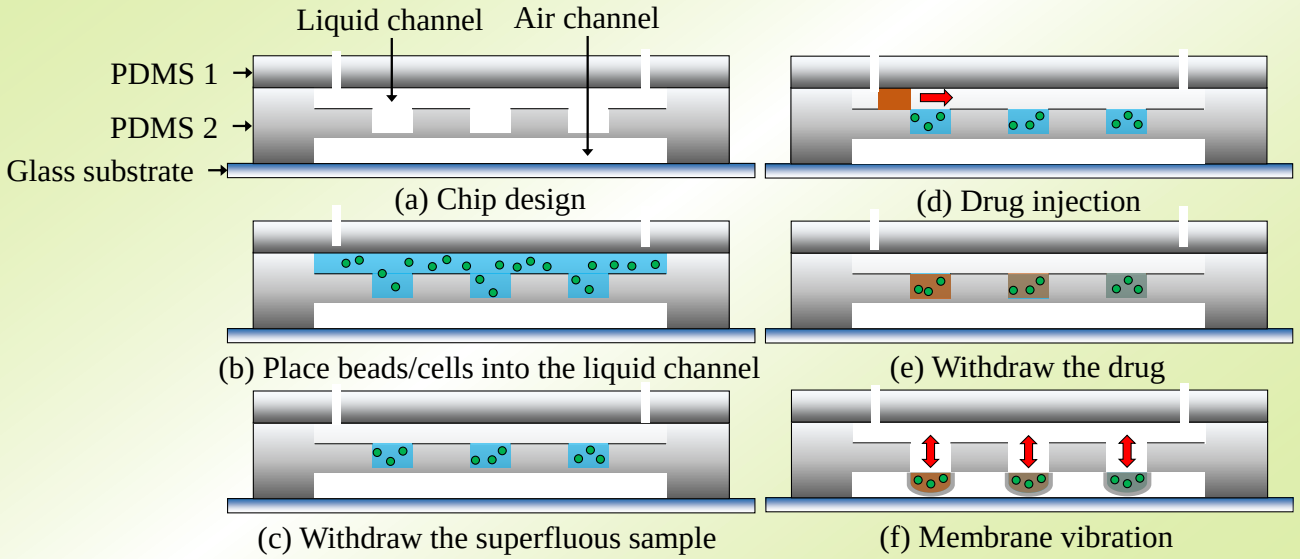
Microencapsulation of Dual-release PLGA Microparticle for Curcumin and Doxorubicin Released in Stages

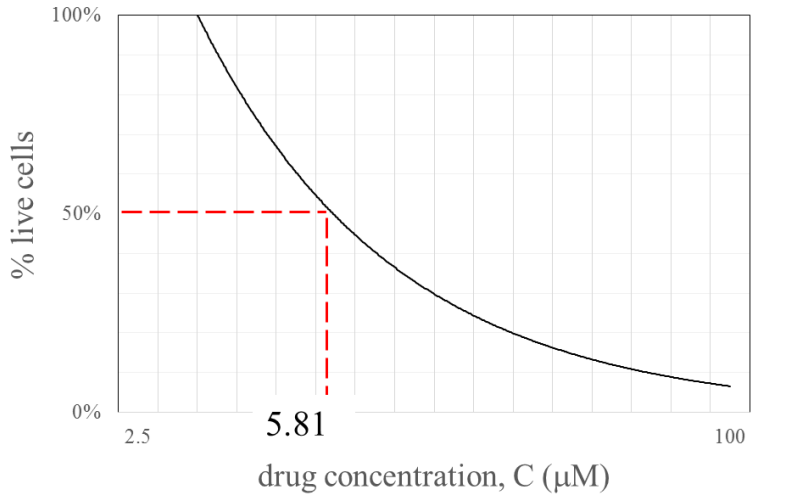
S. I Yeh, C. C. Hau, C. J. Huang and **J. T. Yang***

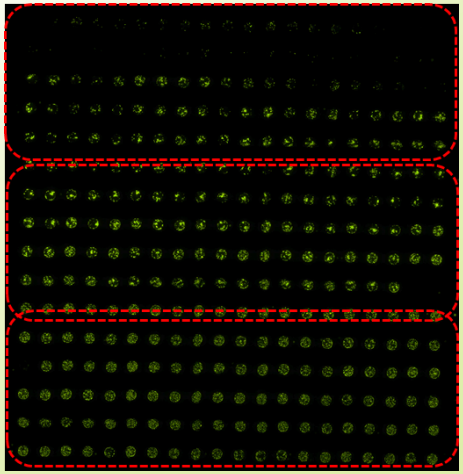
μTAS-2014, San Antonio, USA, October, 2014

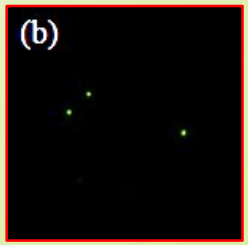
※Cooperating with NTUH

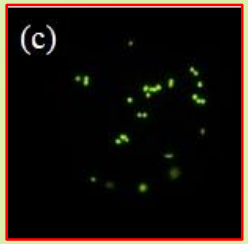


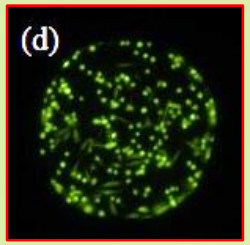




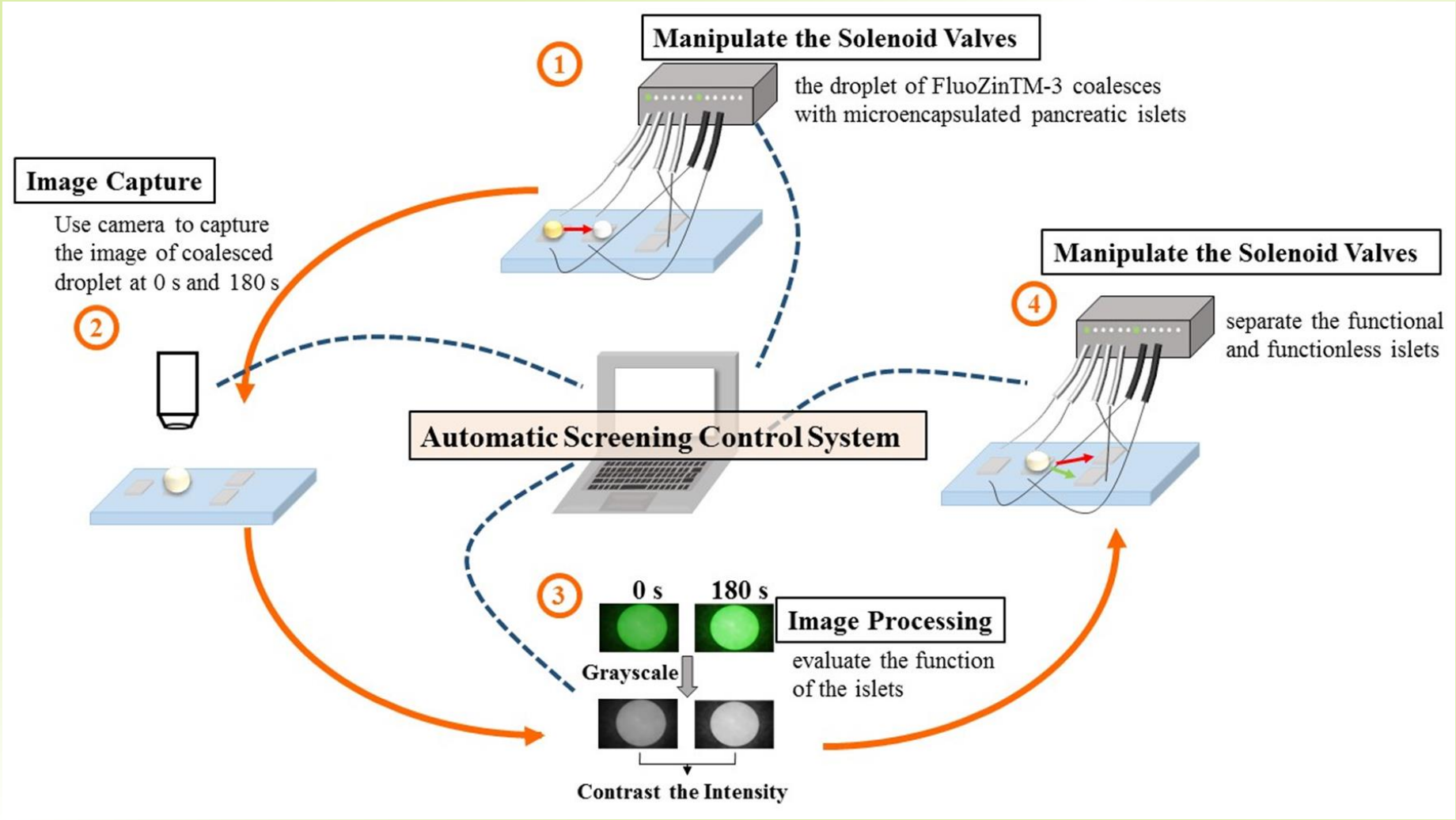






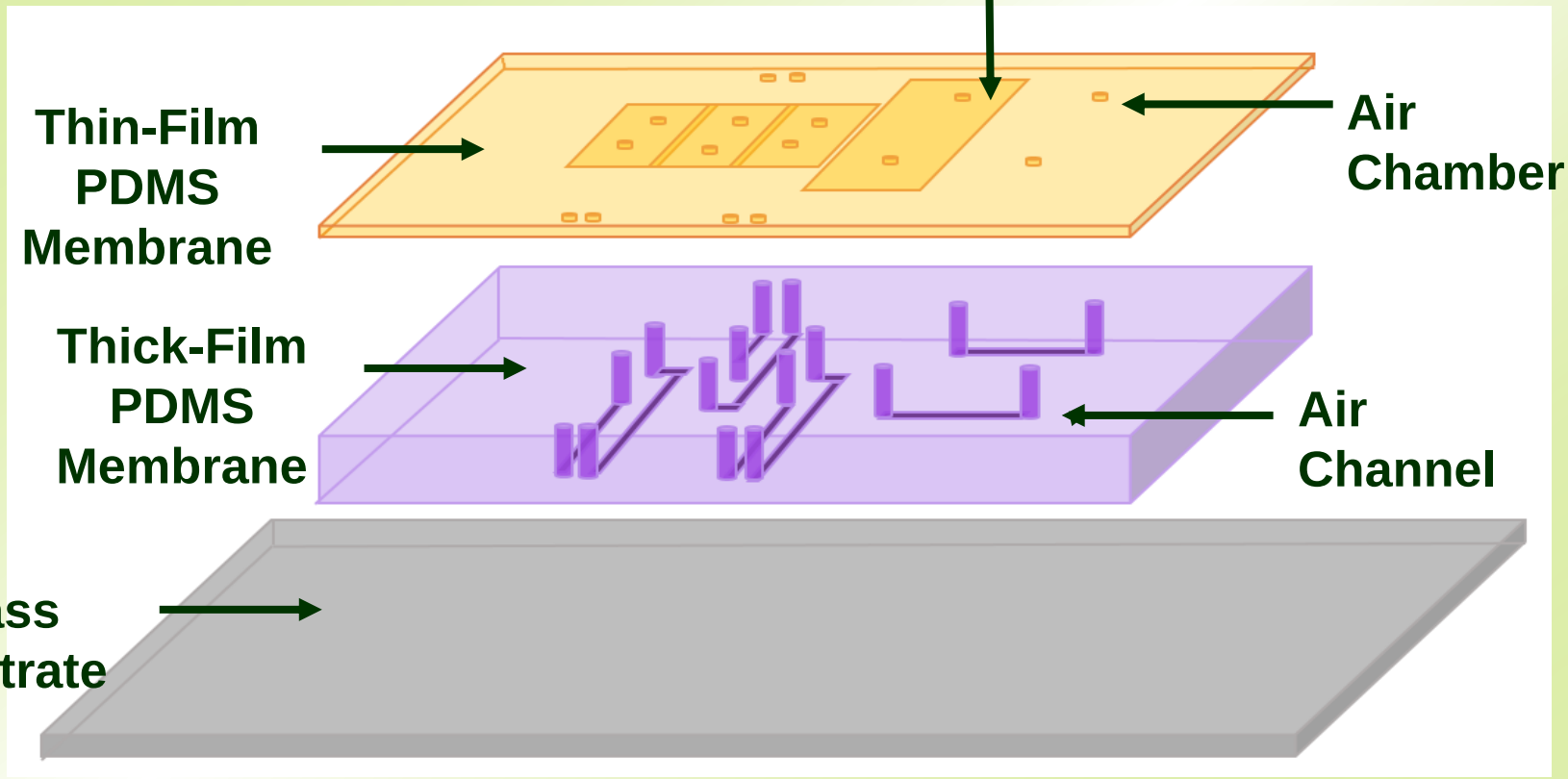


Assessment of Insulin Release Rate and Screening of Islet Cells on a Droplet-Manipulation Platform

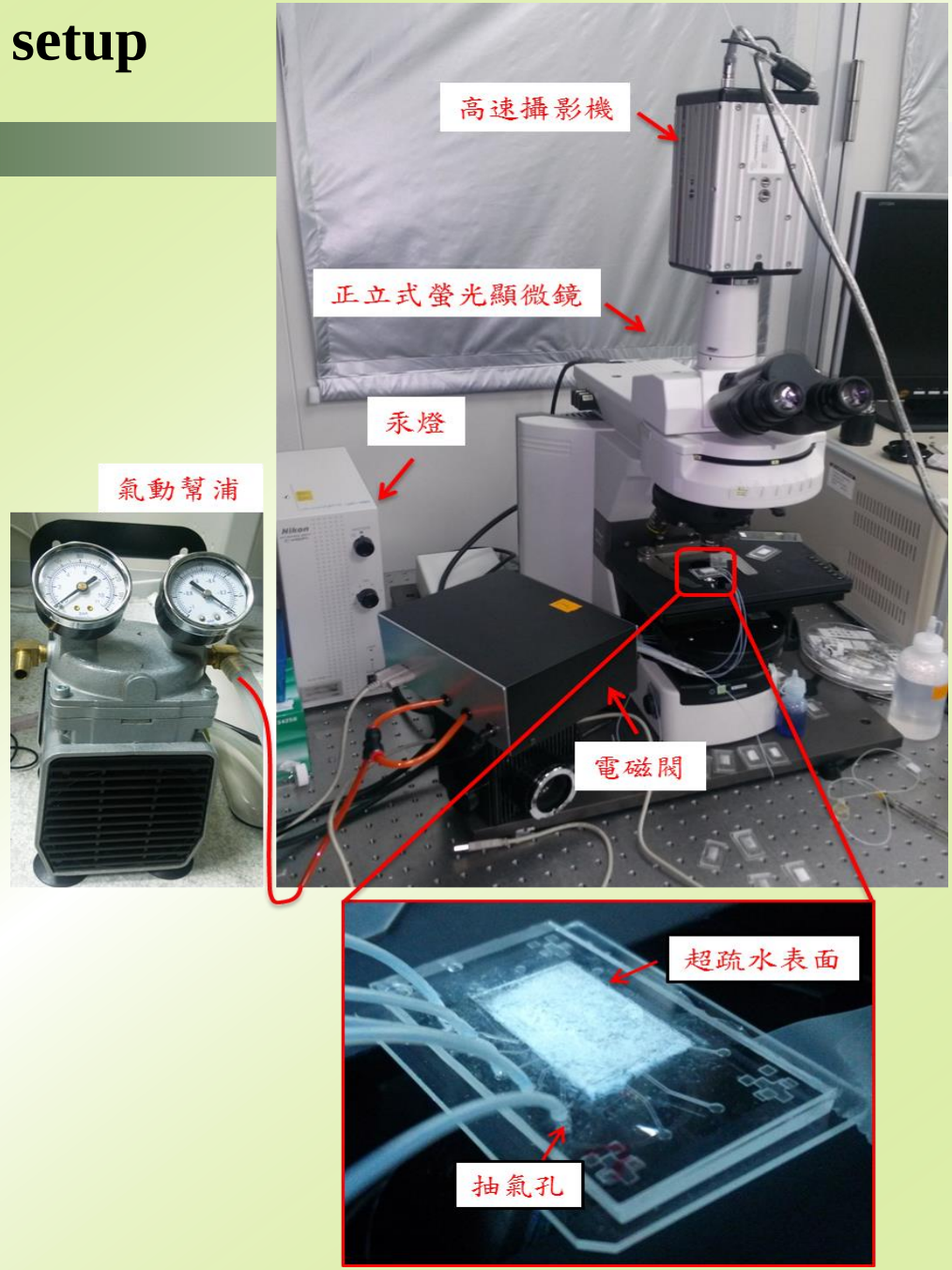


Development of an Automatic Screening System for Islet Function

Chip Design



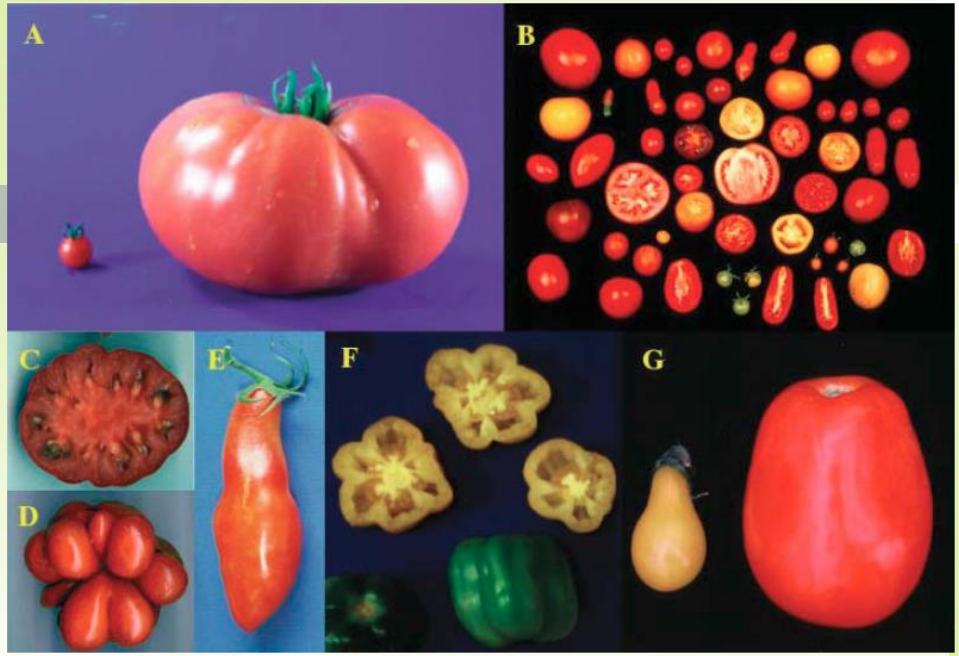
Experimental setup



Tomato & Orchid

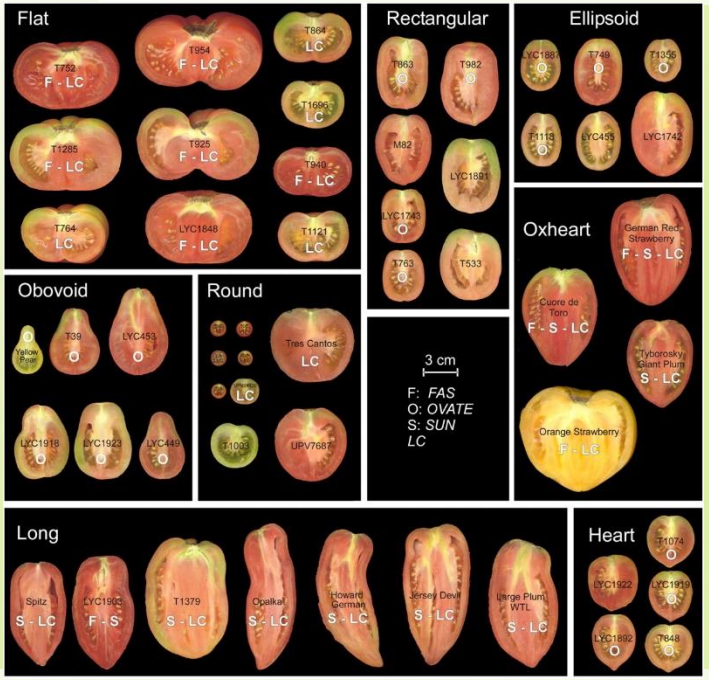
http://juliesgardendelights.com/how-to-grow-184-varieties-of-heirloom-tomatoes-from-seed/

http://gizmodo.com/5917046/what-color-were-tomatoes-before-the-dinosaurs-all-died



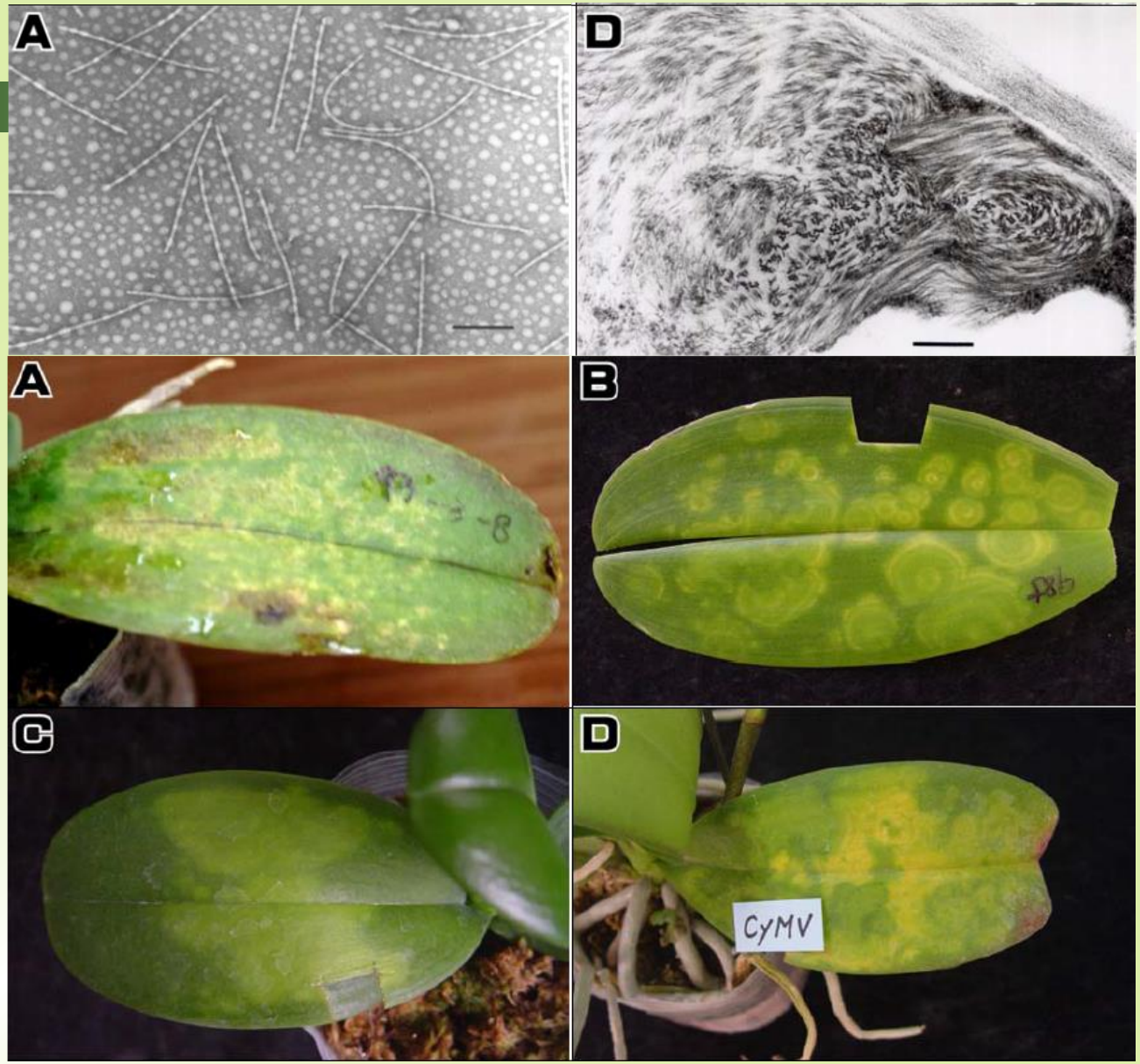
Tanksley ***Plant Cell*** 16 (2004):S181-S189.

Zhang *et al*. ***Nat. Commun.*** 6 (2015):8635.



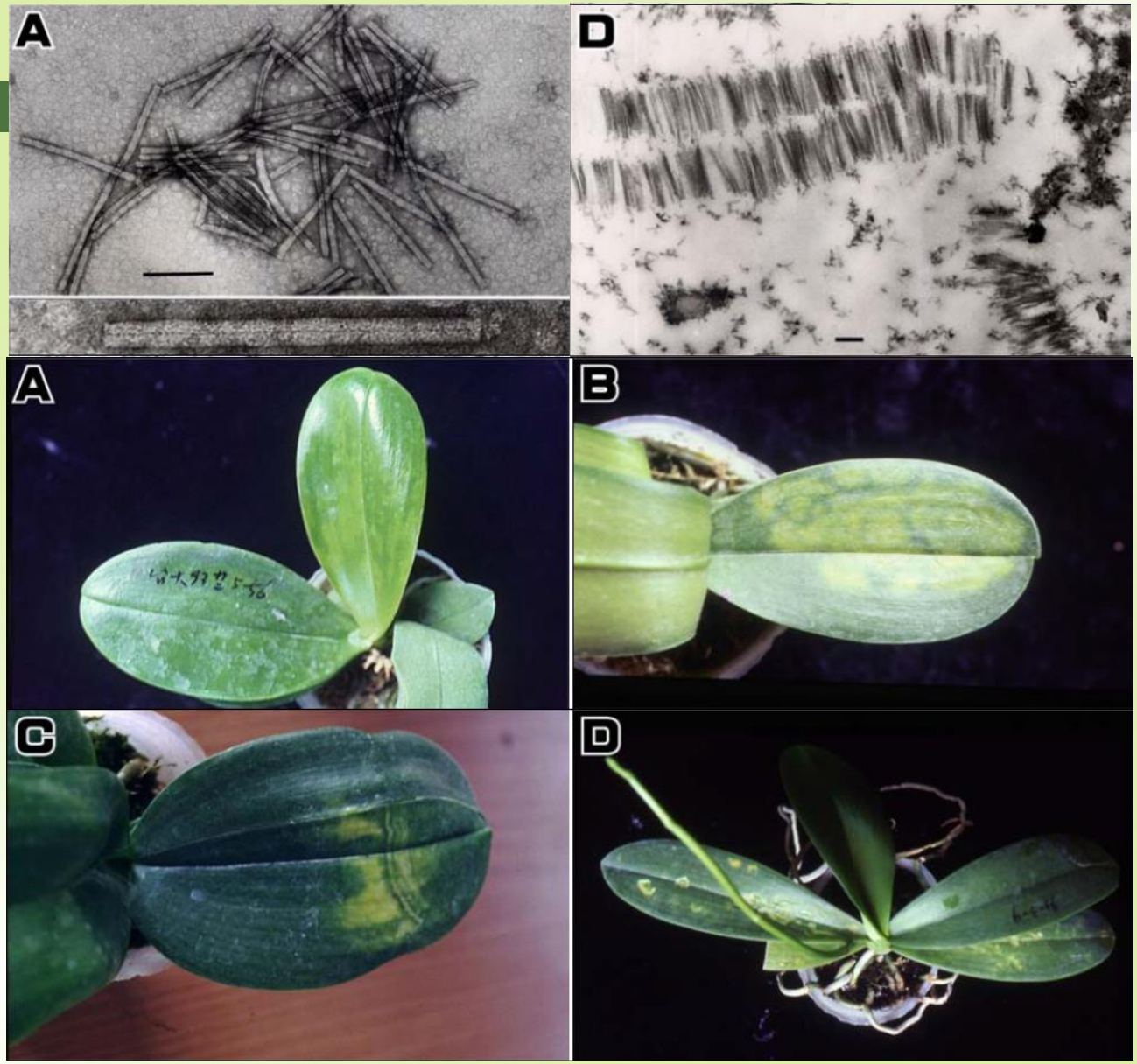
Rodríguez *et al*. ***Plant Physiol.*** 156 (2011):275-285.

CymMV (*Cymbidium mosaic virus*)蕙蘭嵌紋病毒



陳慶忠等 (2006) 齒舌蘭輪斑病毒及蕙蘭嵌紋病毒感染蝴蝶蘭之病徵學及細胞病理學探討。臺中區農業改良場研究彙報93:15-27。

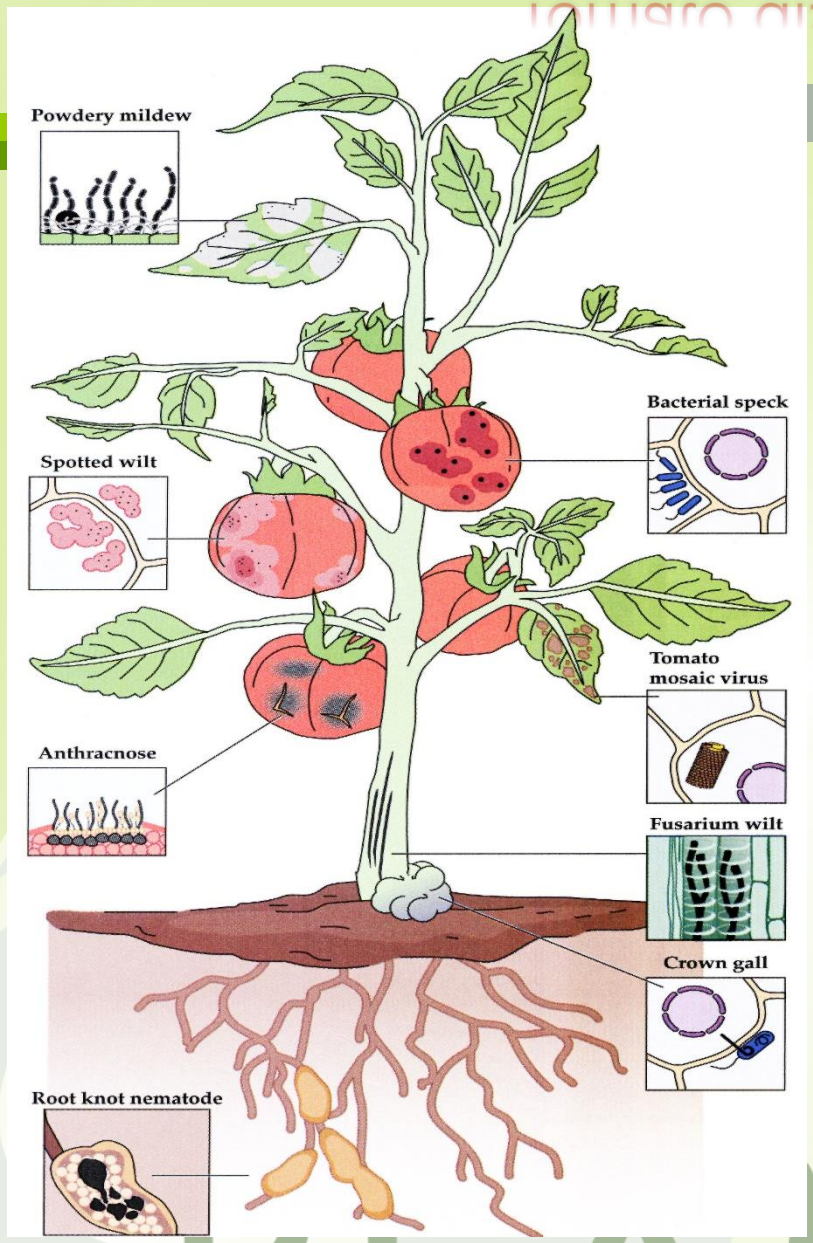
ORSV (*Odontoglossum ringspot virus*) 齒舌蘭輪斑病毒



陳慶忠等 (2006) 齒舌蘭輪斑病毒及蕙蘭嵌紋病毒感染蝴蝶蘭之病徵學及細胞病理學探討。臺中區農業改良場研究彙報93:15-27。

番茄的病毒病主要有番茄嵌紋病毒病、胡瓜嵌紋病毒病、馬鈴薯Y病毒病、番茄斑點萎凋病毒病及**番茄捲葉病**毒病。番茄捲葉病毒病由**Tomato leaf curl virus (TLCV)**或**Tomato yellow leaf curl virus (TYLCV)**所引起，是番茄主要病害之一，病毒感染後造成葉片黃化及捲曲等病徵，所造成番茄經濟損失可高達百分之百。番茄捲葉病毒病只經由一種媒介昆蟲即**銀葉粉蝨**(*Bemisia argentifolii*)傳播，銀葉粉蝨密度越高，番茄捲葉病毒病發生越嚴重。

Tomato disease diagnosis



cf. Buchanan *et al.* (2000) *Biochemistry and Molecular Biology of Plants* pp. 1104 Figure 21.3

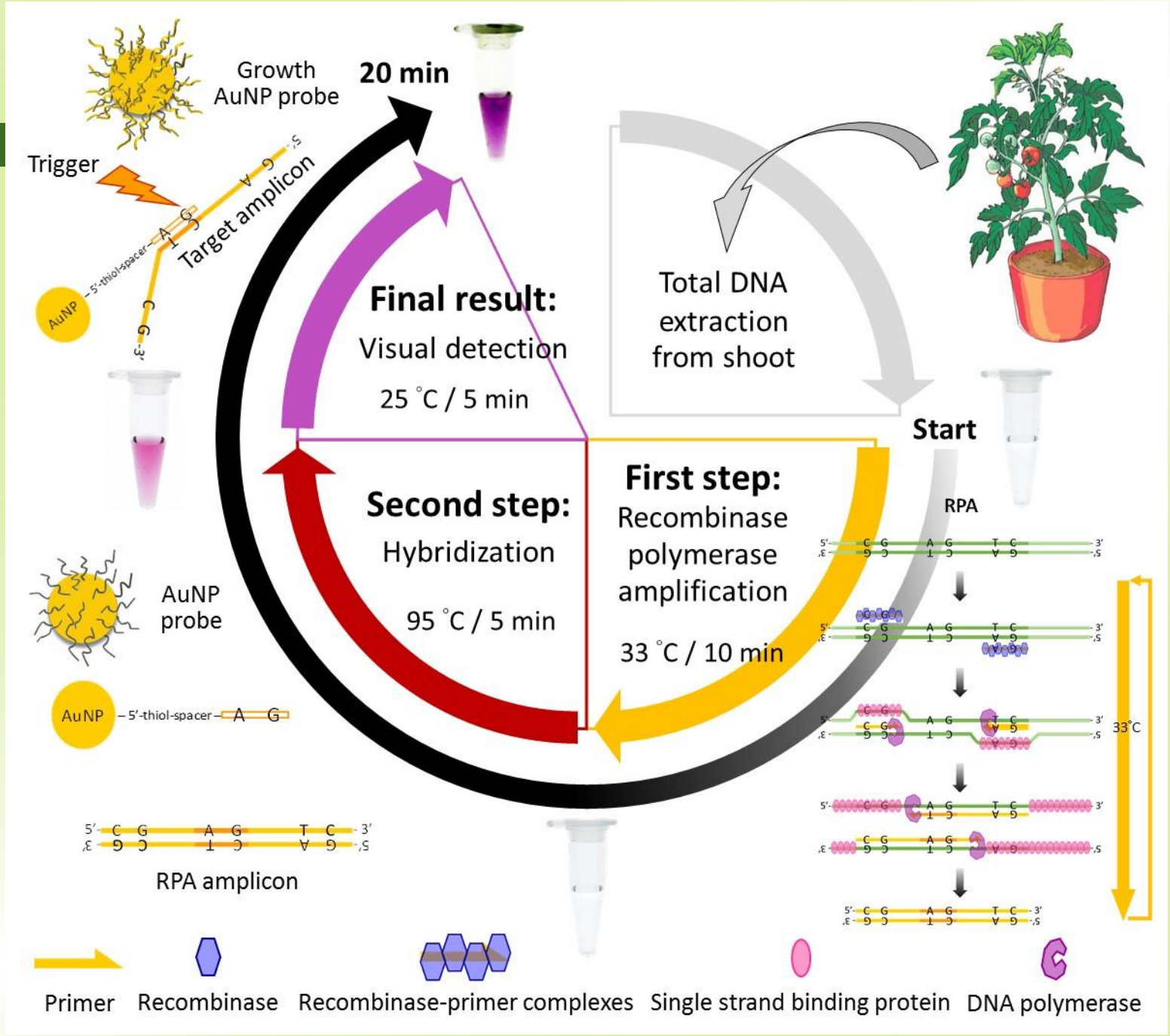
The symptoms applied to monitor tomato diseases are following as below:

1) Problems on leaves
   dark, gray, or white spots; yellowed or mottled foliage; curled leaves

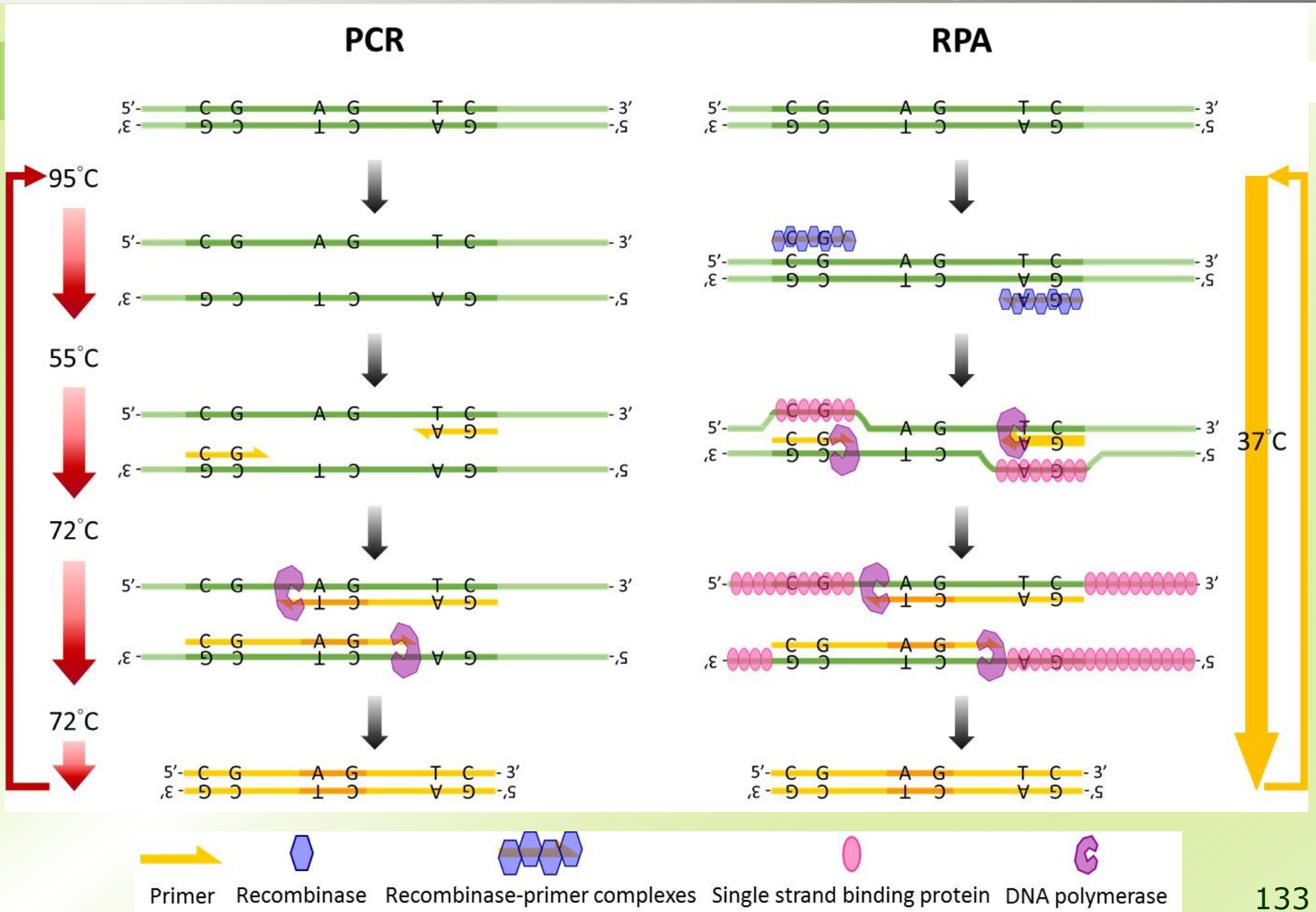
2) Problems on stems
   mushiness, dark, gray, or discolored streaks, mold, stunted growth

3) Problems at the crown
   formations at the plant crown, rotting roots

4) Problems on fruit
   sunken or discolored spots, mottled skin, mold, misshapen or undeveloped fruit

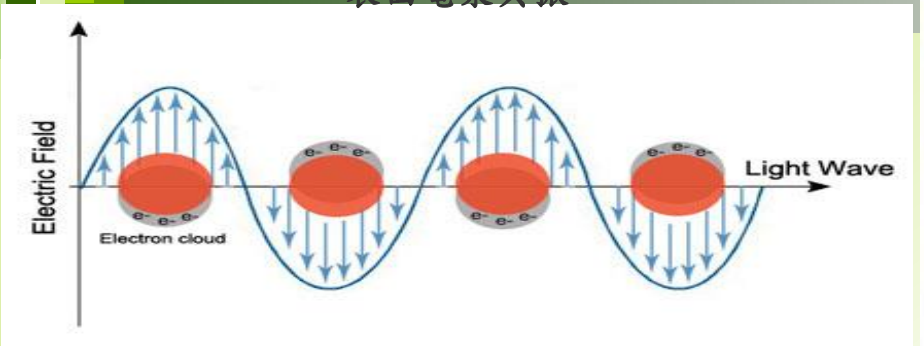

Growth
AuNP probe
20 min
Trigger
Target amplicon
AuNP
– 5'-thiol-spacer –
Total DNA
extraction
from shoot
Start
Final result:
Visual detection
25 °C / 5 min
First step:
Recombinase
polymerase
amplification
33 °C / 10 min
Second step:
Hybridization
95 °C / 5 min
RPA
AuNP
probe
AuNP – 5'-thiol-spacer – A G
33°C
RPA amplicon
Primer
Recombinase
Recombinase-primer complexes
Single strand binding protein
DNA polymerase

Introduction of recombinase polymerase amplification (RPA)



Basic concept of gold nanoparticles (AuNPs)

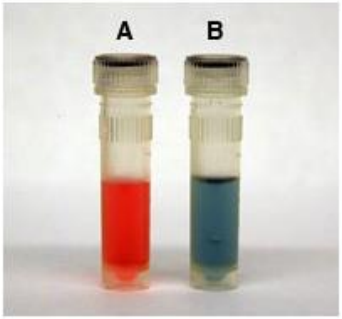
Surface plasmon resonance (SPR)
表面電漿共振

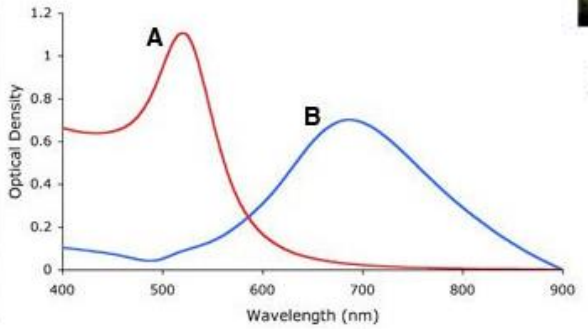


Different sizes of colloidal AuNPs

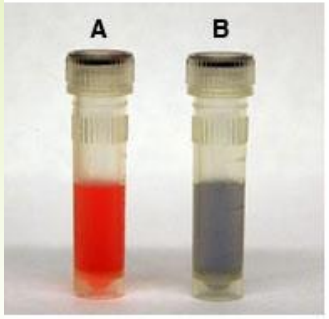
https://www.meritnation.com/ask-answer/question/how-does-size-of-particles-effect-the-colour-of-gold-sol/surface-chemistry/5788885

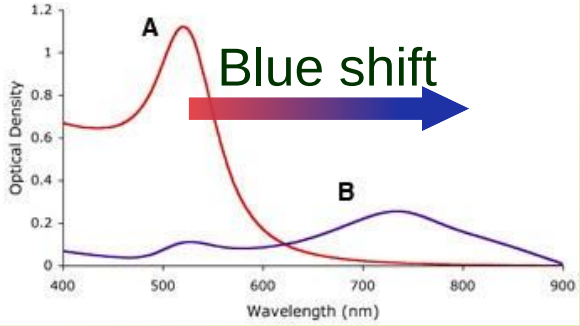
Different sizes and sharps of AuNPs





Aggregation state of AuNPs





http://www.cytodiagnostics.com/store/pc/Gold-Nanoparticle-Properties-d2.htm

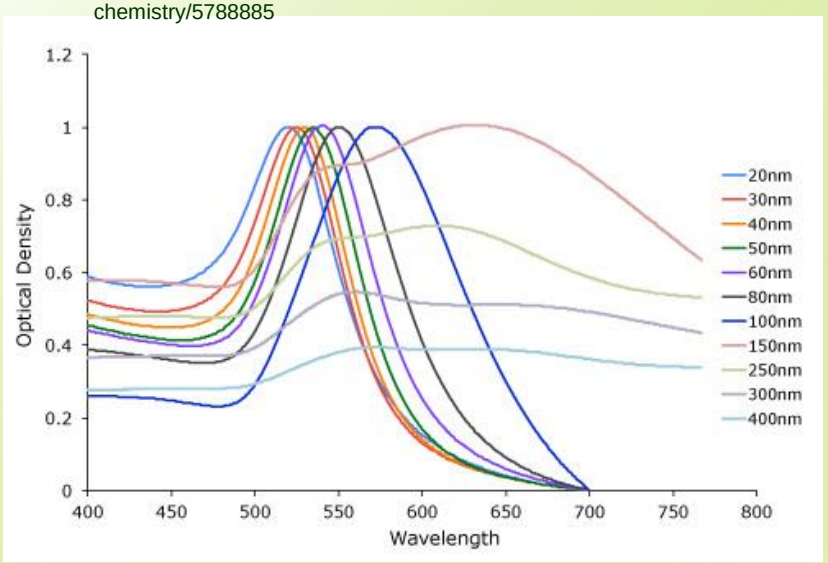
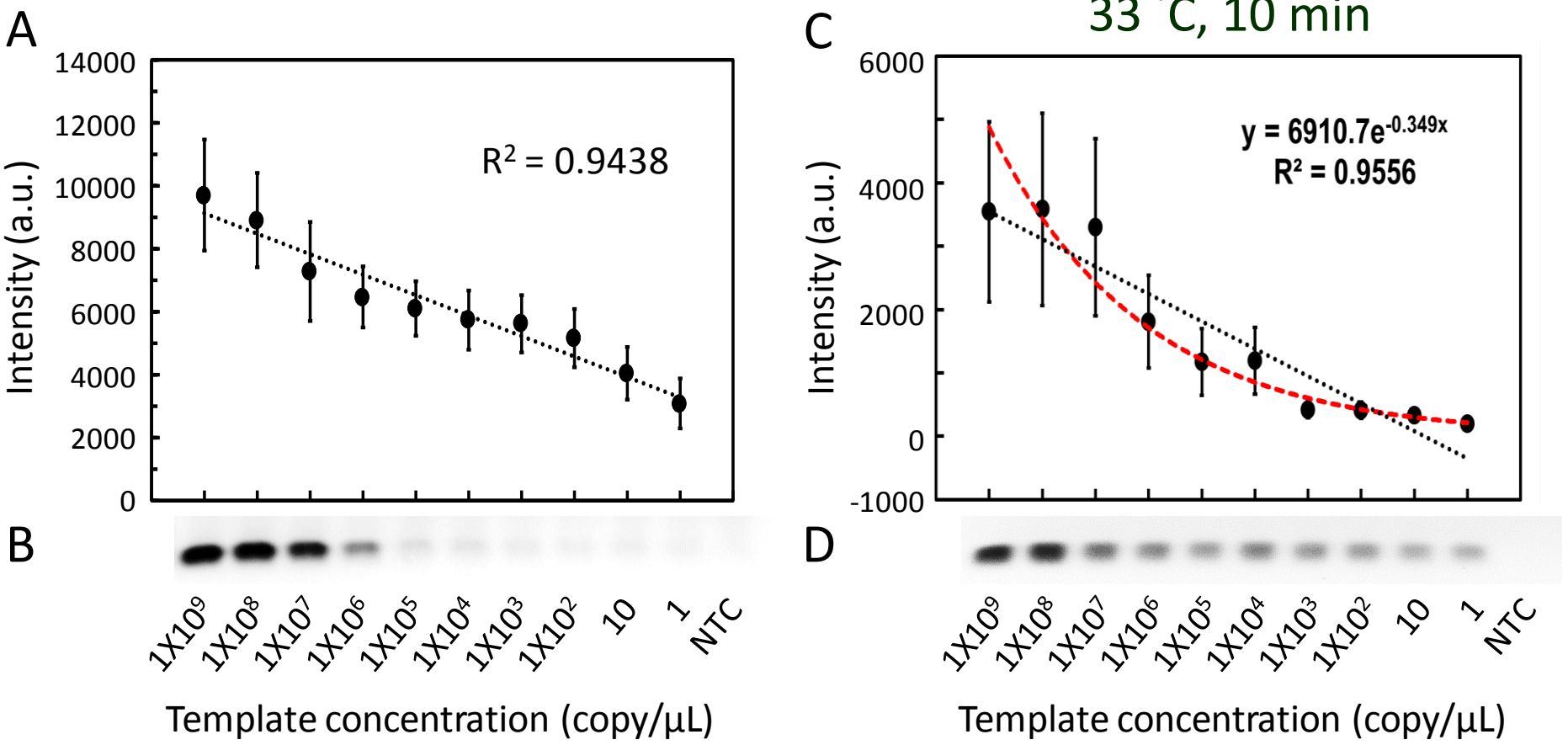


Figure 2. *Gold nanoparticle size dependant surface plasmon resonance. Note the red-shift of the absorption maximum as the gold nanoparticle size increases.*

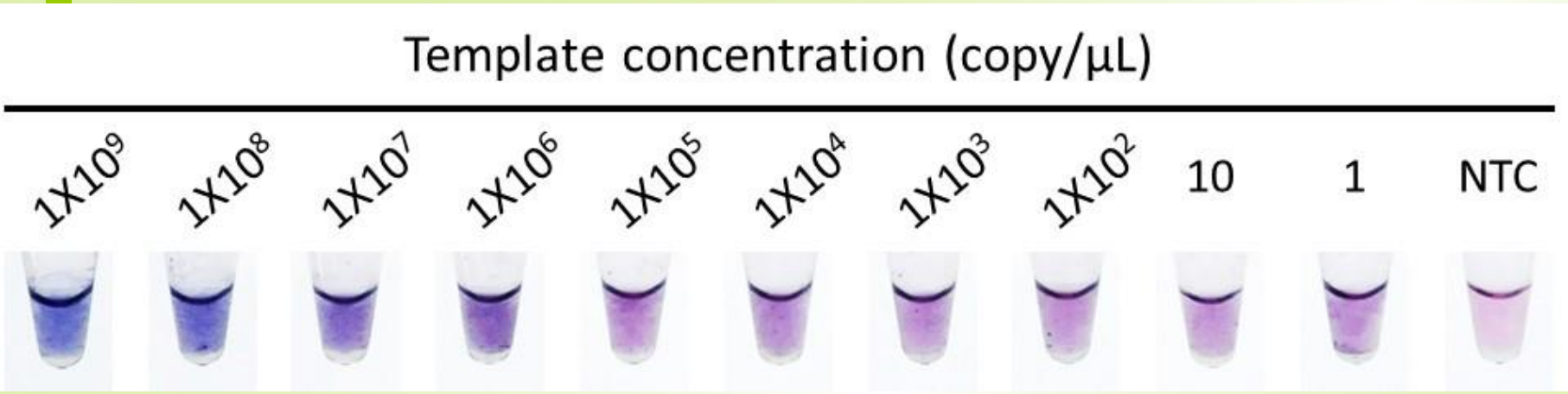
Sensitivity of amplification effect

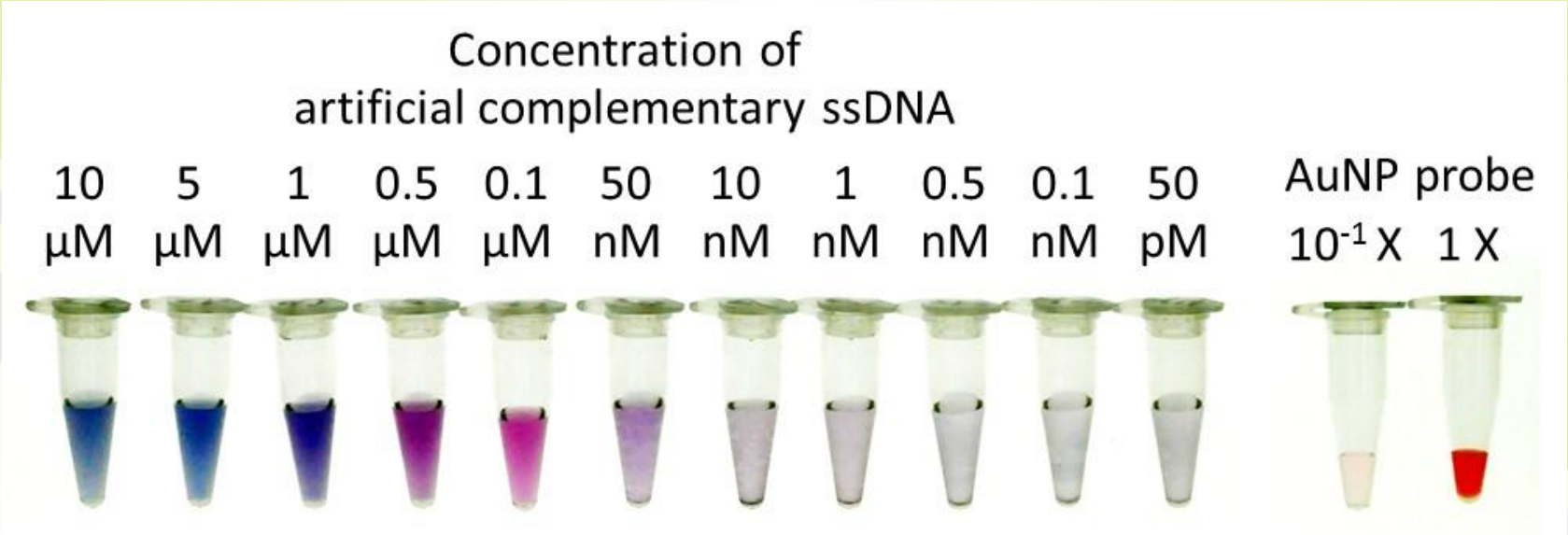
Conventional PCR (10 μL)

RPA (4 μL)
33 °C, 10 min



Sensitivity of colorimetric assay



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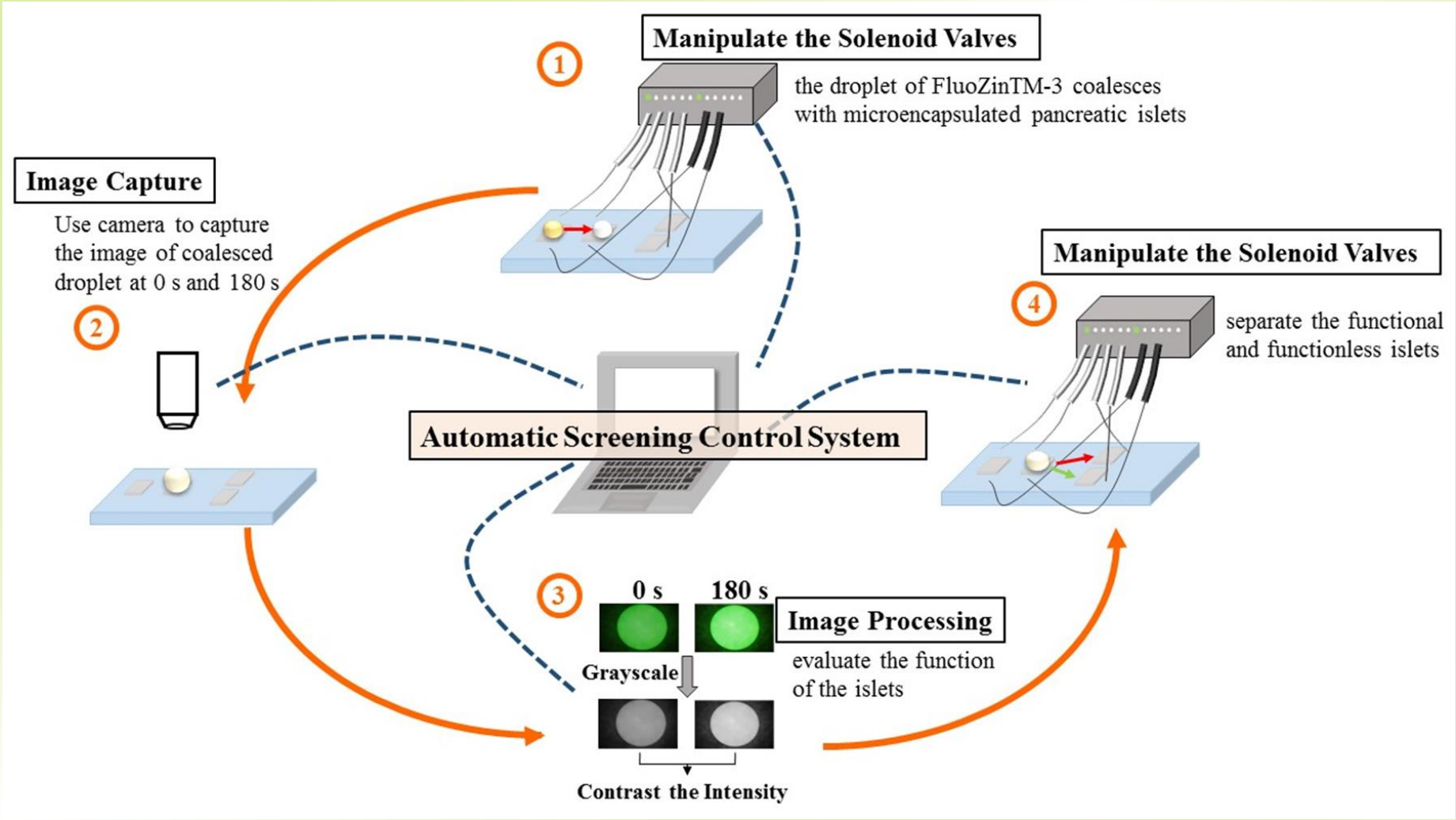


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