國立台灣大學 應用力學研究所實驗室晶片導論

Droplet-Based Biochips

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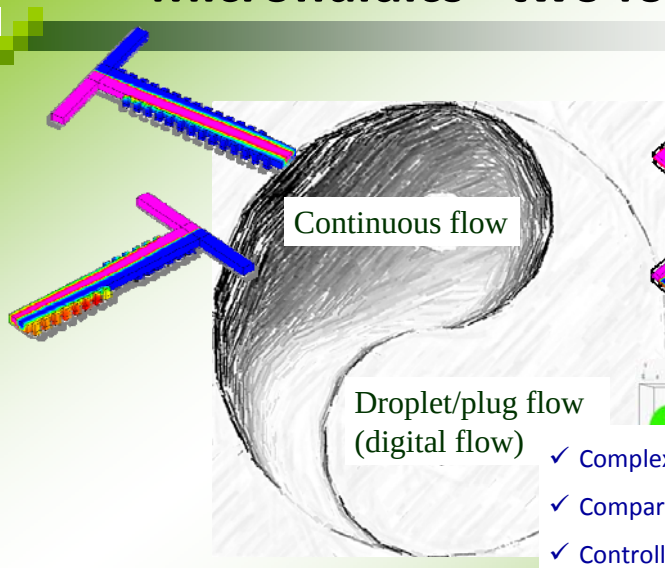
中華民國 一百零二年 三 月十九日

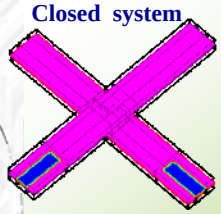
Microfluidics– two folds



Continuous flow

Droplet/plug flow
(digital flow)

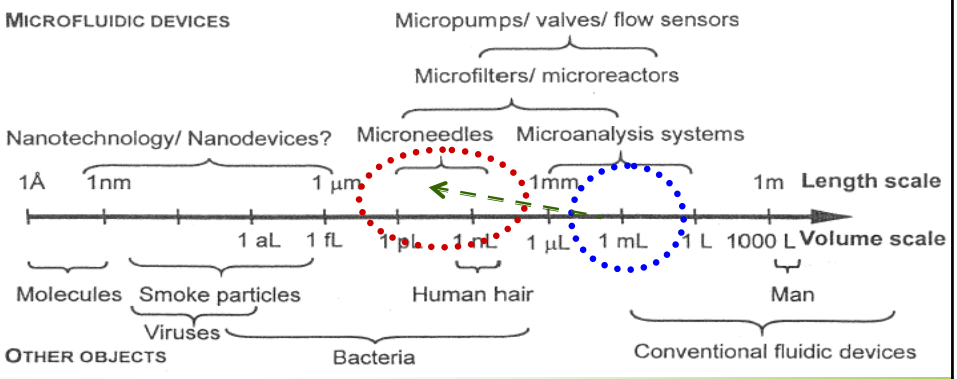
Closed system



Open system

- ✓ Complexity
- ✓ Compartmentalization/isolation
- ✓ Controllability
- ✓ Charm

What is the volume of a droplets ?



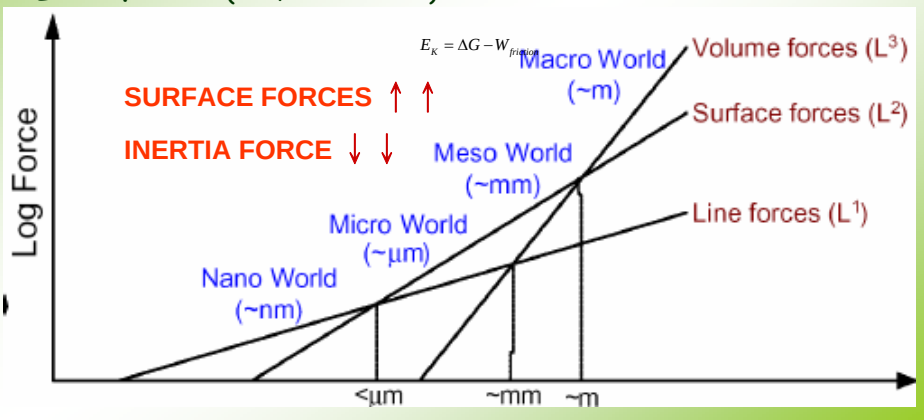
Nguyen and Wereley, 2003

微尺度效應

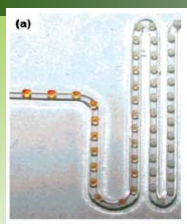
Volume force (mass) ~ d^3

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

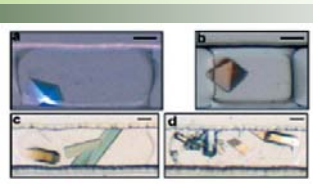
Line force (surface tension) ~ d^1



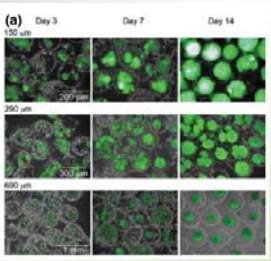
Droplet Applications



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



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



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

Drug discovery

Chemical reactions

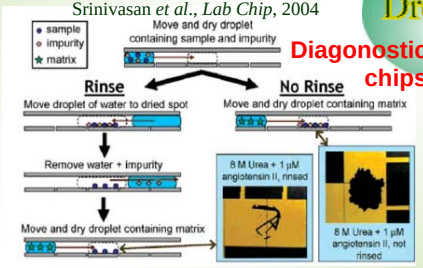
Therapeutic agent delivery

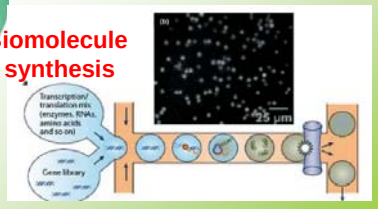
Droplet

Diagonostic chips

Biomolecule synthesis

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



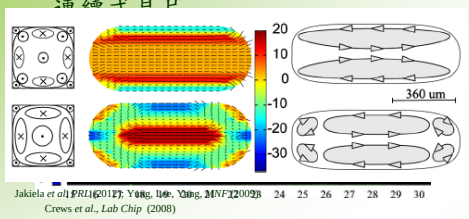


(a) Dittrich *et al.*, *Nat. Rev. Drug Discovery*, 2006
(b) Dittrich *et al.*, *ChemBioChem*, 2005

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

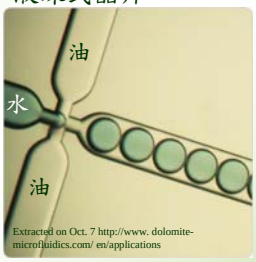
微流體晶片

液珠內流場



Jakiela *et al.*, *PRL* (2012); Yung, Lee, Yang, *MNF* (2009)
Crews *et al.*, *Lab Chip* (2008)

液珠式晶片

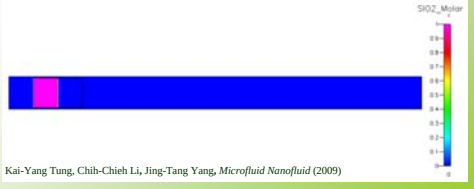


Extracted on Oct. 7 http://www. dolomite-microfluidics.com/ en/applications

液珠式晶片近年來成為主流：

- 試劑量容易調整與量化
- 混合較好、精準度高
- 減少交互汙染疑慮

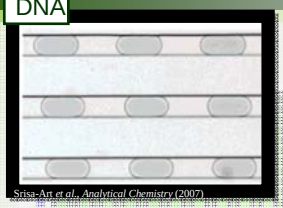
液珠內流場之對稱渦旋



Kai-Yang Tung, Chih-Chieh Li, Jing-Tang Yang, *Microfluid Nanofluid* (2009)

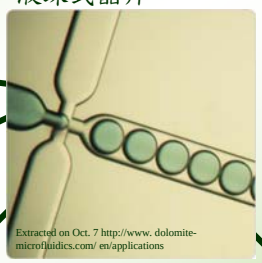
微流體晶片

DNA



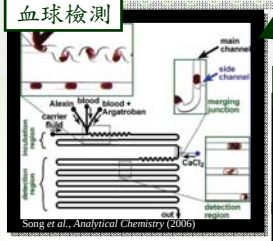
Srisa-Art *et al., Analytical Chemistry* (2007)

液珠式晶片



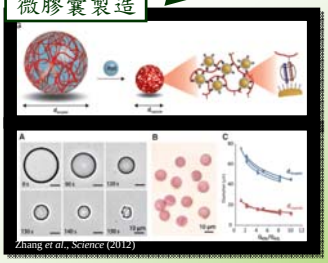
Extracted on Oct. 7 http://www. dolomite-microfluidics.com/ en/applications

血球檢測



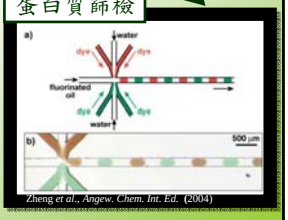
Song *et al., Analytical Chemistry* (2006)

微膠囊製造



Zhang *et al., Science* (2012)

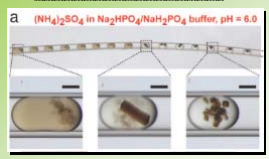
蛋白質篩檢



Zheng *et al., Angew. Chem. Int. Ed.* (2004)

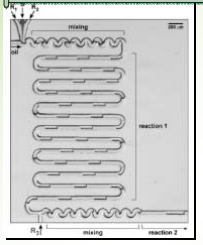
流道內液珠式微流體系統應用

蛋白質合成監控



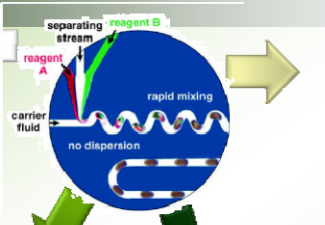
/9Li *et al., P. Natl. Acad.. Sci. USA* , 2006/0

減少縱向擴散

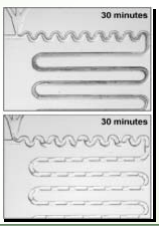


(Shestopalov *et al., Lab Chip*, 2004)

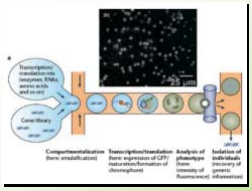
液珠外有薄膜保護隔絕產物沾附流道壁面



奈米粒子合成



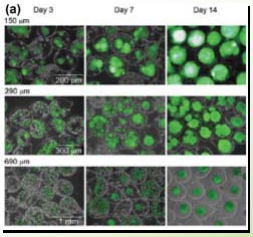
醫藥檢測篩選



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

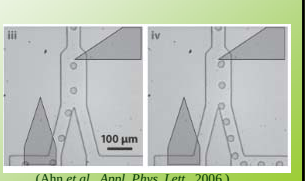
對個別液珠檢測篩選

細胞包覆



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

高密閉性，可做細胞包覆，並平行監控。

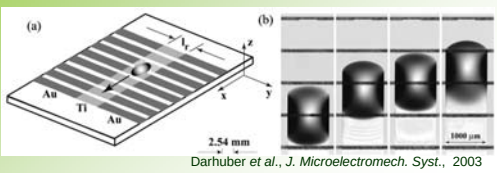


(Ahn *et al., Appl. Phys. Lett.*, 2006)

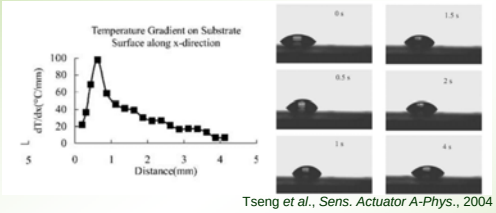
微液珠驅動機制 I

熱能趨動法

熱毛細現象(thermocapillary)：液珠從表面溫度較高區移動到較低區。



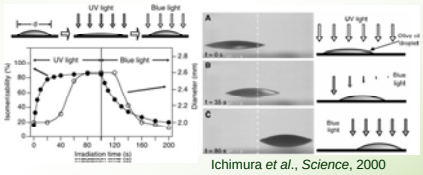
Darhuber *et al.*, *J. Microelectromech. Syst.*, 2003



Tseng *et al.*, *Sens. Actuator A-Phys.*, 2004

利用微機電壓印技術，將具有不同表面自由能的高分子化學薄膜沉積於PDMS表面，再轉印到矽晶片表面，以此方式控制微液珠傳輸方向與路徑。

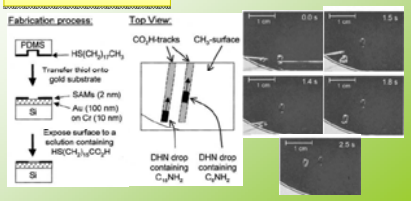
光能趨動法



Ichimura *et al.*, *Science*, 2000

晶片表面塗佈光感同分異構物，利用兩種光源搭配不同的照射方向與強度，可調控表面自由能差值，移動速度慢。

化學能趨動法

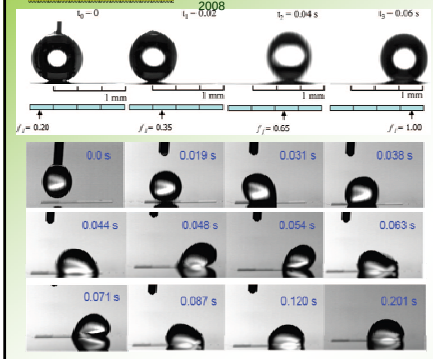


Lee and Laibinis, *J. Am. Chem. Soc.* , 2000

微液珠驅動機制 II

奈微米結構

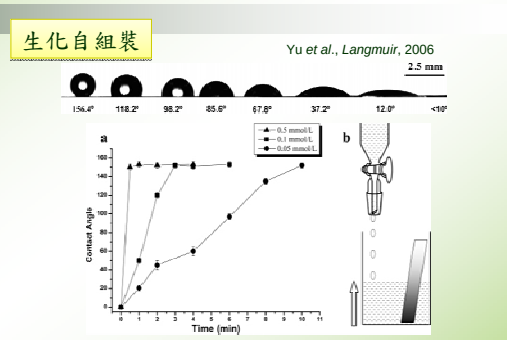
Yang *et al.*, *J. MEMS*, 2006, *Langmuir*, 2008

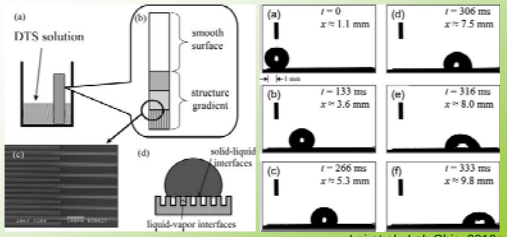


利用表面微結構、自組裝矽烷類分子，造成表面親疏水梯度，以趨動微液珠。並可利用雙複合結構表面達成超長距離傳輸。

生化自組裝

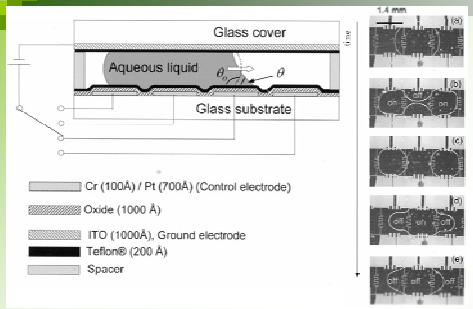
Yu *et al.*, *Langmuir*, 2006



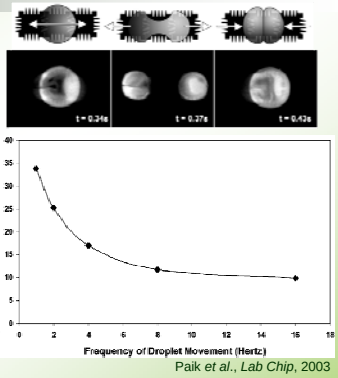


Lai *et al.*, *Lab Chip*, 2010a

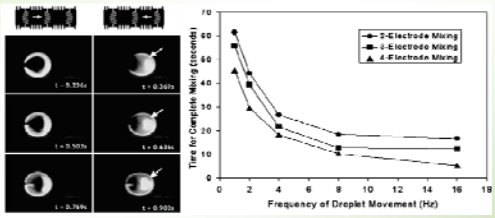
EWOD 驅動/操控微液珠



Cho *et al.*, J. *Microelectromech. Syst.*, 2003



Paik *et al.*, *Lab Chip*, 2003



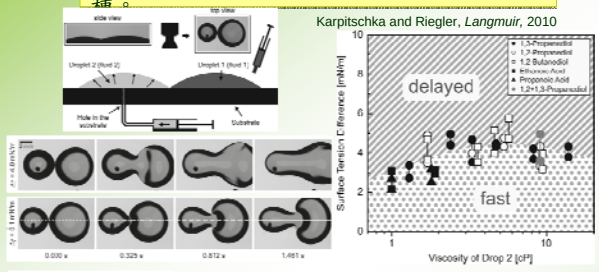
Paik *et al.*, *Lab Chip*, 2003

藉由電極之排列設計與電路之控制，進行各種液珠操控之設計，包括液滴產生、切斷、分離與傳輸。利用液珠來回傳遞，或切割和合併，都可達到混合的效果。

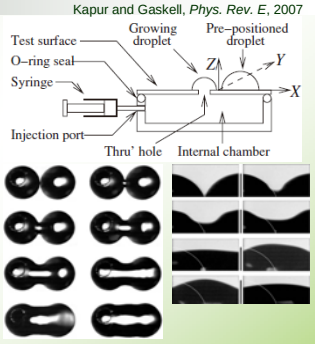
微液珠碰撞與融合

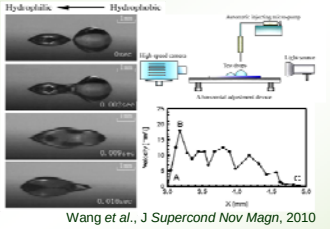
表面張力及黏滯性不同的液珠，接觸後的接合現像，可分為延遲接合與快速接合兩種。

Karpitschka and Riegler, *Langmuir*, 2010

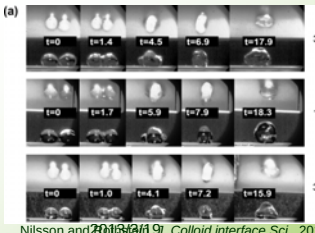


Kapur and Gaskell, *Phys. Rev. E*, 2007

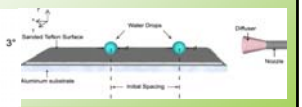




Wang *et al.*, J *Supercond Nov Magn*, 2010



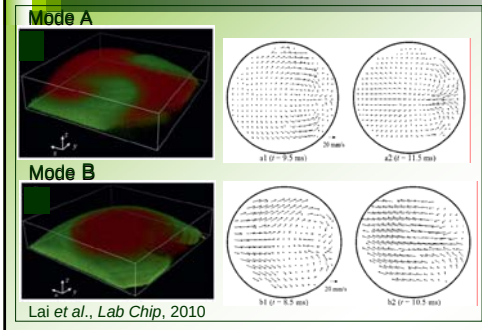
Nilsson and Bergeron, *J. Colloid interface Sci.*, 2011



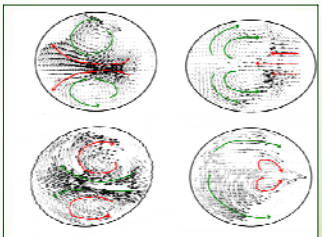
目前微液珠融合的相關研究，仍以輪廓變化以及流體混合為主

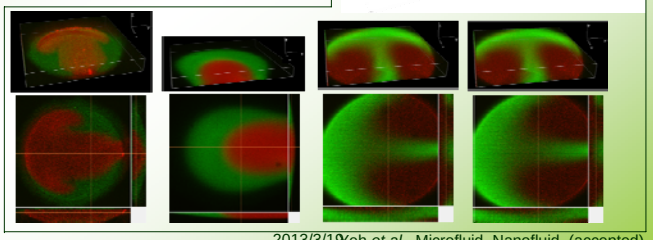
微液珠碰撞融合行為

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。



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

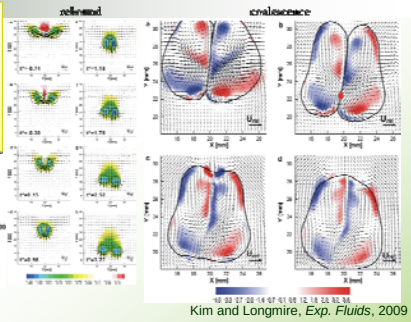


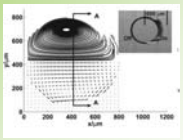


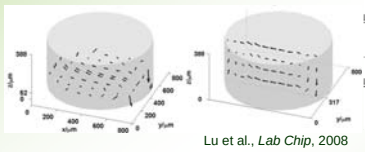
Yeh *et al.*, Microfluid. Nanofluid. (accepted)

微液珠內部流場分析

早期的研究是使用micro-PIV觀察流道內液珠內部流場，並用以說明混合現像。近年來利用共軛焦顯微術的輔助，可得到液珠內部三維流場速度變化。

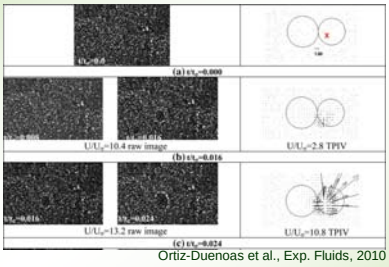




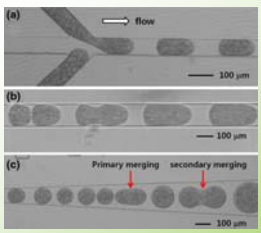


Lu et al., *Lab Chip*, 2008

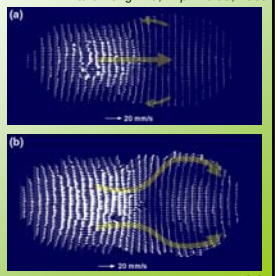
Kim and Longmire, *Exp. Fluids*, 2009



Ortiz-Duenoas et al., Exp. Fluids, 2010

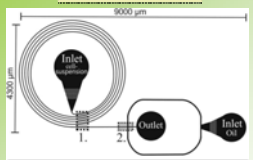


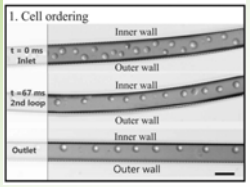
Jin and Joo, Exp. Fluids, 2012



管道內微液珠生成與操控

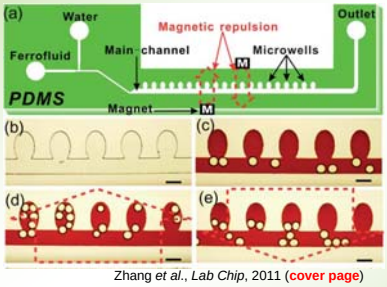
Cell ordering





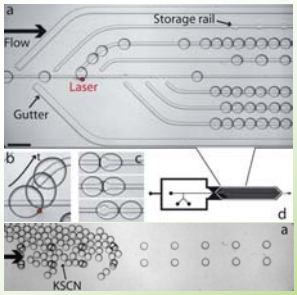
Kemna *et al.*, *Lab Chip*, 2012

Manipulate droplet using hydrophobic ferrofluid



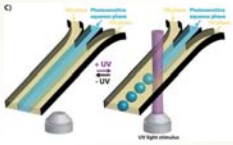
Zhang *et al.*, *Lab Chip*, 2011 (**cover page**)

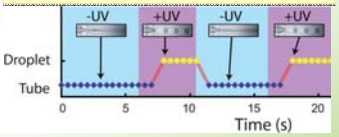
Rails and anchors



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

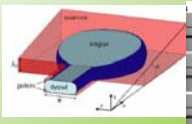
Droplet generation by light actuation





Diguet *et al.*, *Lab Chip*, 2011 (**cover page**)

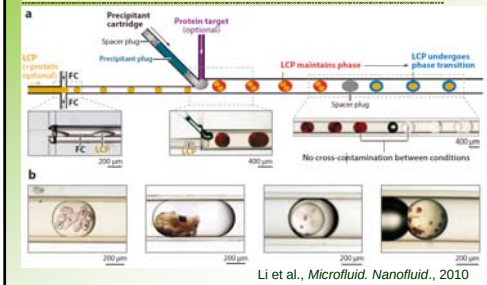
Manipulation of drops without any flow of the external phase



Dangle *et al.*, *2012 μTAS*

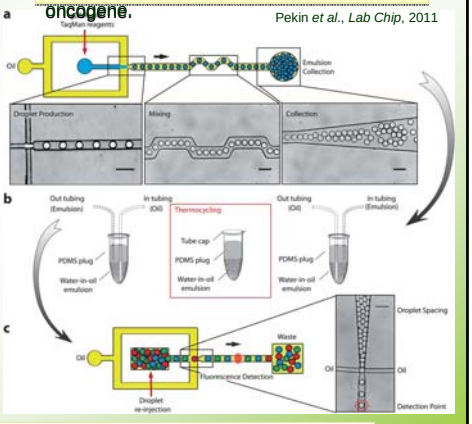
液珠式微反應器

Droplet-based microfluidic system for membrane crystallization within lipidic mesophases

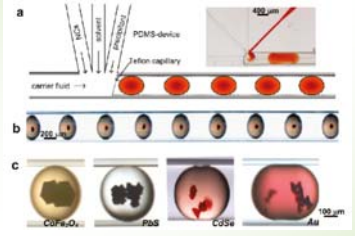


Li et al., *Microfluid. Nanofluid.*, 2010

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

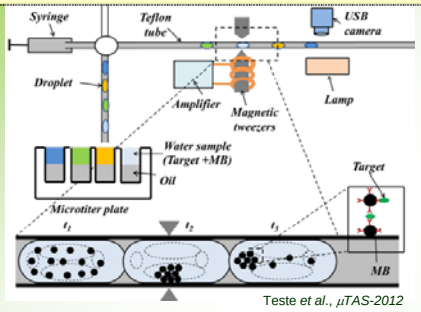


Bodnarchuk, *J. Am. Chem. Soc.*, 2011

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

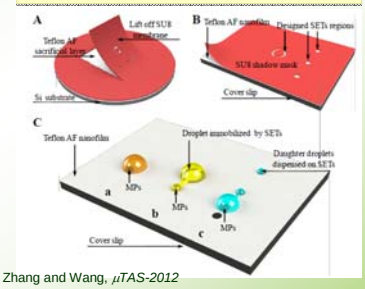
微液珠最新發展-- 磁力驅動

Immunoagglutination assay by combining magnetics beads

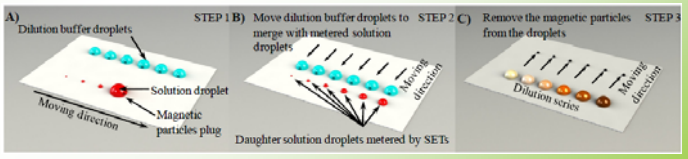


Teste *et al.*, *μTAS-2012*

surface energy traps enabled magnetic droplet manipulation platform



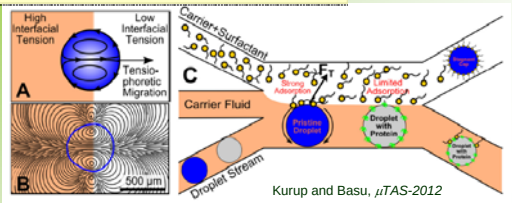
Zhang and Wang, *μTAS-2012*



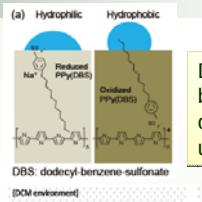
2013/3/19

微液珠最新發展 – 微液珠操控

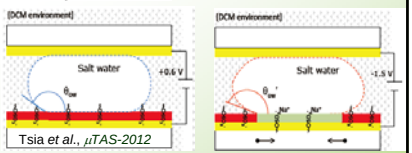
drop sorting based on chemical contents



Kurup and Basu, *μTAS-2012*

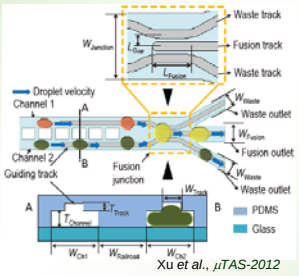


Droplet manipulation by tunable wetting on smart polymer at ultra-low voltages



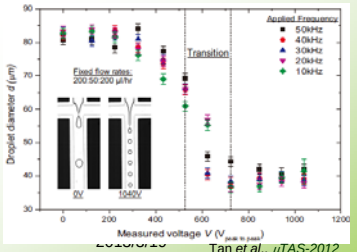
Tsia *et al.*, *μTAS-2012*

Fusion and sorting of two parallel trains of droplets



Xu *et al.*, *μTAS-2012*

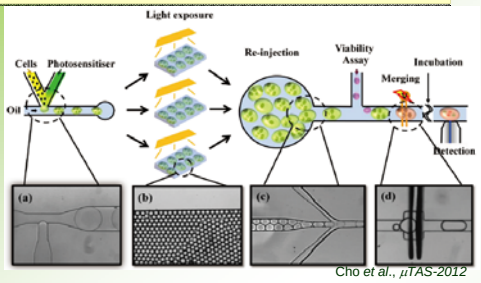
control the size of droplets



Tan *et al.*, *μTAS-2012*

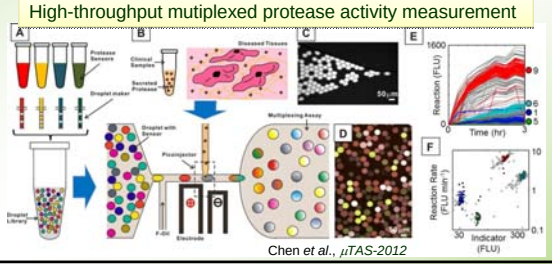
微液珠最新發展— 反應器

High-throughput cytotoxicity screening of photosensitizers against microbial organisms



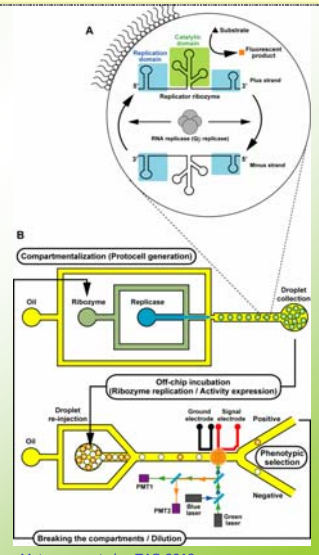
Cho *et al.*, *μTAS-2012*

High-throughput mutiplexed protease activity measurement



Chen *et al.*, *μTAS-2012*

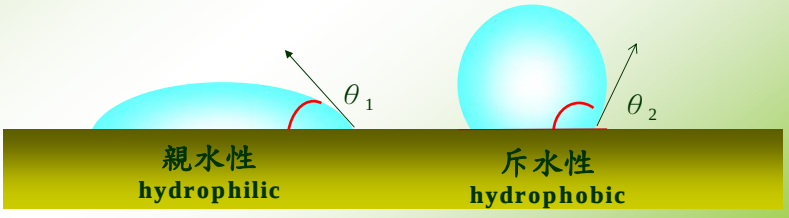
Droplet-based proto-cellular compartments



Matsumura *et al.*, *μTAS-2012*

親水性與疏水性

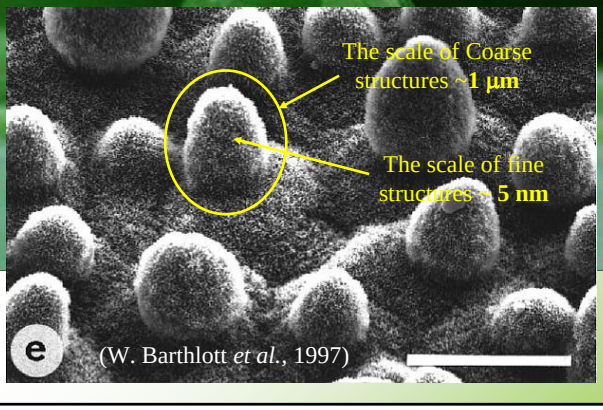
- 由水滴與表面之接觸角作為其親、疏水性之判斷：
- 接觸角 < 90° ⟹ 親水性(hydrophilic)表面，如 θ_1
- 接觸角 > 90° ⟹ 斥水性(hydrophobic)表面，如 θ_2



Lotus leaf

Lotus leaf, Super-hydrophobic surface

Apparent contact angle, θ_c ~160.4 °

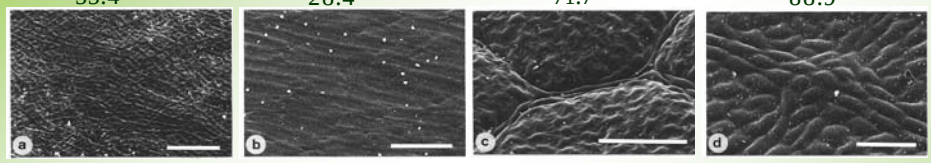


(W. Barthlott *et al.*, 1997)

Hydrophilic and Hydrophobic Features of Leaves

wetted plant leaf

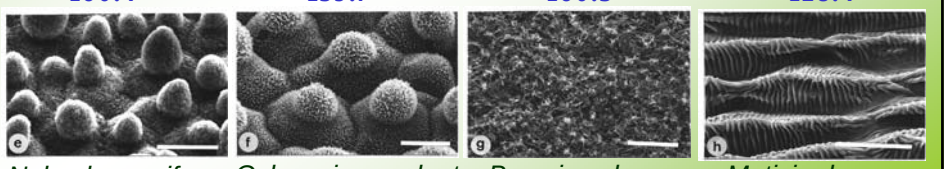
55.4° 28.4° 71.7° 88.9°



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

non-wetted plant leaf

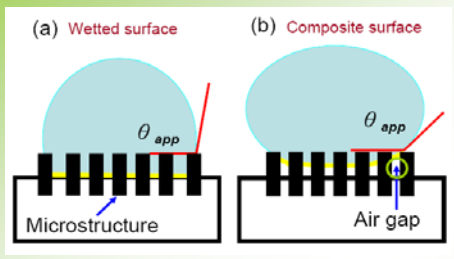
160.4° 159.7° 160.3° 128.4°



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

(Barthlott *et al.*, 1997)

Schematics of Surface Effects



■ **Smooth surface** $\cos\theta_o = (\gamma_{SV} - \gamma_{SL})/\gamma_{LV}$

Young equation

■ **Wetted surface** $\cos\theta_{app} = r\cos\theta_0$

Wenzel equation

■ **Composite surface** $\cos\theta_{app} = f_1\cos\theta_1 + f_2\cos\theta_2$

Cassie and Baxter Eq.

■ $\theta = 110^o$

Smooth surface

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

Surface with micro-structure

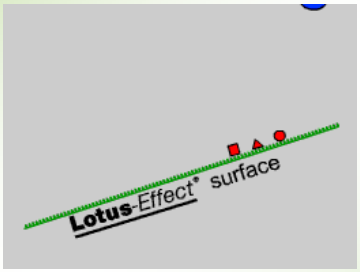
■ **composite surface** $\theta \sim 160^o$

Surface with hybrid structure

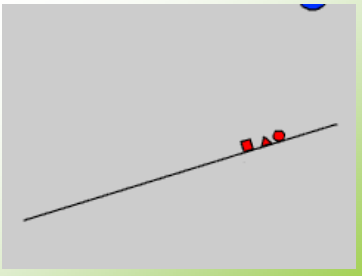
仿生動力機械實驗室 楊鏡堂教授

自清潔效應

- 斥水粗糙表面
  - 水滴滾動
  - 表面污物可由水滴帶走



- 斥水平滑表面
  - 水滴滑動
  - 污物沾附於表面

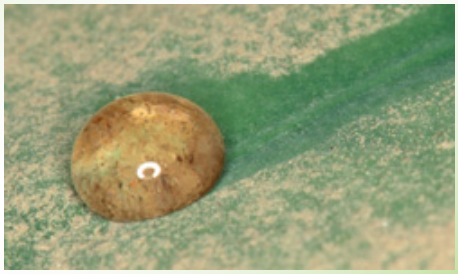


(http://www.botanik.uni-bonn.de/system/lotus/de/lotus_effect_multimedia.html)

自清潔效應 (Self-Cleaning Effect)

由於蓮葉表面之特殊微結構，可減少微塵、水滴與葉面之接觸面積，使其不易沾附葉面。

- 葉面污物易隨水滴自蓮葉表面滑落。



(http://www.botanik.uni-bonn.de/system/lotus/de/lotus_effect_multimedia.html)

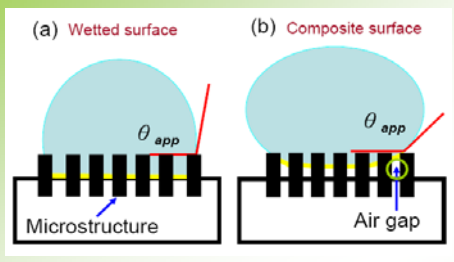
Technology

J. T. Yang, 20081116

Schematics of Surface Effects

蓮葉效應之圖解

楊鏡堂教授, 台大機械系



■ θ = 110°

smooth surface

■ 5-10 mm roughness θ ~ 135°

microstructures

■ **Smooth surface** $\cos\theta_o = (\gamma_{SV} - \gamma_{SL})/\gamma_{LV}$

Young equation

■ **Wetted surface** $\cos\theta_{app} = r\cos\theta_0$

Wenzel equation

■ **Composite surface** $\cos\theta_{app} = f_1\cos\theta_1 + f_2\cos\theta_2$

Cassie and Baxter Eq.

■ Composite surface θ ~ 160°

microstructures & nanostructures

不同溶液與蓮葉之接觸情形

- 高黏滯流體(膠水)　•斥水性染料 (斥油性顏料)

(http://www.botanik.uni-bonn.de/system/lotus/de/lotus_effect_multimedia.html)

蓮花噴霧劑

• BASF蓮花噴霧劑是一種由奈米微粒及拒水性聚合物混合組成的鍍膜噴劑。

• 右圖為經BASF蓮花噴霧劑處理之木質表面與水珠接觸情形。

• 可應用在紡織、皮革及建築材料上。

(http://www.basf.com/)

奈米塗料

STO 公司：

- 圖為表面塗佈Lotusan塗料之壁面與水珠接觸情形。
- 此種塗料可使建築物具有容易清潔、易維護、不易沾污、不易毀損等好處。

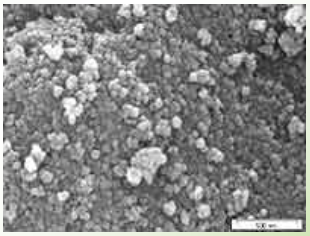
(http://www.lotusan.de/lotusan/_02_wissen/index.jsp)

楊鏡堂教授網站

奈米粒子表面應用

Creavis 公司：

右圖是奈米粒子覆蓋表面之掃瞄式電子顯微鏡(SEM)圖。



應用此種奈米粒子表面之產品

此奈米粒子表面產生機制，已發表於：US 20030013795 A1

(http://www.creavis.com/en/default.cfm)

不溼性抗污布料

- **iTV 公司：**
  - 開發出仿蓮葉自清潔效果之紡織材料。
  - 此紡織具有不沾水、不沾油污之特性。
  - 可使表面常保乾燥、無污。

(http://www3.itv-denkendorf.de/read.asp?tid=show&id=239&lang=en)

奈米彩晶塗料

光陽公司--奈米彩晶塗裝：

- 表面光澤及觸感較一般塗料光滑細緻。
- 不易沾染污垢、超耐髒。
- 對氣候變化有極大的適應性。
- 耐侵蝕、不易褪色。
- 硬度較一般塗料高，不易產生刮痕。

(http://www.kymco.com.tw/tw/news/news_01.asp?NewsID=17)

奈米馬桶

和成公司：

- 奈米馬桶--和成ADB (Anti-Dirt-Bacteria)。
- 將奈米釉藥覆蓋在陶瓷表面，釉料粉體約50奈米大小。
- 添加銀離子形成高溫抗菌劑，滅菌率達99%。
- 衛浴設備不易附著污垢亦不易產生臭味。

(http://www.hcgnet.com.tw)

Research Actions inspired by Lotus Leaf and Plants

BEAM Lab at NTU

楊鏡堂 特聘教授

jtyang@ntu.edu.yw

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

研發策略與步驟

探索生存適應的物理

(Life among the Formulae of Physics)

⇩

模仿生物智慧

⇩

科技創新

Biophysics → Biomechanics → Biomimetics

Lotus and Microchips

J. T. Yang, 20091026

Objectives of Our Research

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
生醫製藥領域之最高桂冠

Droplet spontaneous moving and reacting on a microchip

Lotus leaf

The first idea :

- We have integrated the nano/micro fabrication to mimic the morphology of a lotus leaf and made the hybrid structures on the solid surfaces.
- Such an artificial surface would be similar to a lotus leaf with superhydrophobicity.

Contact Angle & Surface Wettability

(a) Smooth surface (b) Wetted surface (c) Composite surface

droplet γ_{LV} θ_0 θ_w θ_c

(a) PPFC, microstructure stature of 3.2 μm

(b) PPFC, microstructure stature of 24.1 mm

126.1° 124.8°

157.6° 158.0°

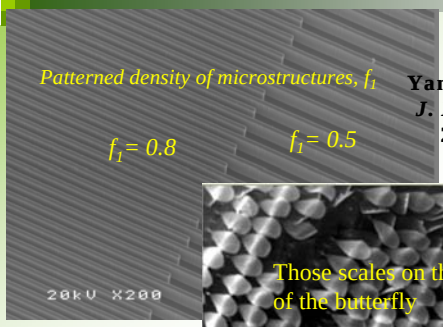
Collapsed droplet Suspended droplet

Sm… Ju… co… les…

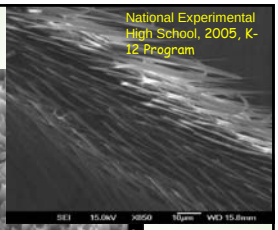
…rface …r Eq. (1944) $\theta_0 + f_1 - 1$

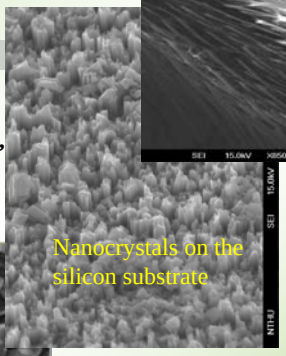
…parameter: …on of …density of …ures, f_1

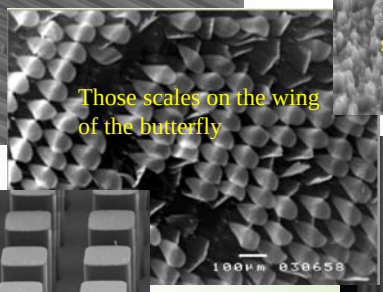
Surface Science & Art

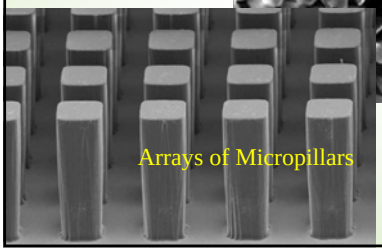


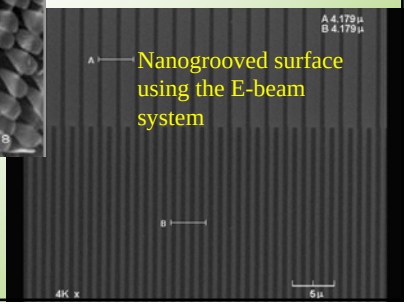
Yang et al., *J. MEMS*, 2006



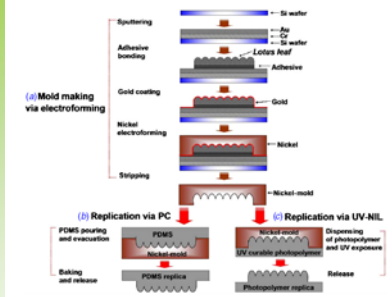


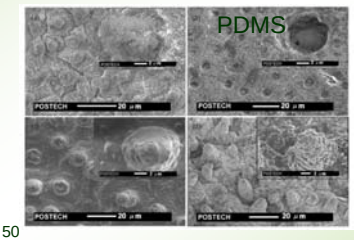






Artificially Superhydrophobic Surfaces





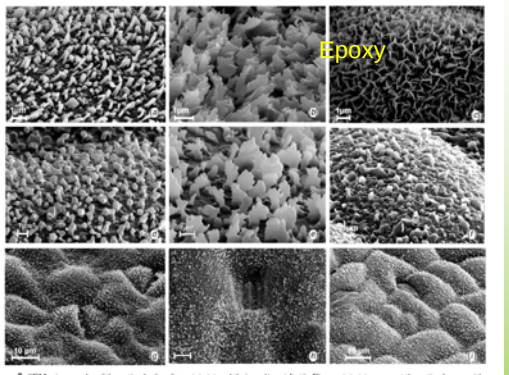


Figure 7. SEM micrographs of the native leaf surfaces (*a*)-(*c*) and their replicas (*d*)-(*i*). Figures (*a*)-(*c*) represent the native leaves with wax crystals: *Lindera obtusiloba*: wax rodlets (*a*), *Iris germanica*: parallel-oriented wax platelets (*b*) and *Babtisia australis*: wax platelets arranged in a dense network (*c*). *L. obtusiloba* leaf replication with 10 g cm^{-2} pressure is shown in (*d*) and (*g*). For the replication of the *I. germanica* wax platelets only 7.5 g cm^{-2} were applied (*e*), (*h*). (*f*) and (*i*) show that waxes of *B. australis* leaves were only partly replicated; thus the surface structure of the replica (*f*) is quite different from the original waxes (*c*).

Lee, S. M., and Kwon, T. H. 2007. *J Micromech Microeng*, Vol. 17(4), pp. 687-692.

- **Koch, K., Schulte, A. J., Fischer, A., Gorb, S. N., and Barthlott, W. 2008. *Bioinspir Biomim*, Vol. 3(4), pp. 046002.**

Transport and Manipulation of a Droplet

- Apparent contact angle & the strength of hyd
- The prin mic tran

Direction of actuation force and movement

Ele

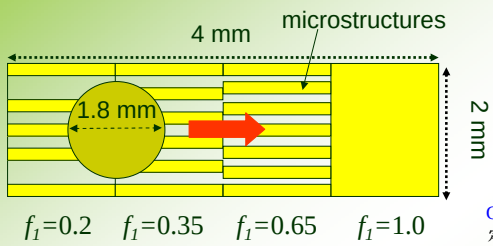
Mic

The second main ideas:

- By means of modulating the patterned density of microstructures, f_1, a transport path with a surface gradient has been created.
- A single droplet will move spontaneously along a specified direction from the surface with a lower patterned density to that with a higher one.

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 :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 …

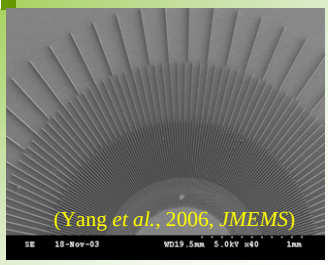
藉由液珠在移動前後穩態表面自由能的轉換，扣除因遲滯力和黏滯力所造成的摩擦能損和液珠表面震盪的內能損耗，應該等於液珠移動時的平均動能。

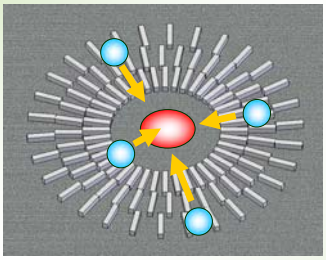
$$\Delta Gs_{12} - G_b - W_{vis} - G_{shape} = \frac{1}{2}mv^2$$

Available (theory prediction and measurement)

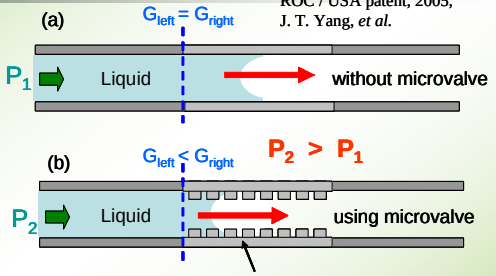
Yang et al., Langmuir, 2008
(times cited: 16)

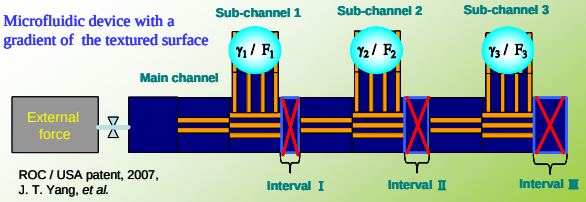
Engineering Application & Patents





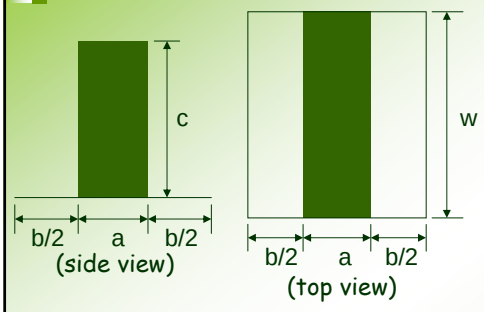
ROC / USA patent, 2005,
J. T. Yang, *et al.*

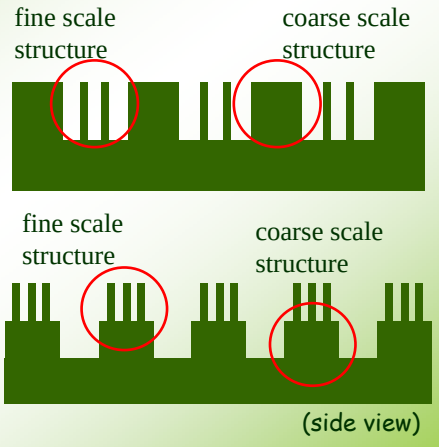




ROC / USA patent, 2007,
J. T. Yang, *et al.*

複合表面結構設計





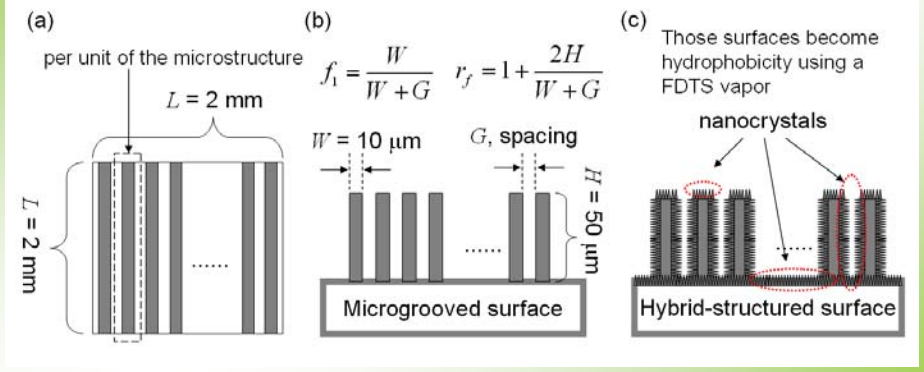
$$r = \frac{A_{actual}}{A_{projected}} \qquad r = 1 + \frac{2c}{a+b}$$

$$f_1 = \frac{A_{S-L}}{A_{total}} \qquad f_1 = \frac{a}{a+b}$$

$r \rightarrow$ 接觸模式

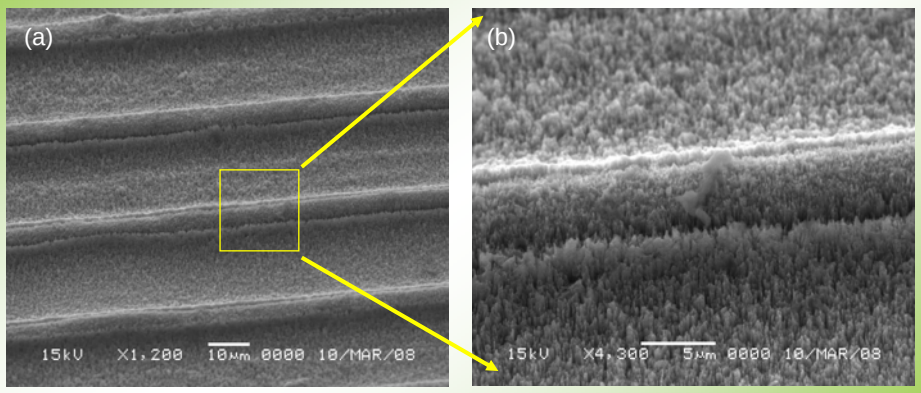
$f_1 \rightarrow$ 計算接觸角度

Schematic of geometric parameters of each microgrooved pad.



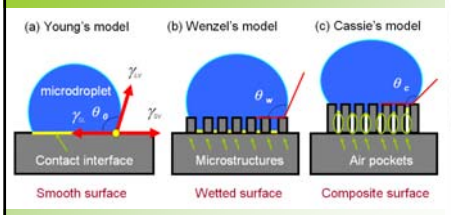
Z. H. Yang, C. Y. Chiu, J. T. Yang,* and J. A. Yeh, 2008, "Hybrid-Structured Surfaces with Ultra-Hydrophobic Character using Micro/Nanofabrication," *submitted to Applied Physics Letters.*

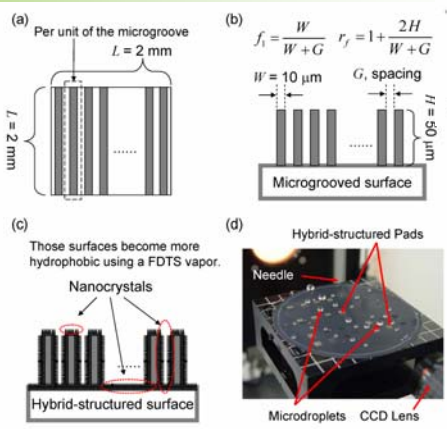
Hybrid structured surfaces

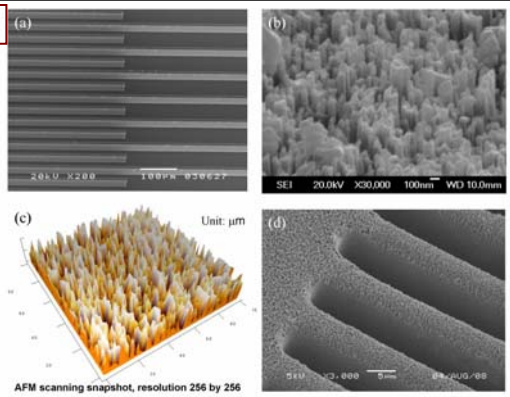


Photographic Scans of a Hybrid Structured Surface with a SEM: (a) The Sight Field at a Small Magnification; and (b) The Sight Field at an Increased Magnification

Yang *et al.*, *JMM*, 2009 *(times cited: 13)*



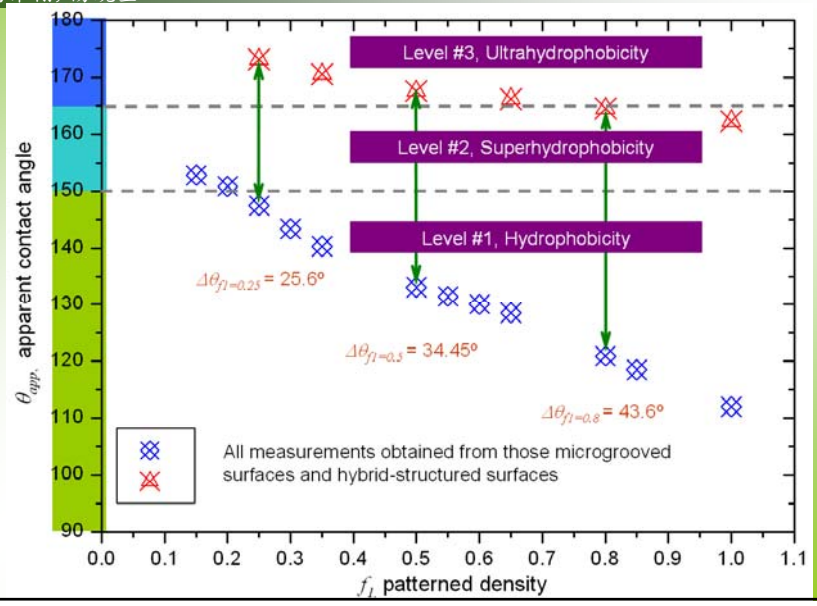




- Hybrid-structured surfaces consisting of microgrooves and nanocrystals have been realized via an integration of nano/microfabrication.
- The nanocrystal-decorated microgrooves were arranged and fabricated on a silicon substrate followed by vapor deposition of a fluorinated self-assembled monolayer (FDTS), yielding an ultra-hydrophobic surface.

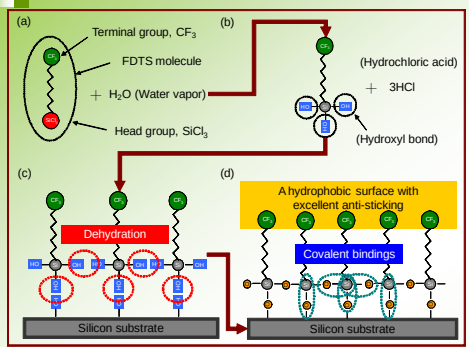
Surface Hydrophobicity of Three Levels

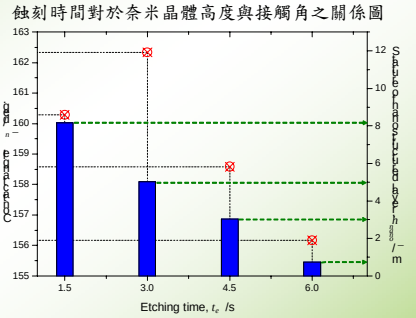
楊宗翰, 楊鏡堂

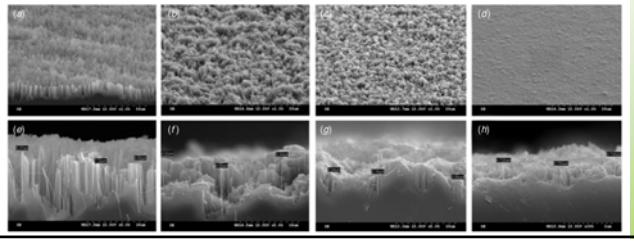


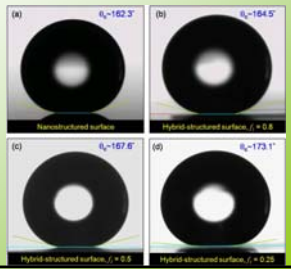
分子自組裝技術應用於表面改質

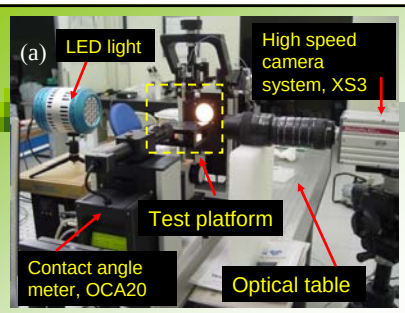
Yang *et al.*, *JMM*, 2009; ***IOP Select; JMM Highlights of 2009***

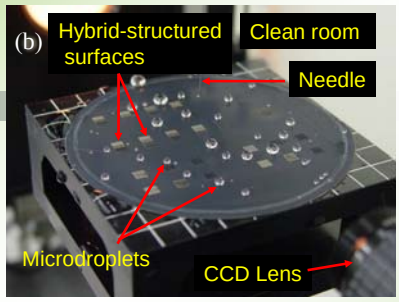


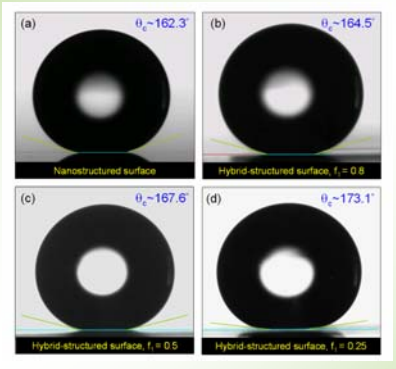


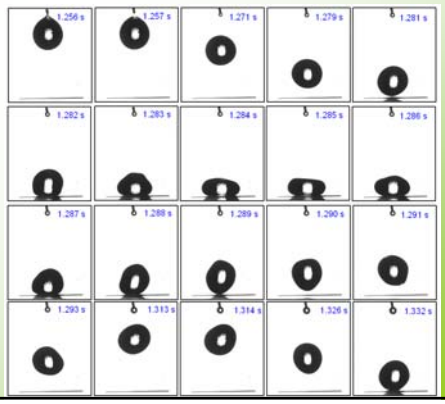










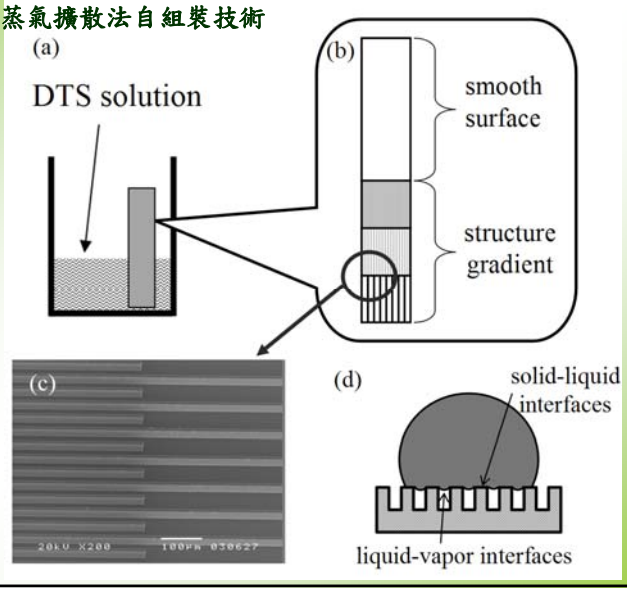


A droplet is falling on Si surface

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

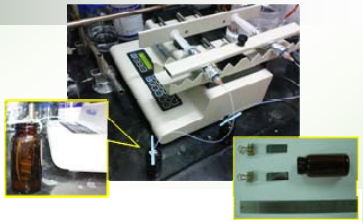
Lai, Yang, Shieh, *Lab Chip*, 2009

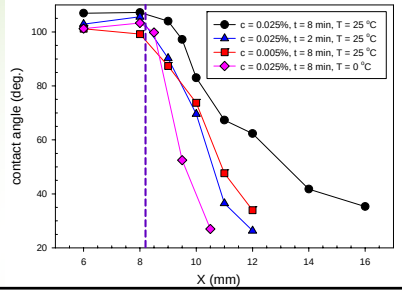
FDT

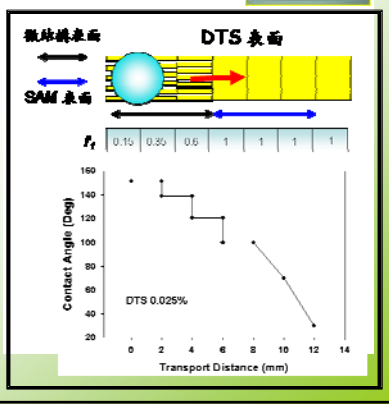
DTS

滴定法

蒸汽法



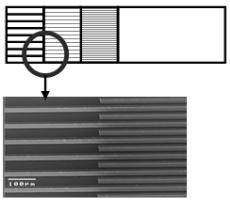




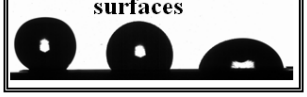
A biochemical droplet transporting across superhydrophobic to hydrophilic surfaces.

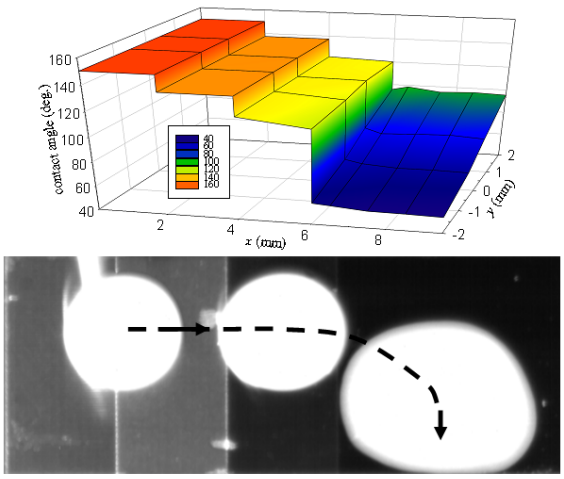
Lai, Yang,* Shieh, *Lab Chip* 2009 ***(times cited: 13)***

a microstructure and SAM composition gradient surface



transport of droplets across superhydrophobic to hydrophilic surfaces



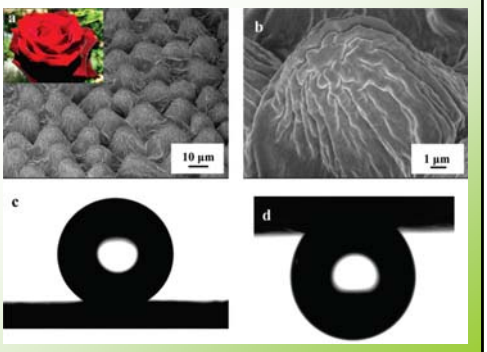


a double-direction gradient

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.



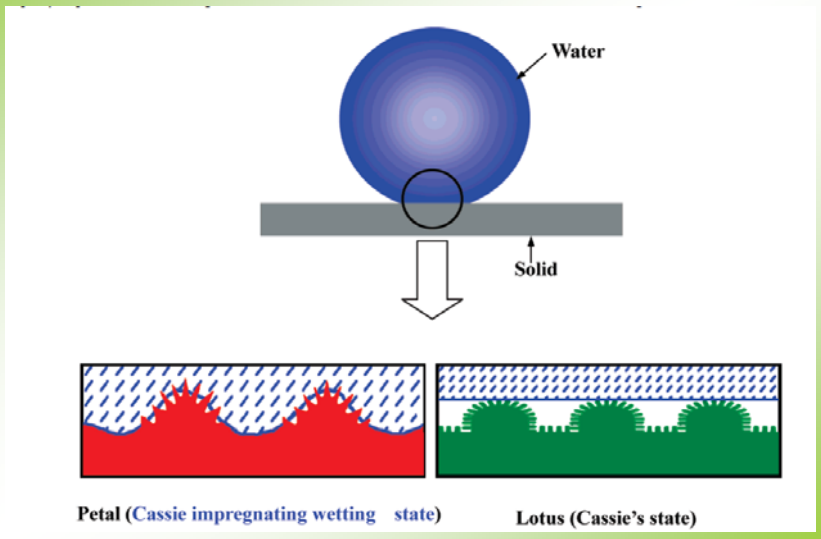
Petal Effect:

A Superhydrophobic State with High Adhesive Force

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

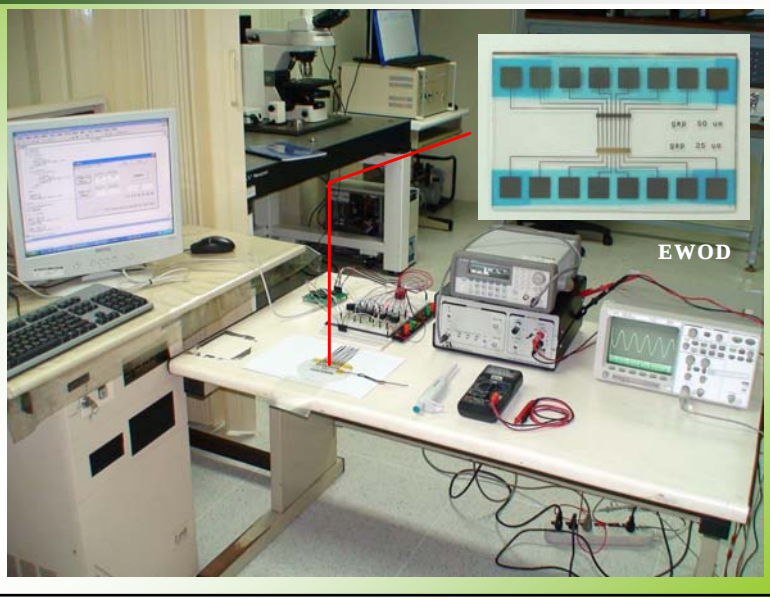
Feng et al., Langmuir, 2008.

Petal Effect and Lotus Effect



SEM, AFM, and Platform for Biochips

楊鏡堂教授, 台大機械系



Application

Research Motive

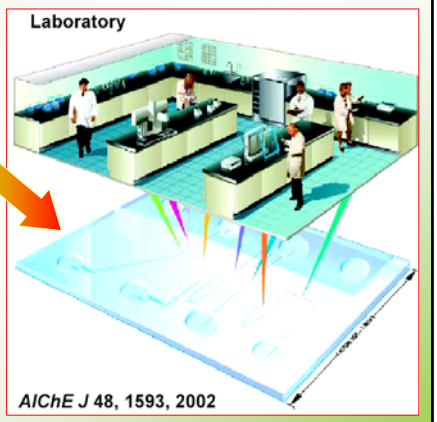
past

Manz *et al.*, *SNA-B*. 1990

current

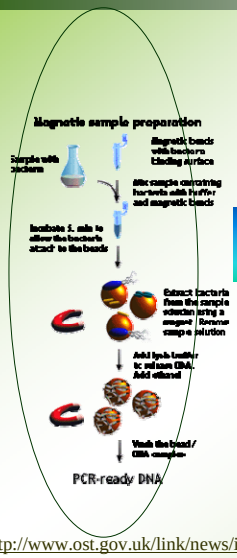
future

Miniaturization
Automation
Safety



General flow chart of a chemical analysis

(Manz et al., Sens. Actuators, 1990)



sampling

Transport

Sample pretreatment

Transport

Detection

Transport

Ideal chemical sensor

TAS

μ-TAS

Ref. : http://www.ost.gov.uk/link/news/images/9903chip.jpg ; http://w4.siemens.de/en2/html/press/newsdesk_archive/index.html ; www.genpoint.com/ Files/illustration.html http://www.ost.gov.uk/link/news/images/9903chip.jpg ; http://www.giannigiorgetti.com/pcr/

Droplet Technology

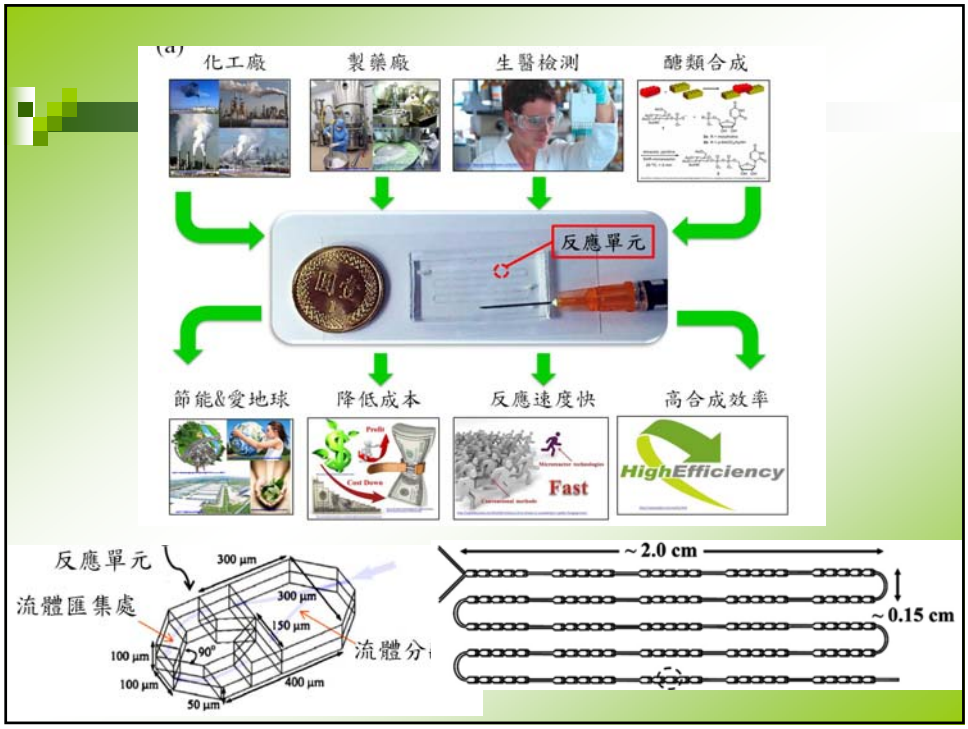
Droplet

RainDance Technologies

The RDT 1000 produces picoliter-volume droplets at the rate of 10 million discrete PCR reactions per hour.

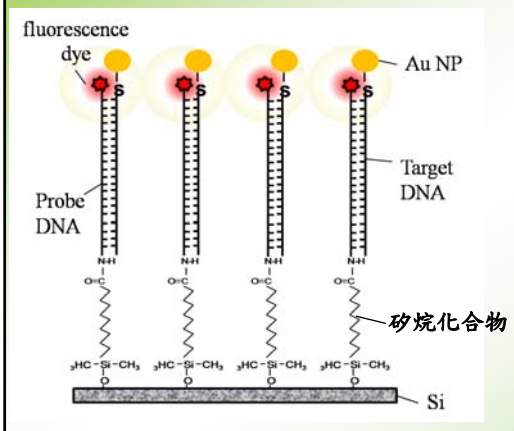
- Formulate
- Load
- Combine
- Mix
- Split
- Timing
- Store
- Sequential add
- Detect
- Direct

From http://www.raindancetechnologies.com/tech.html

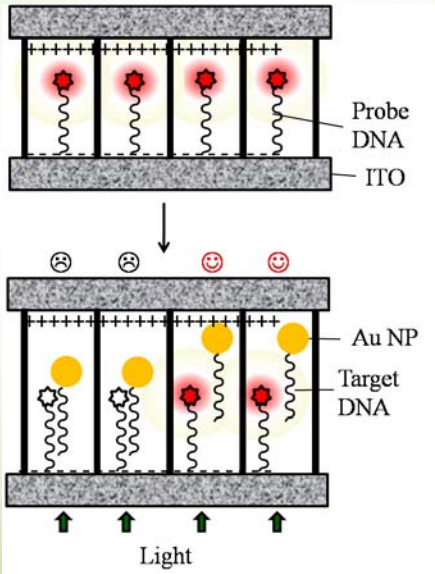


利用生化自組裝技術製作生化薄膜之感測裝置

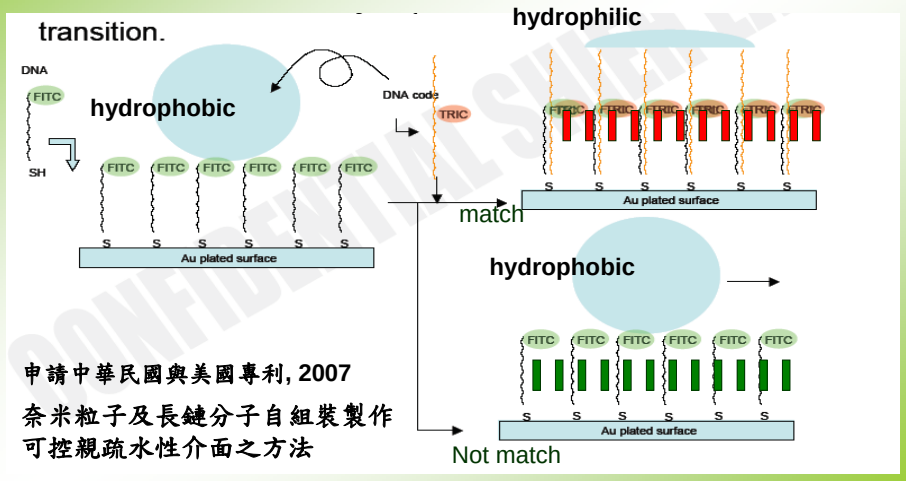
Yang *et al.*, ROC Patent, 2009.



利用氨基 (-NH_2 group) 與
羧酸基 (-COOH group) 鍵結



A novel method of self-assembling nano-particles or long chain molecules for the formation of surfaces with controllable wettability

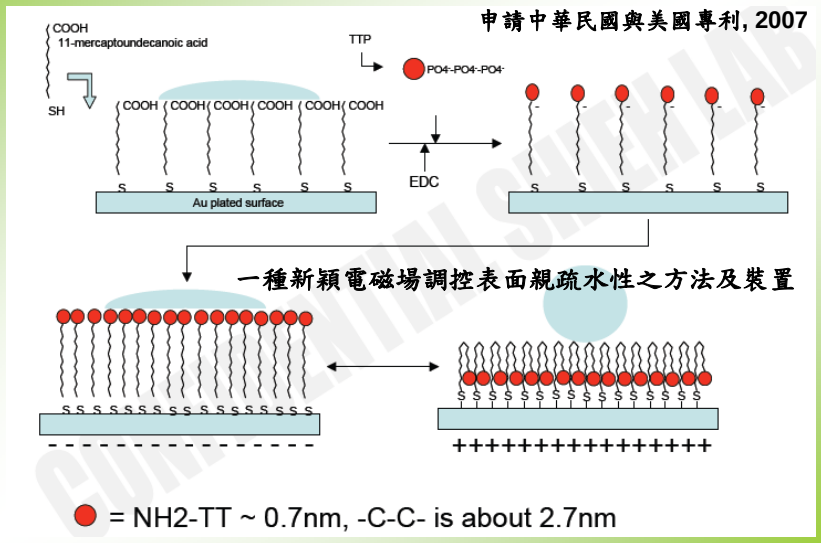


申請中華民國與美國專利, 2007

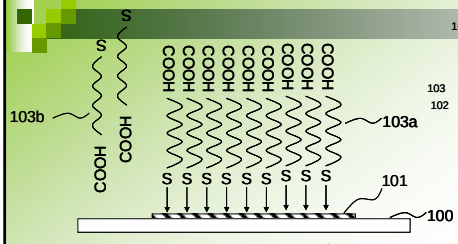
奈米粒子及長鏈分子自組裝製作可控親疏水性介面之方法

A novel method and control devices for changing wettability on solid surface by electric or magnetic field

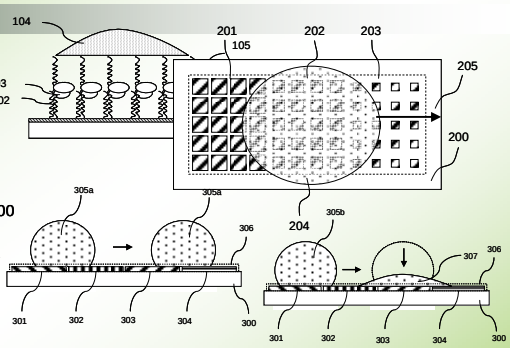
申請中華民國與美國專利, 2007



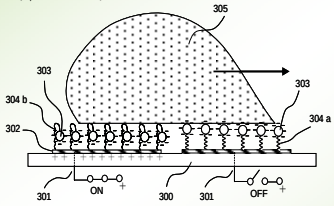
2008年奈米自組裝專利五項圖解(楊鏡堂教授與謝達斌醫師)



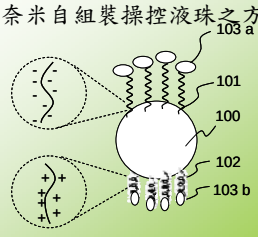
奈米粒子及長鏈分子自組裝製作可控親疏水性介面之方法



生物奈米自組裝操控液珠之方法及裝置



一種新穎電磁場調控表面親疏水性之方法及裝置

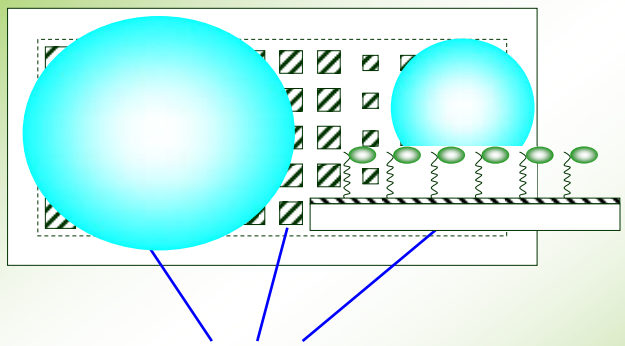


一種具超高解析度奈微米顯示元件之裝置

以奈米自組裝製造非均勻表面性質奈微米粒子之方法

A Patent- Manipulate Droplet by SAM

Droplet transport



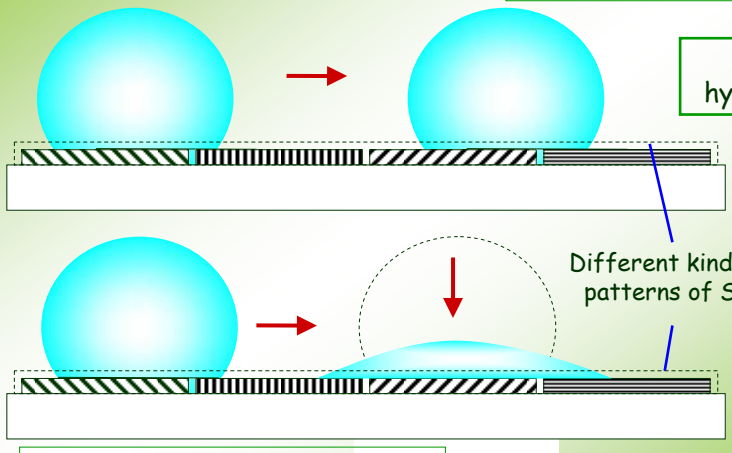
Different patterns of SAM

楊鏡堂，謝達斌，邱朝陽，楊宗翰，張佑民，陳逸臨，2007,“生物自組裝操控液珠及檢測之方法及裝置，”申請中華民國及美國發明專利(No. 096114775, 96/04/26 立案).

A Patent：Manipulate Droplet by SAM

Bio-molecule detection

DNA in the droplet doesn ‘t hybridize with the DNA connected to the substrate

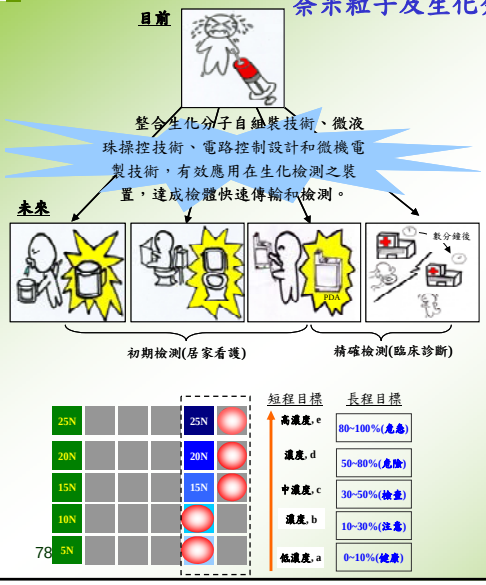


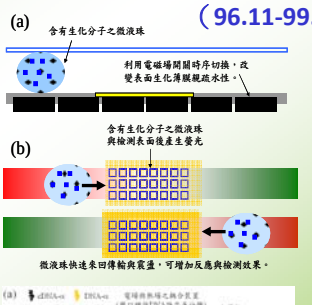
DNA in the droplet hybridize with the DNA connected to the substrate

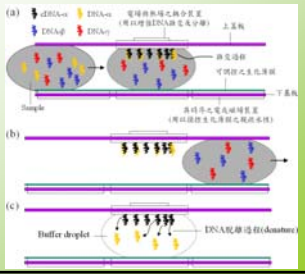
hydrophobic → hydrophilic

國科會前瞻優質生活環境科技跨領域研究計畫

奈米粒子及生化分子自組裝製作可控親疏水性介面晶片（96.11-99.10）



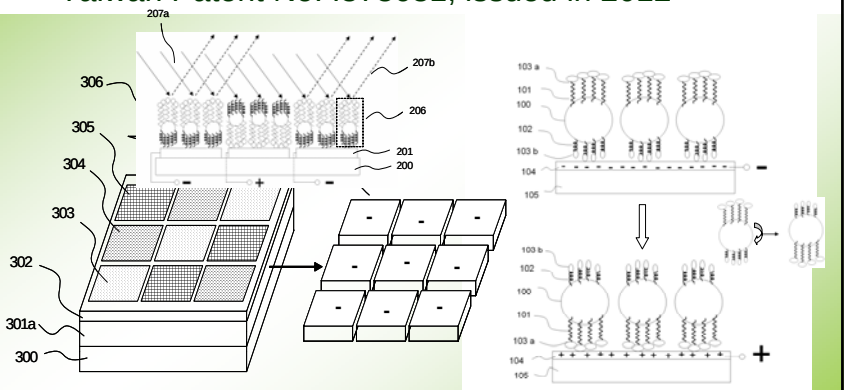




A novel fluorescent device with ultra-resolution and its application (一種具超高解析度奈微米顯示元件之裝置)

J. T. Yang,* D. B. Shieh, W. F. Fang, C. Y. Chiu, T. L. Tasi, and Y. N. Wu

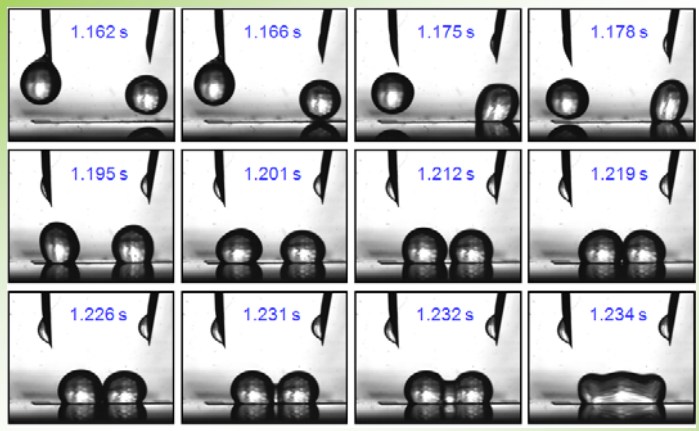
Taiwan Patent No. I373681, issued in 2012



由於不同區域之分子表層各具不同的電性及親疏水性，經由電場與表面分子層的控制，即可對於奈米粒子之方向排列加以操控，不同的面朝向觀測端，可製造出不同顏色或灰階的效果，因而得以應用於各種顯示裝置和感應元件。

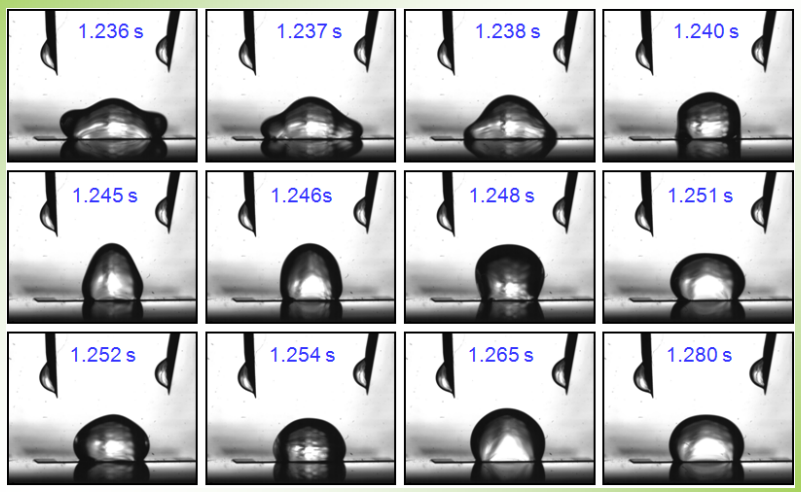
Mixing and Reaction within Droplets

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 .

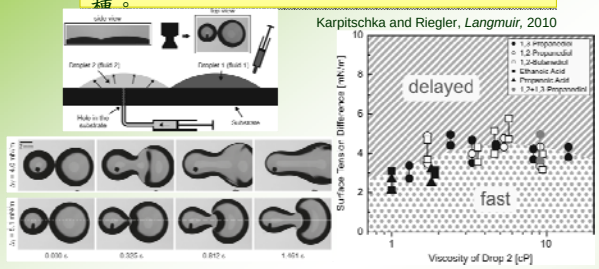
Sequence of images during two droplets collision (2)



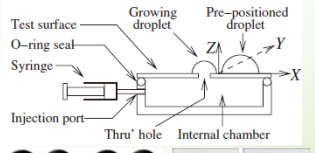
微液珠碰撞與融合

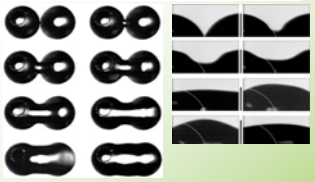
表面張力及黏滯性不同的液珠，接觸後的接合現像，可分為延遲接合與快速接合兩種。

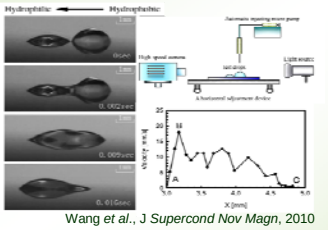
Karpitschka and Riegler, *Langmuir*, 2010



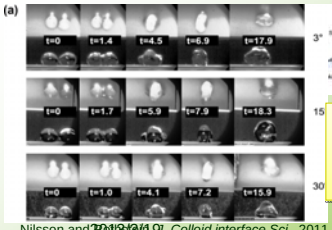
Kapur and Gaskell, *Phys. Rev. E*, 2007



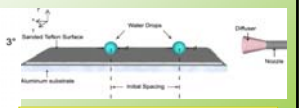




Wang *et al.*, J *Supercond Nov Magn*, 2010



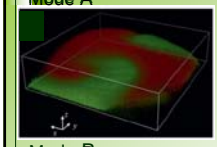
Nilsson and Bolognesi, *J. Colloid interface Sci.*, 2011

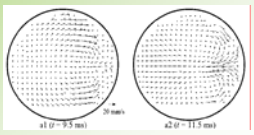


目前微液珠融合的相關研究，仍以輪廓變化以及流體混合為主

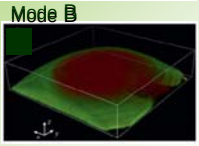
微液珠碰撞融合行為

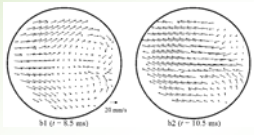
Mode A





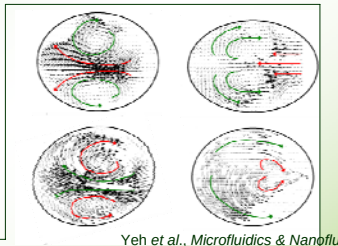
Mode B



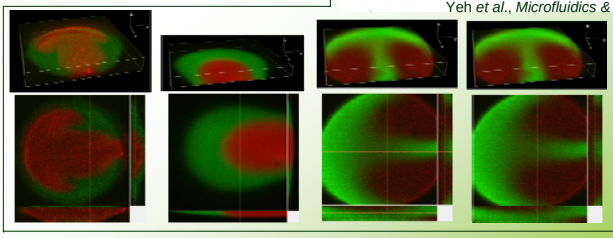


Lai *et al.*, *Lab Chip*, 2010

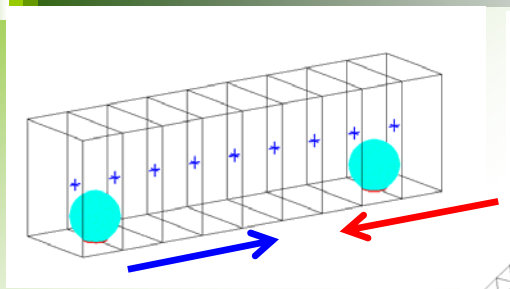
使用micro-PIV以及共軛焦顯微鏡進行微液珠融合過程的行為分析，結合流場與三維混合圖形探討不同流體之融合行為差異。

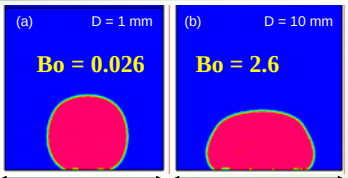


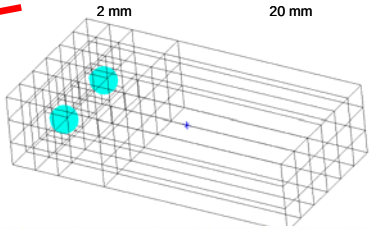
Yeh *et al.*, *Microfluidics & Nanofluidics*, 2012

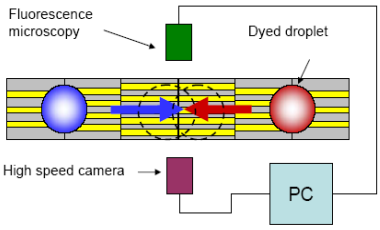


Numerical Simulation



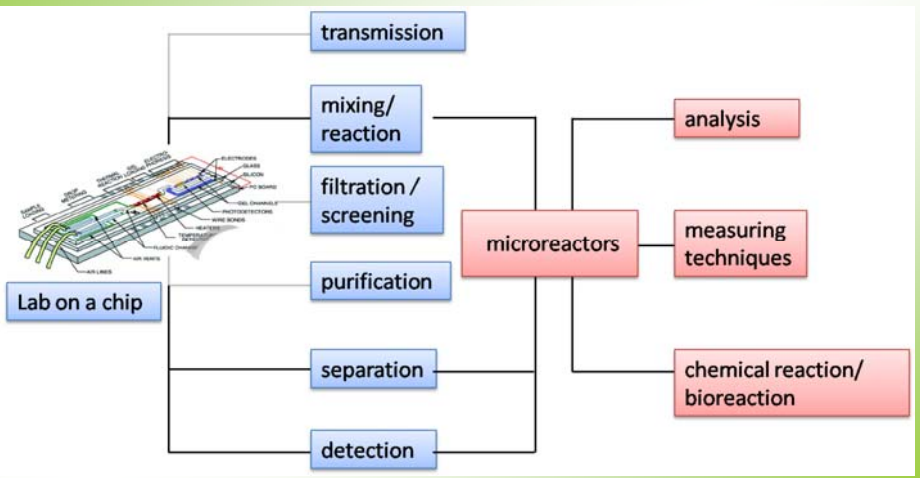






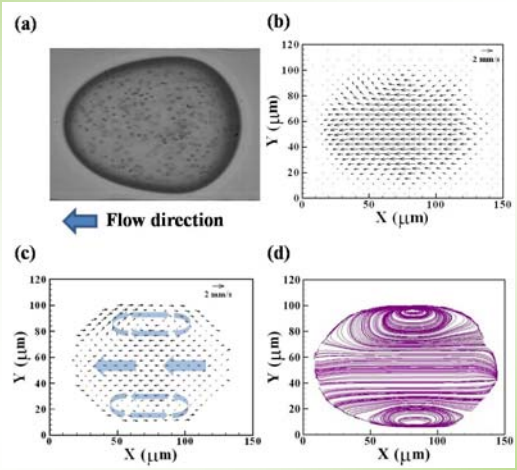
Collision and Mixing of two Droplets

Research Targets in bio-medical diagnosis



Droplets in a Straight Channel

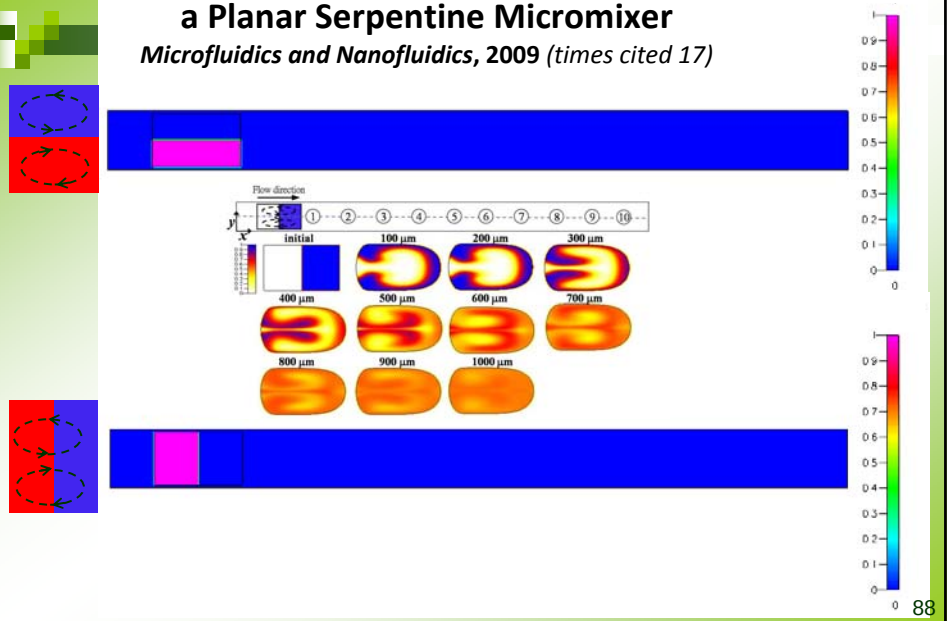
Tung, Li,, and Yang, *Microfluidics & Nanofluidics*, 2009



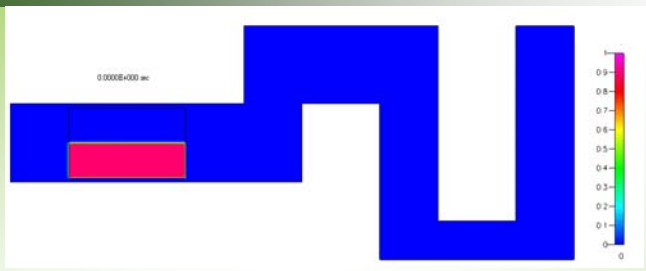
Micro-PIV measurement of the velocity field inside an aqueous moving droplet. (a) Orginal image, (b) velocity field, (c) velocity field after subtracting velocity of the droplet and (d) the streamlines at the center of the droplet.

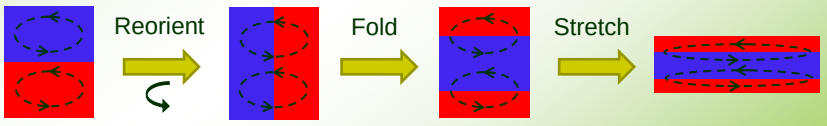
Mixing and Hydrodynamic Analysis of a Droplet in a Planar Serpentine Micromixer

***Microfluidics and Nanofluidics*, 2009** *(times cited 17)*



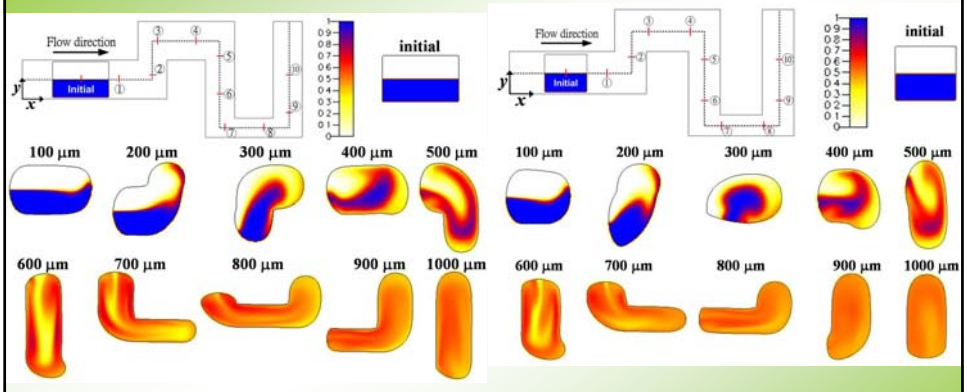
Mixing Mechanism





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

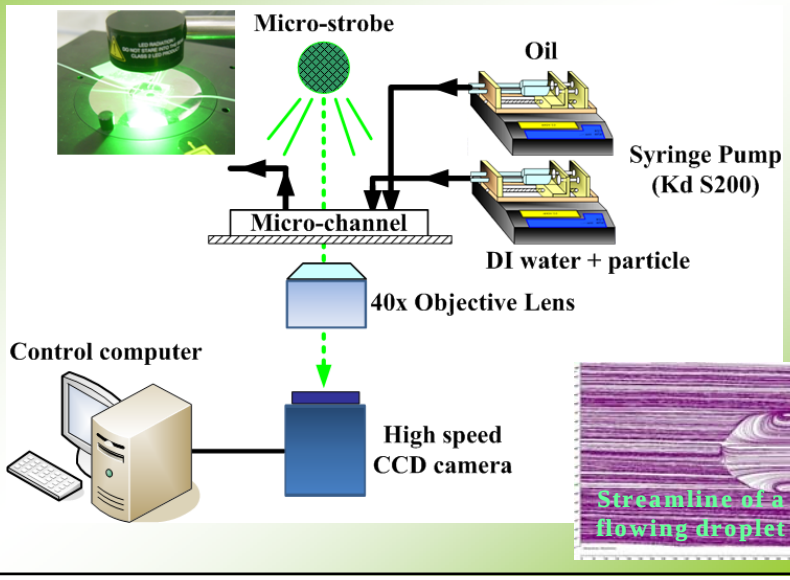
Droplet in PSM– Numerical Simulation



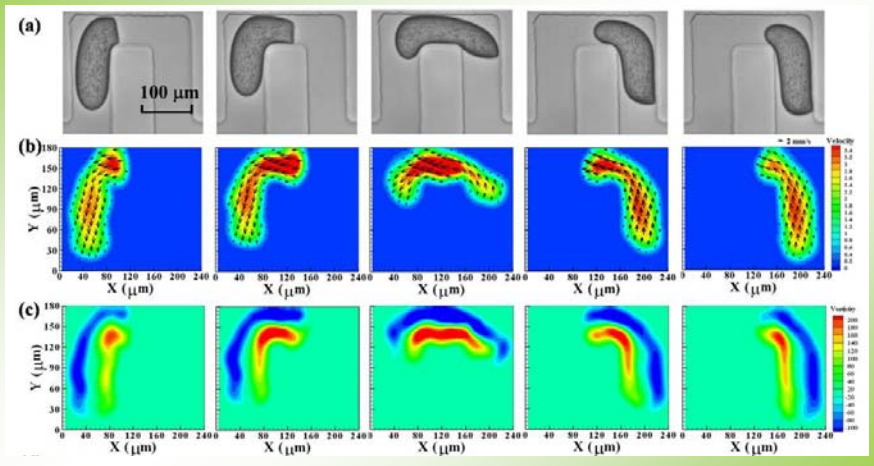
2D simulations showing dye mixing inside droplets in which bye is injected throughout the bottom half of the droplet (150 μm & 100 μm) in a PSM.

Schematics of μ-PIV Measurement

童凱煬 李志杰 楊鏡堂 *Microfluidics and Nanofluidics, 2009*



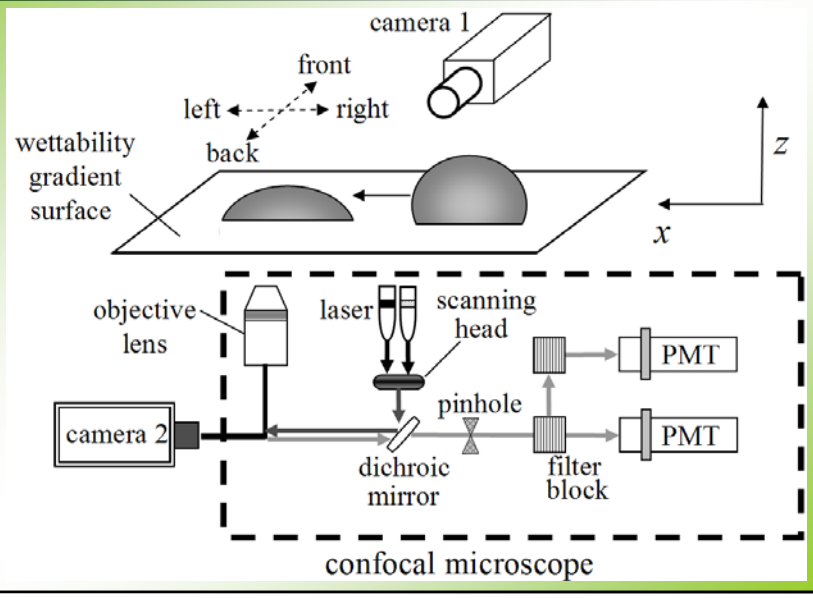
Droplet in PSM– PIV Measurement



- Original droplet images
- Original contour and vector of velocity field inside the droplet along PSM.
- Contour plot of vorticity inside the droplet along PSM.

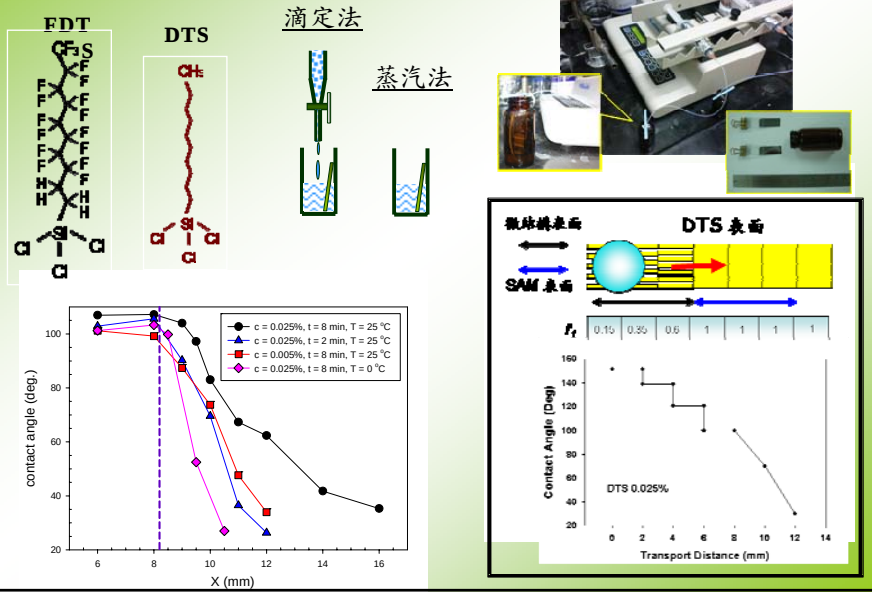
Multi-color Micro-PIV & Species Concentrations

Lai and Yang, *Lab Chip*, 2010



A Microchip using SAM & Gradient Surfaces

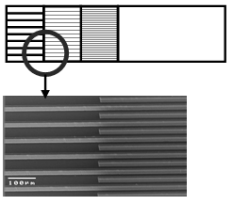
Lai, Yang, Shieh, *Lab Chip*, 2009



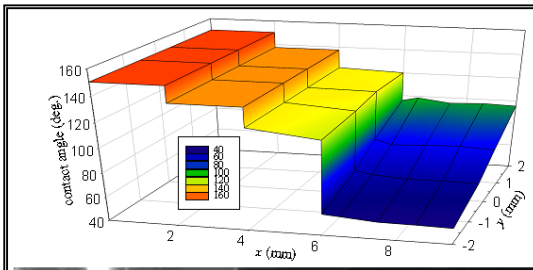
A biochemical droplet transporting across superhydrophobic to hydrophilic surfaces

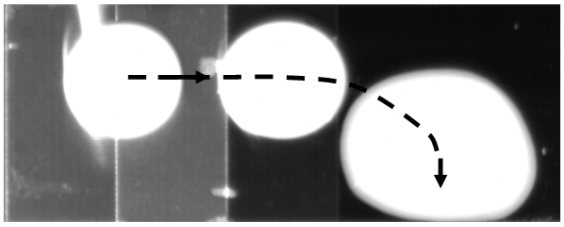
Lai, Yang,* Shieh, *Lab Chip* 2010

a microstructure and SAM composition gradient surface



transport of droplets across superhydrophobic to hydrophilic surfaces

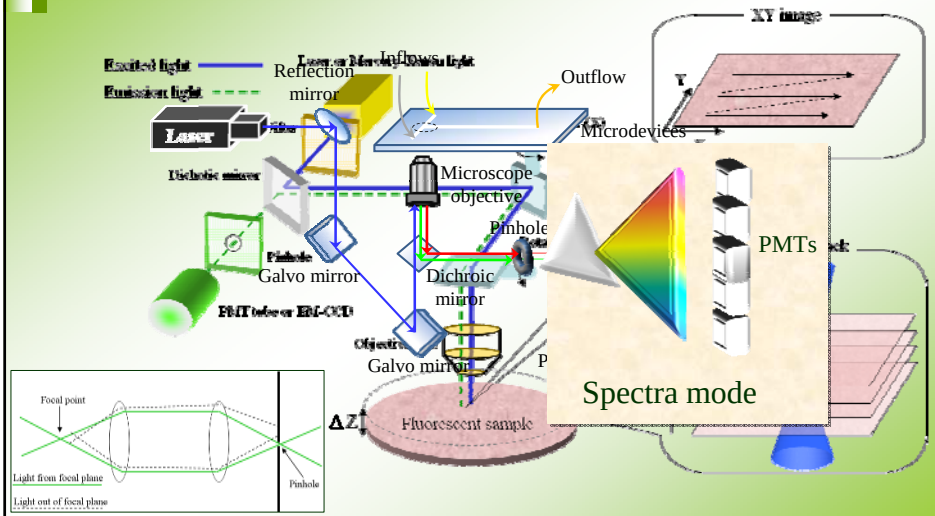




a double-direction gradient

Confocal Fluorescence Microscopy

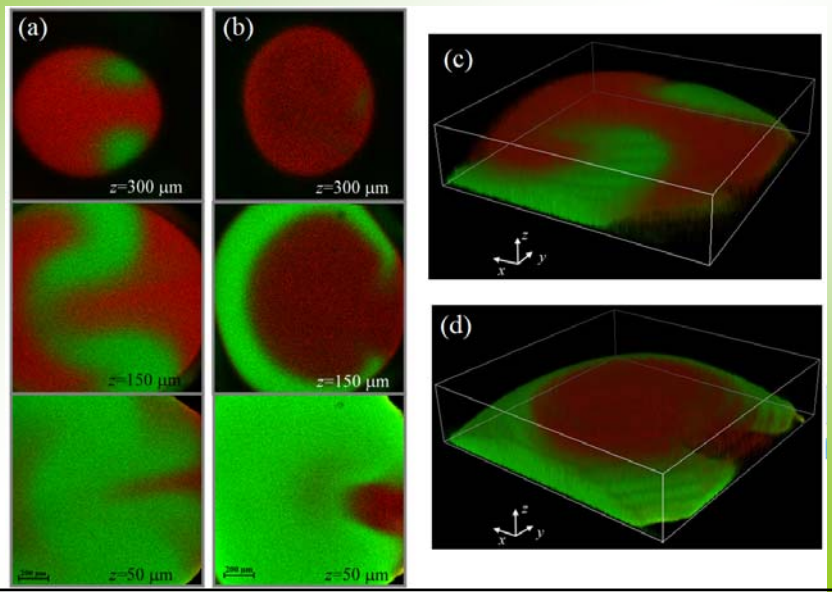
Beam Lab., NTU



DNA hybridization in Reaction Channels

Lab Chip, 2010; Beam Lab., NTU

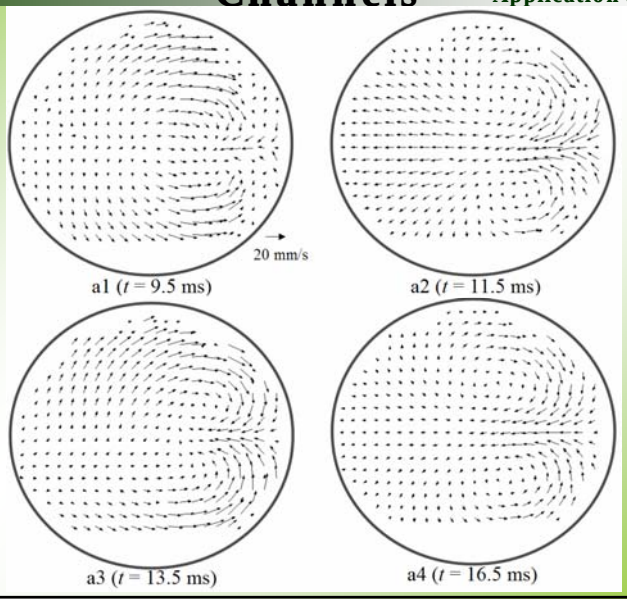
Application and pilot-test



DNA hybridization in Reaction Channels

Beam Lab., NTU

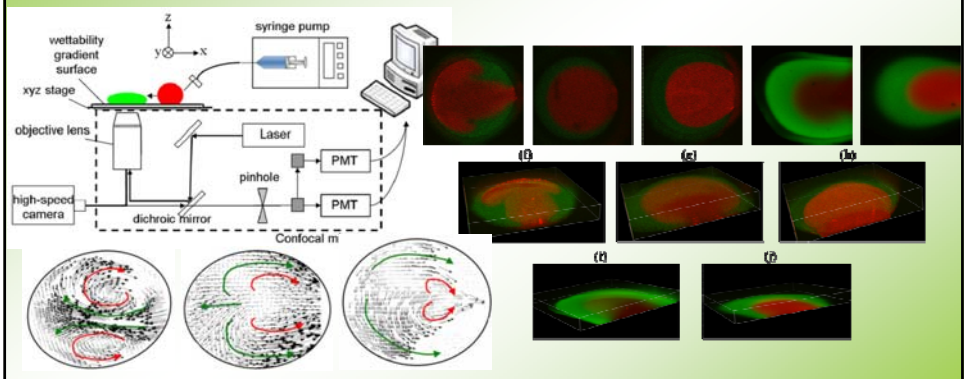
Application and pilot-test



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***

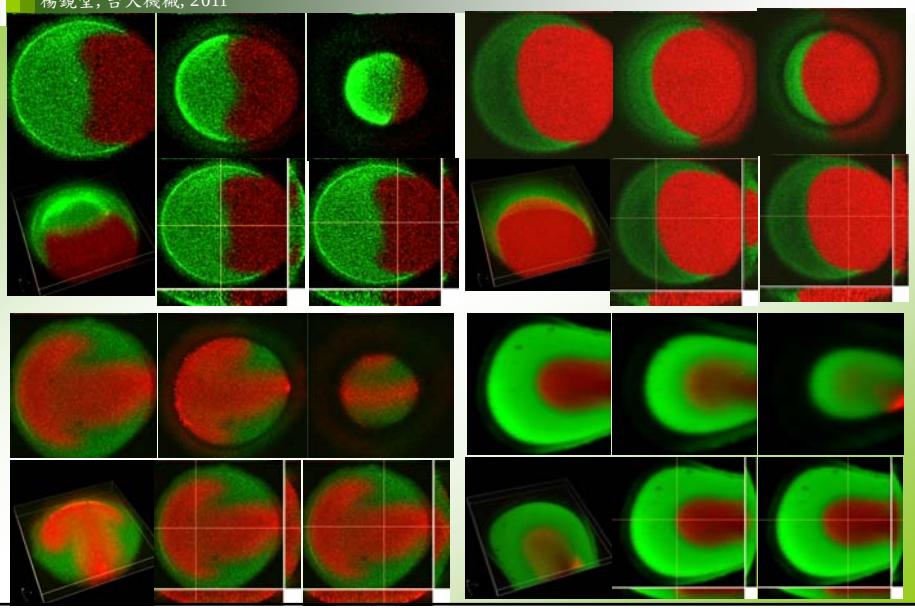
Microfluidics and Nanofluidics, doi: 10.1007/s10404-012-1096-2, 2013



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.

Reconstruction of Species Concentrations Interior the Colliding Droplets

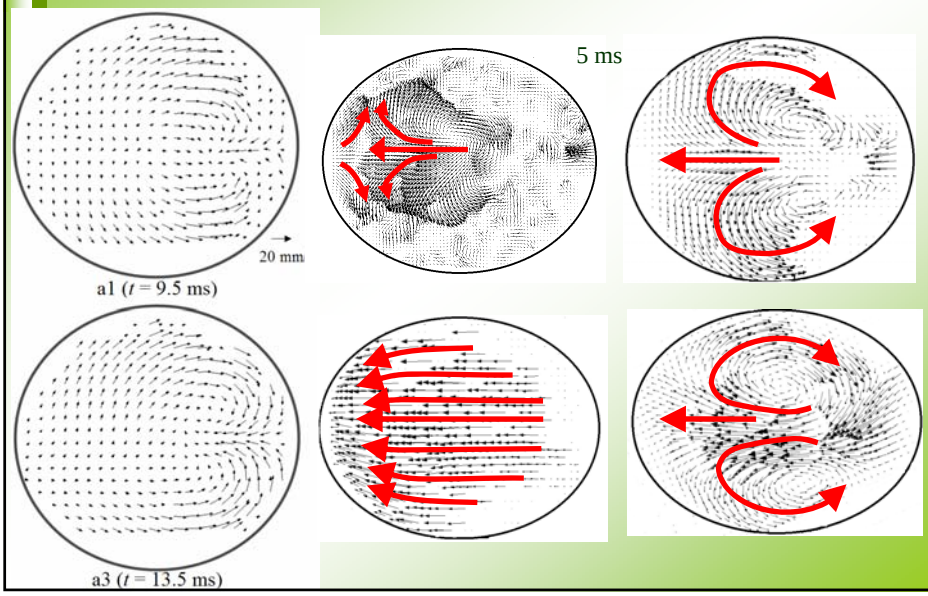
楊鏡堂, 台大機械, 2011



Flowfield Measured with Micro-PIV in Two Coalescenced Droplets

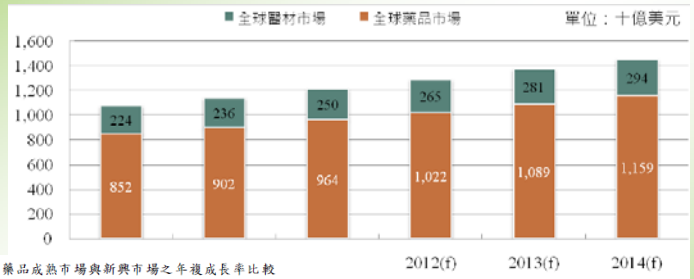
Beam Lab., NTU

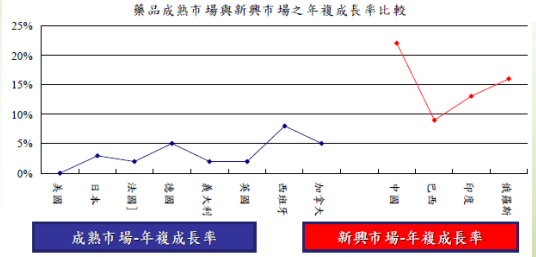
Application and pilot-test



Next-generation microfluidic system for *drug screening* and *cell analysis*

全球生醫產業產值預測





- 新興國家-主要以金磚四國為例(中國、巴西、印度、俄羅斯) 將扮演全球市場成長關鍵角色
- 2008-2013年全球藥品市場年複合成長率為3%-6%。
- 歐美新進大國之藥品市場已趨於成熟，成長率維持在1-3%。
- 新興國家藥品市場未來將持續大幅成長，預期年複合成長率為14%-16%

資料來源:工研院產經中心 (IEK)

100-102年度奈米國家型科技計畫

應用奈升液珠操控技術於高通量細胞測試之可調式奈微複合結構平台

Tunable nano/micro-composite structure platform for high throughput cell analysis *via* manipulating nano-liter droplets

2011/08/01-2014/07/31, NTD 8,000,000 (2011)/7,000,000 (2012)

計畫主持人: 楊鏡堂 終身特聘教授, 國立台灣大學機械工程學系

計畫共同主持人: 陳文鍾 教授, 國立台灣大學醫學院急診醫學科

周涵怡助理教授, 國立台灣大學醫學院口腔生物科學研究所

應用於生化微液珠操控及檢測之可調式奈微複合結構平台開發 (總計畫及子計畫一)

計畫共同主持人: 陳志臣 講座教授兼工學院院長, 國立中央大學機械學系

孫珍理 副教授, 國立台灣大學機械工程學系

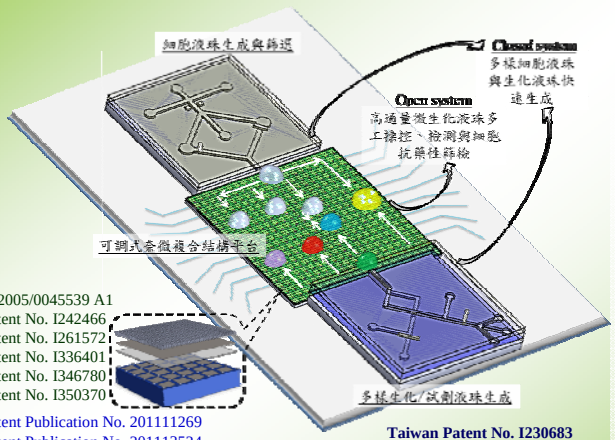
微流道內奈微液珠動力操控及其與開放式系統整合之研究 (子計畫二)

計畫共同主持人: 許佳賢 助研究員, 國家衛生研究院醫工組

陳致真 助理教授, 國立清華大學奈微所

奈微液珠細胞包覆與抗癌藥物篩選應用之研究 (子計畫三)

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**

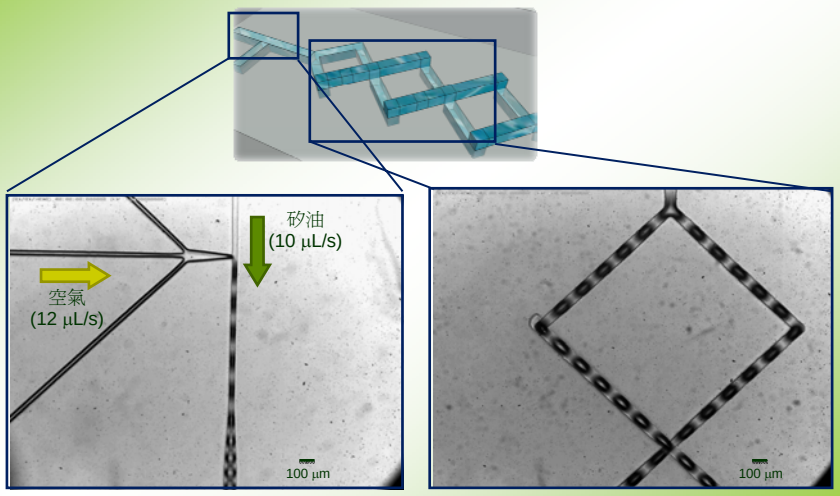
✓包覆細胞或試劑(候選藥物)的微液珠可被**有效地篩選、分類與運用，避免細胞與試劑浪費**

✓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**

Preliminary Tests

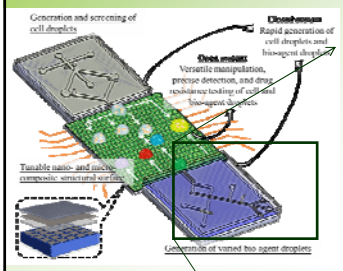
Yang *et al.*, *Microfluidics & Nanofluidics*, 2011



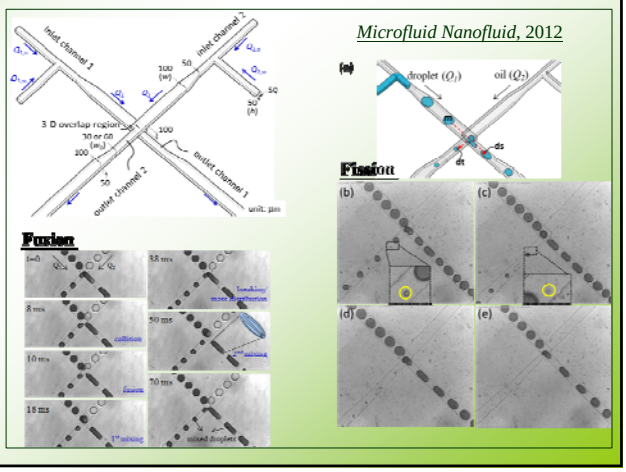
張偉軍碩士論文, 2011

Beam Lab

Next-generation microfluidic system for *drug screening* and *cell analysis*



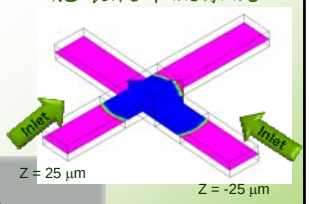
藥品液珠產生元件（十字交疊流道）

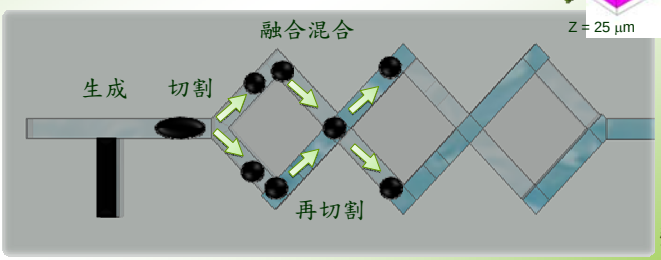


液珠在流道中的切割、融合與混合機制研究

Yang *et al.*, *submitted to Lab Chip*, 2011

本研究主要目的在探討兩股液珠流(droplet flow)在十字交疊流道中的交互作用，包含液珠融合、混合效率及切割現象。以實驗數據分析融合條件，並以數值模擬最佳化幾何設計，進而將其應用在加強微反應器的混合效率，及液珠混合與否的操控上，能讓液珠流系統有更多元的發展空間。

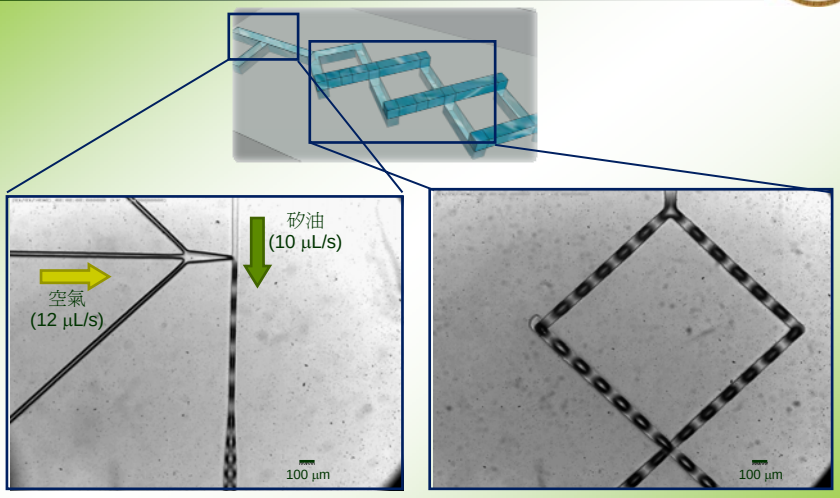




張偉軍碩士論文, 2011

Preliminary Tests

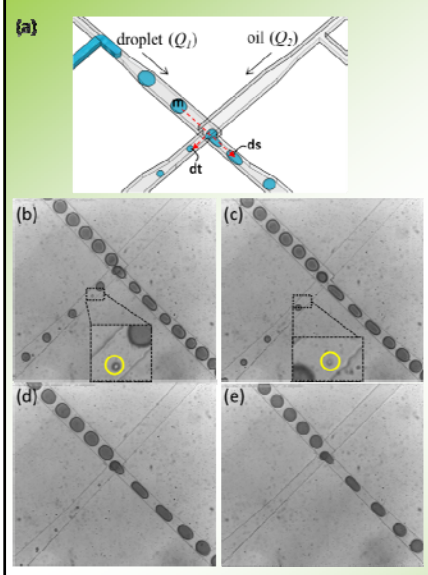
Yang *et al*., *submitted to Lab Chip*, 2011

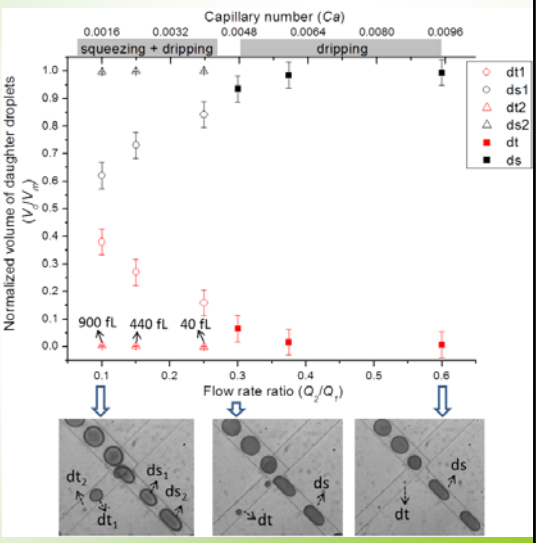


張偉軍碩士論文, 2011

Droplet Fission

Submitted to MNF, 2011

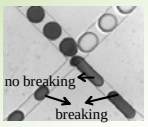
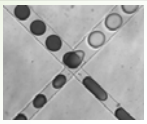
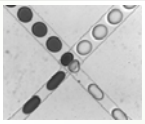
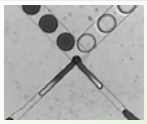
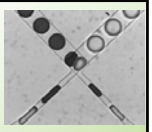




Film of droplet fission

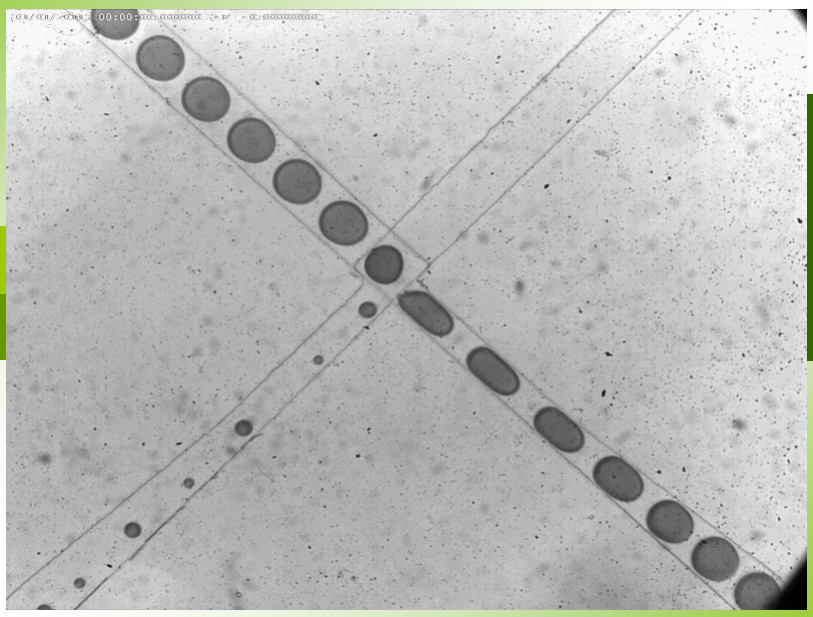
Droplet Fusion and Mixing

Submitted to MNF, 2011

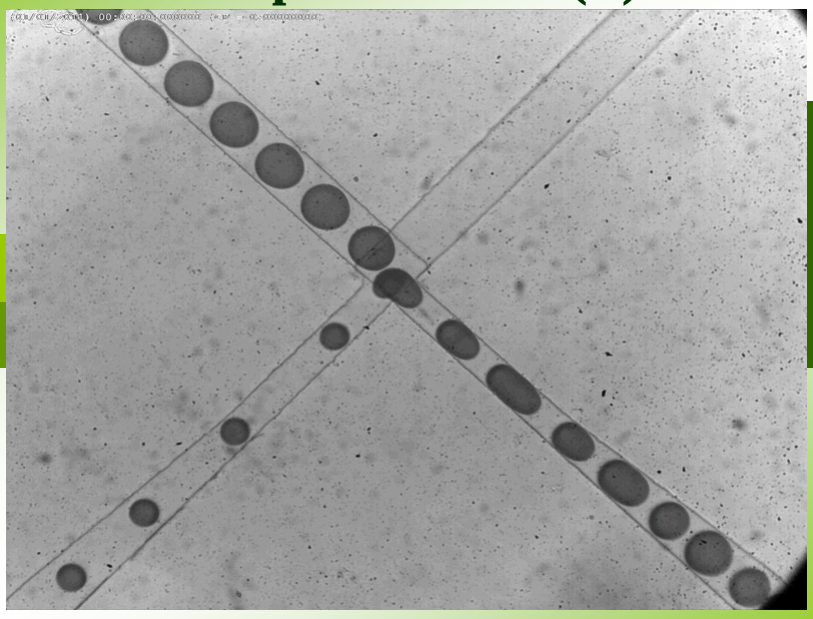
Initial width of the outlet channels (w_o)	60 μm			30 μm	
Flow rate (μL min^{-1})	$Q_1=Q_2<0.6$ ($Ca<0.0048$)	$1<Q_1=Q_2<1.6$ ($0.0079<Ca<0.0127$)	$2<Q_1=Q_2$ ($0.0159<Ca$)	$Q_1=Q_2<0.2$ ($Ca<0.0016$)	$0.4<Q_1=Q_2$ ($0.0032<Ca$)
					
	Fusion Unstable breaking	Stable fusion Stable breaking	No fusion No breaking	Stable fusion Stable breaking	No fusion Breaking
Fusion process	During the two droplets impact with each other. (side-by-side)		none	During the two droplets tend to separate. (decompression)	none
Breaking process	Asymmetric breaking		none	More symmetric breaking	
Mixing process	• Stretching and folding at the 3-D overlap region. • Agitating by two inversely recirculating flows at the narrower straight outlet channel.		none	Agitating by two inversely recirculating flows at the narrower straight outlet channel.	none

Film of droplet fusion

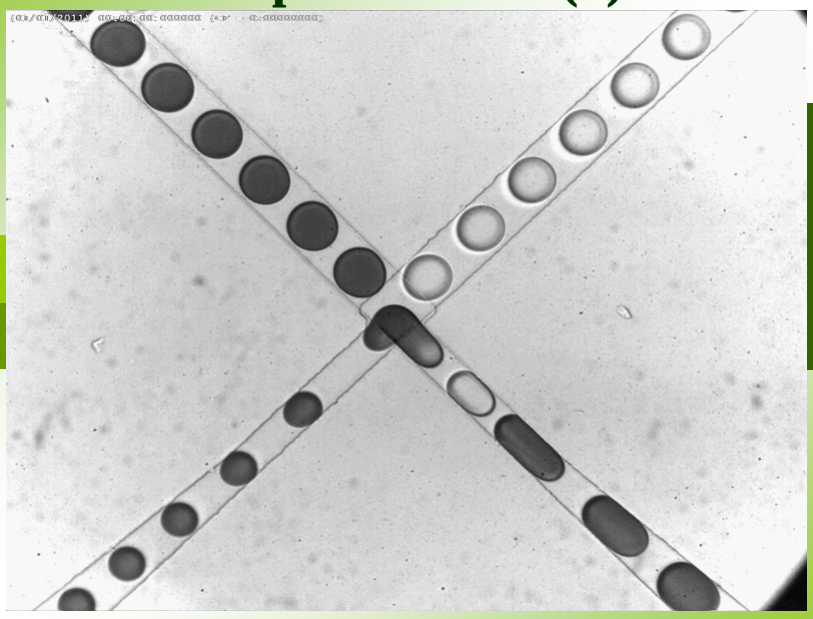
Droplet Fission (1)



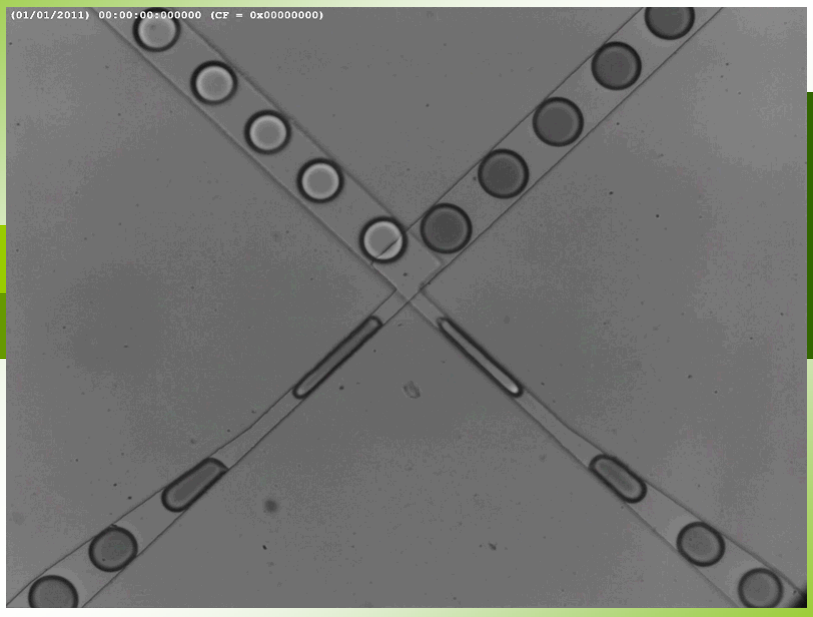
Droplet Fission (2)



Droplet Fusion (1)

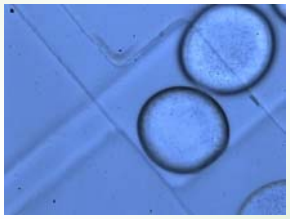


Droplet Fusion (2)

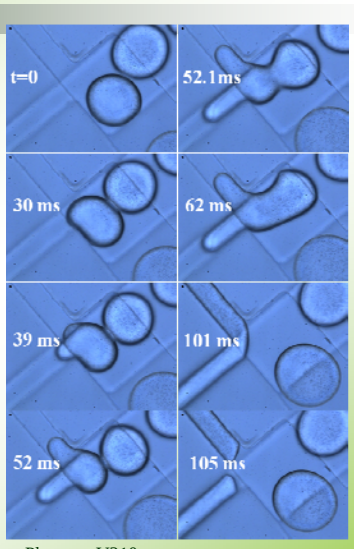


Visualization of Droplets Fusion and Fission

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



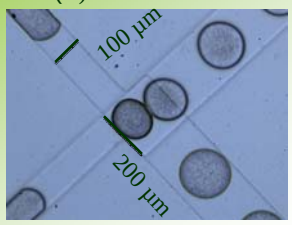
Frame rate：6000 fps
Spatial resolution：2.13
μm/pixels



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

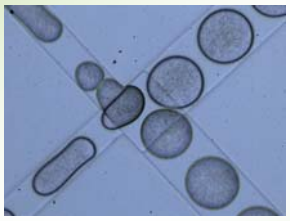
Mechanism
Droplets Fusion, Fission, and Distribution

(a.) fusion and fission



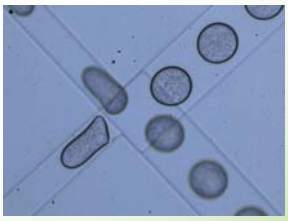
Deep of single layer: 51 µm
DI water: 0.5 µl/min
Silicone oil: 1 µl/min
Re: 0.031 ; Ca: 0.0006

(b.) fission and distribution

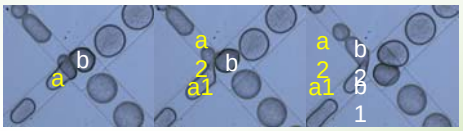


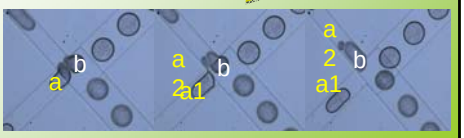
Deep of single layer: 51 µm
DI water: 2 µl/min
Silicone oil: 2 µl/min
Re:0.083 ; Ca: 0.0016

(c.) fission and distribution

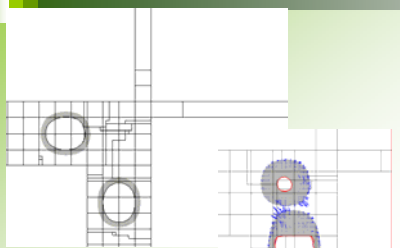


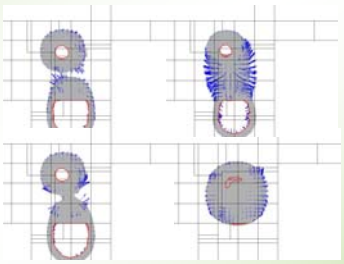
Deep of single layer: 51 µm
DI water: 2 µl/min
Silicone oil: 5 µl/min
Re: 0.145 ; Ca: 0.0028

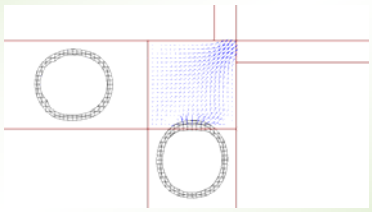


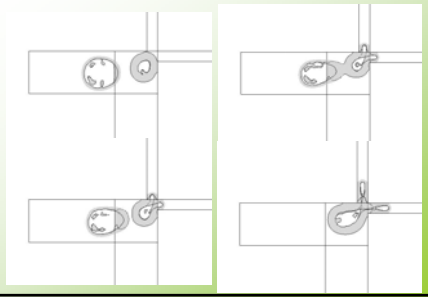


Droplets Simulation

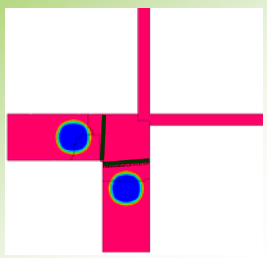




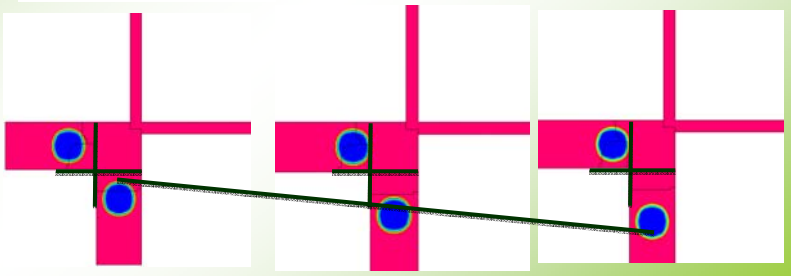




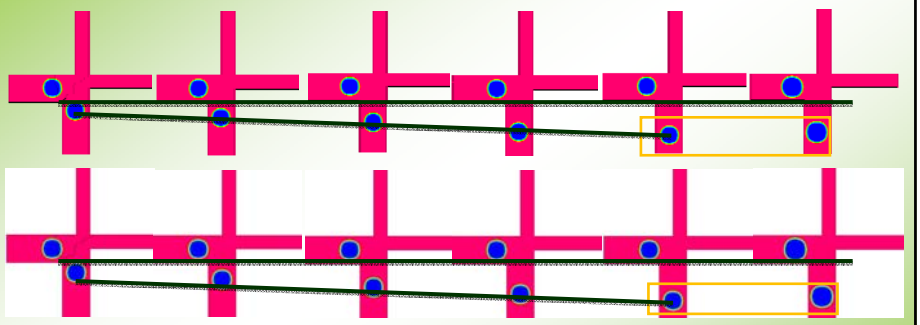
Droplets simulation 200-50 (2D)



- 液珠起始位置不同會影響液珠進入縮口流道的行為
- 影響因素:
  1. 縮口大小 2. 液珠大小 3. 液珠前後距離

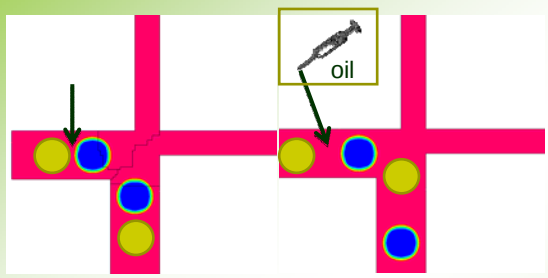


Droplets simulation 200-100 (2D)

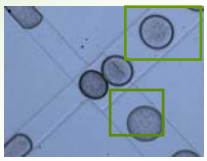


- 液珠起始位置不同會影響液珠進入縮口流道的行為
- 影響因素: 1. 縮口大小 2. 液珠大小 3. 液珠前後距離(相位差)

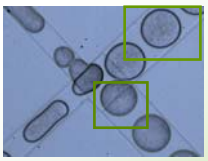
How to control distance between droplets?



- 實驗中液珠大小因為上游T型流道不同流率而改變。
- 液珠之間的距離會影響液珠進入十字交疊處的行為



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



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

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

影響因素: 1. 縮口大小 2. 液珠大小 3. 液珠前後距離

Future Work

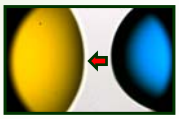
- 設計濃度分配觀測晶片
  （液珠融合、濃度變化、及時改變濃度）
- 找出完整液珠式濃度稀釋流速範圍
- 設計液珠切割質量分配實驗
- 液珠濃度稀釋晶片實際應用

New Topics

Mixing Test— food coloring & chemical reaction

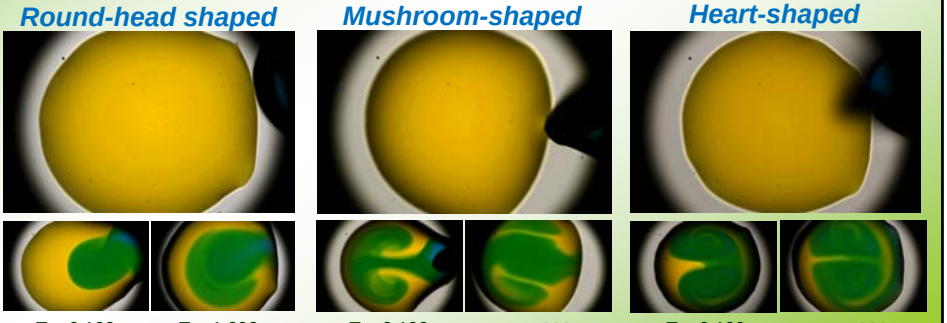
Sometimes a color change is the result of a chemical reaction. Sometimes it is just the result of mixing colors.

Tartrazine (stationary droplet)



Indigo Carmine (moving droplet)

Round-head shaped *Mushroom-shaped* *Heart-shaped*



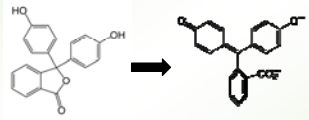
T = 0.100 s T = 1.000 s T = 0.100 s T = 1.000 s T = 0.100 s T = 1.000 s

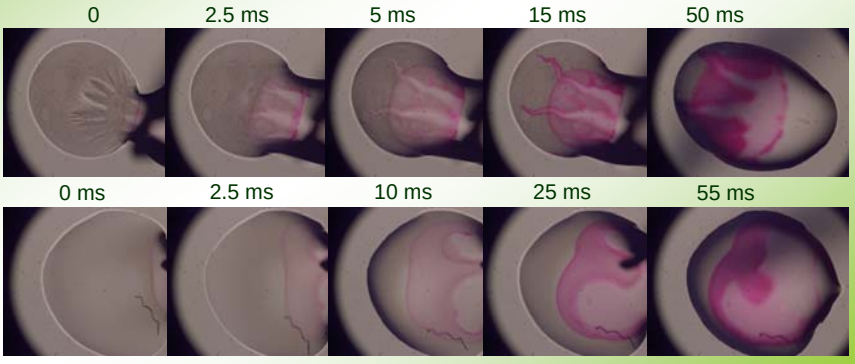
1280 × 800 pixels, 3200 fps, 512X Slow motion

Chemical Reaction in Colliding Droplets

酚酞是一種弱有機酸，pH＞10時爲粉紅色的醌式結構，
是一種常用的酸鹼指示劑。

酚酞+ NaOH (PH=12)　　3200 fps

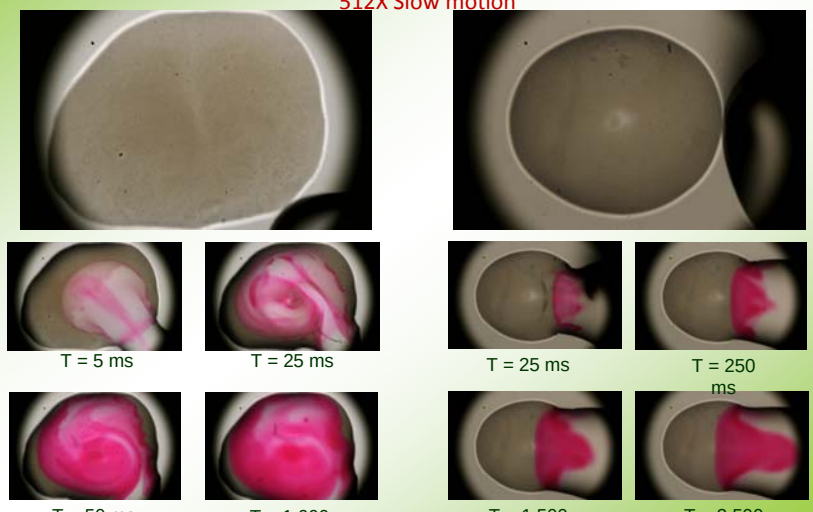




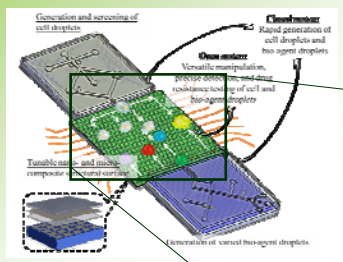
Beam Lab

Chemical Reaction in Droplets

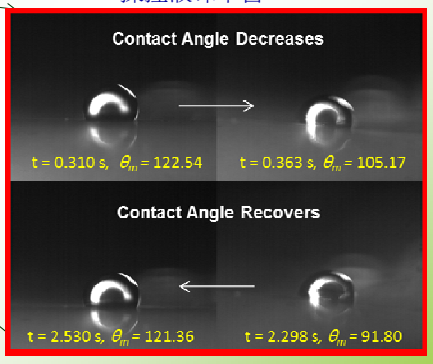
Mode C　　1280 × 800 pixels, 3200 fps
512X Slow motion　　*Mode D*



Next-generation microfluidic system for *drug screening* and *cell analysis*



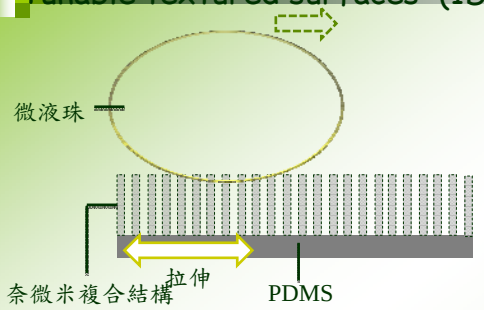
操控液珠平台

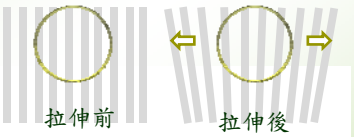


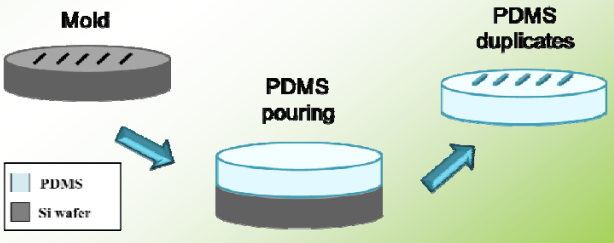
申請專利中

Droplet/plug-based microfluidics (open syste

Tunable textured surfaces (1D)



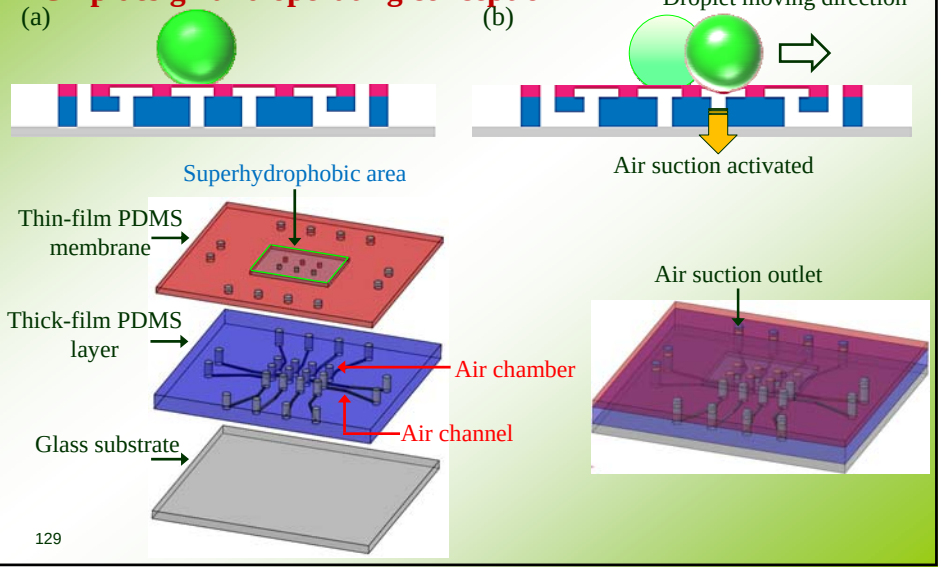




申請專利中

A Pneumatic Open-Surface Microfluidic Platform for Droplet Manipulation

Chip design and operating conception



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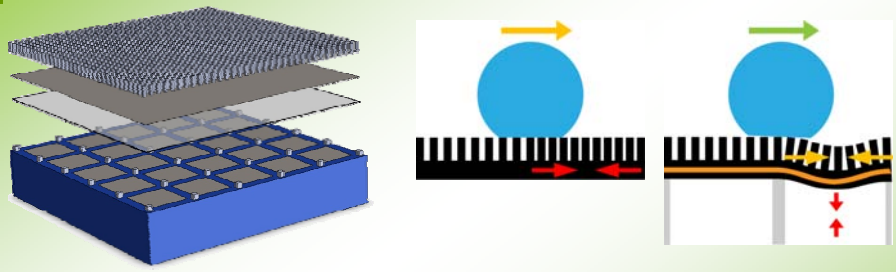
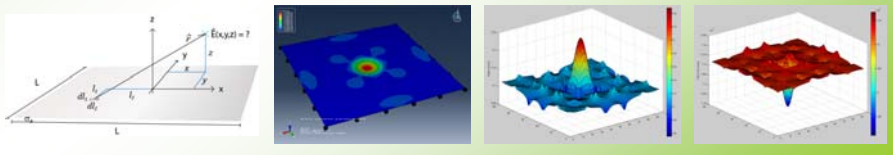
Droplet/plug-based microfluidics (open system)

Tunable textured surfaces (2D)

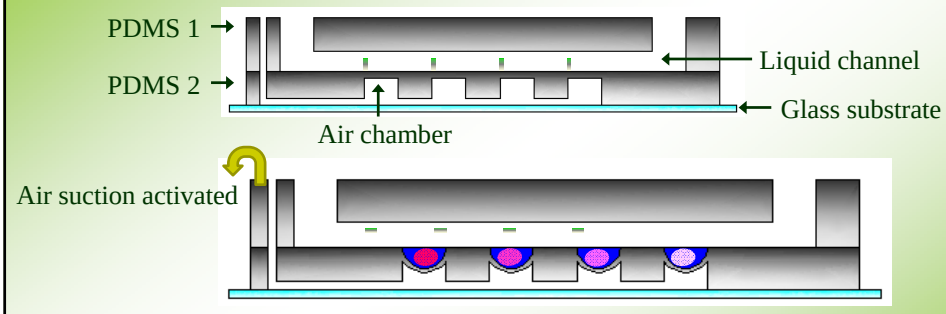


靜電力拉伸 → 彈性材料變形 → 結構密度改變 → 液滴表面自由能梯度



申請專利中

Encapsulation of single cells to evaluate the cytokines & protein of WBC in animals receiving different therapies

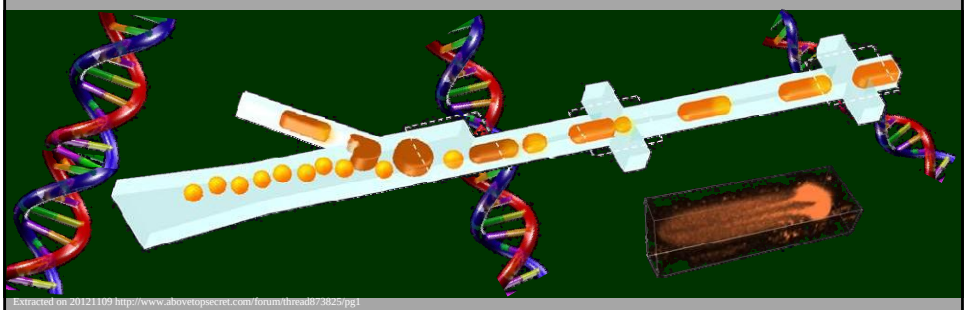


1. Droplets generation
2. Particle test
3. Single Cell encapsulation
4. Drug therapies

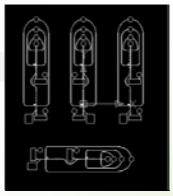
2012中華民國立學學會年會暨第36屆全國力學會議
The 36th National Conference on Theoretical and Applied Mechanics

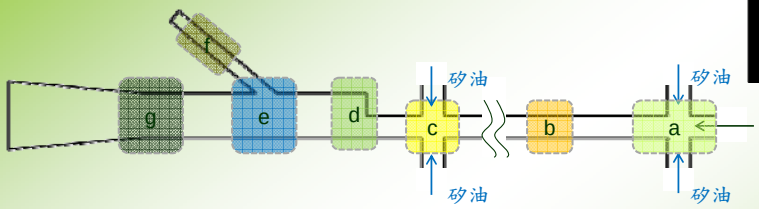
DNA 濃縮暨分離之液珠式微型全分析系統

Droplet-based Micro Total Analysis Device to Enrich and to Separate Hydrophobically Functionalized DNA in Free-Flow Microdroplet

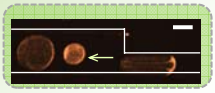


DNA濃縮與分離—實驗影像

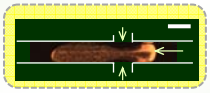




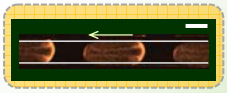
d. 流道擴張



c. 液珠分割

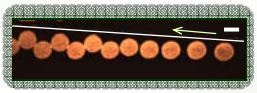


b. DNA 聚集濃縮

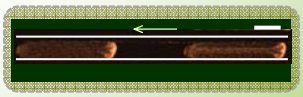


a. 液珠生成

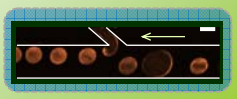
g. 高濃度尾端液珠(rear droplet)收集



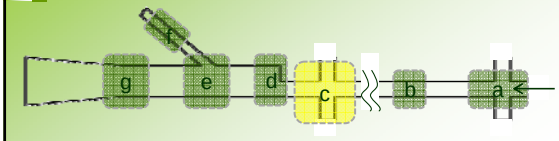
f. 前端液珠(front droplet)收集

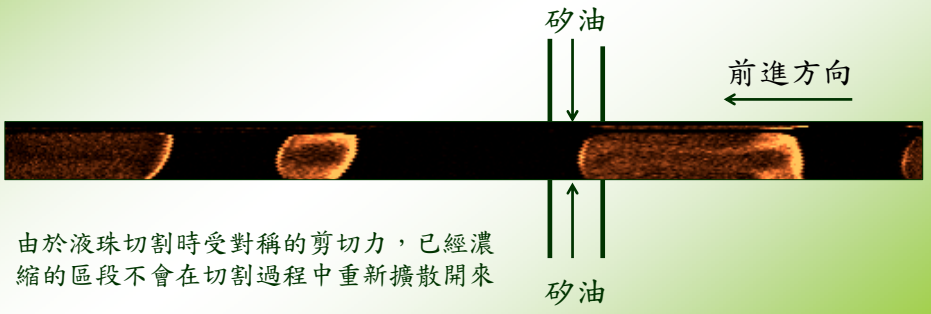


e. 液珠分類



DNA濃縮與分離—液珠分割

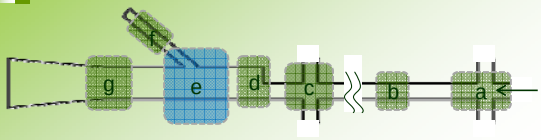




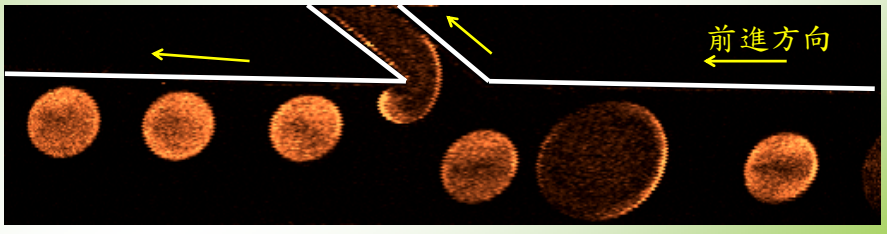
由於液珠切割時受對稱的剪切力，已經濃縮的區段不會在切割過程中重新擴散開來

結果與討論

DNA濃縮與分離—液珠分類



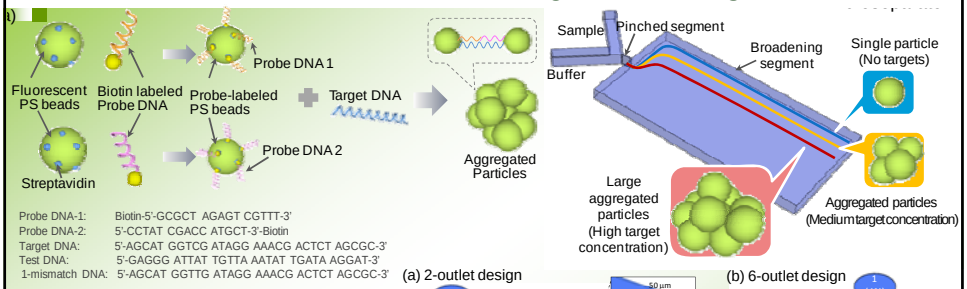
TAMRA-labeled
DNA 溶液



Aggregation-based Detection of DNA in a Microseperator

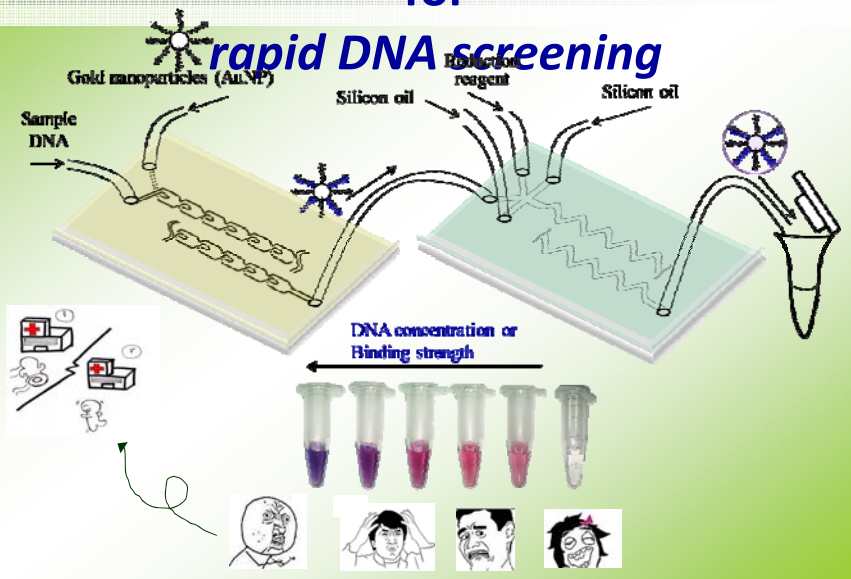
Biosensors and Bioelectronics (in revision), 2012

Y. T. Chen, Y. C. Liu, W. F. Fang, and **J. T. Yang,***

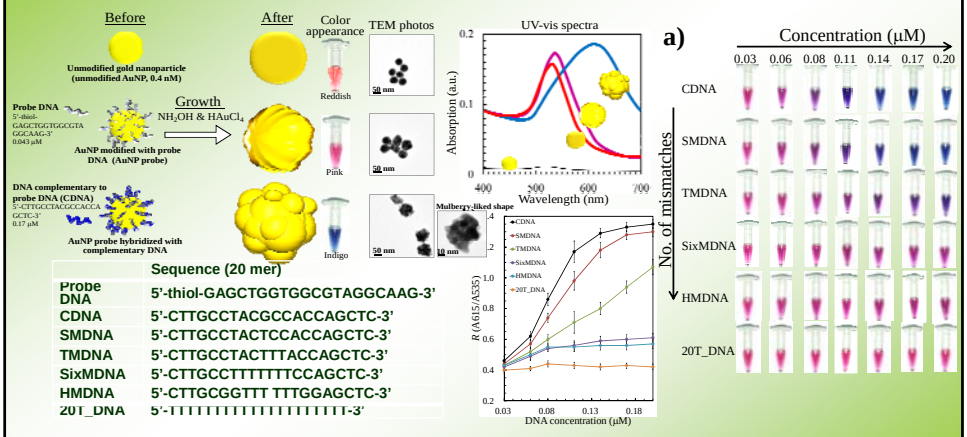


A novel aggregation-based method to execute oligonucleotide detection in a PFF (pinched flow fractionation) microseparator is proposed and developed. The label-free target DNA hybridizes with the probe DNA on the surface of microspheres and causes the polymeric aggregate, thus enlarging the average size of the aggregated particles.

Next-generation microfluidic system for *rapid DNA screening*



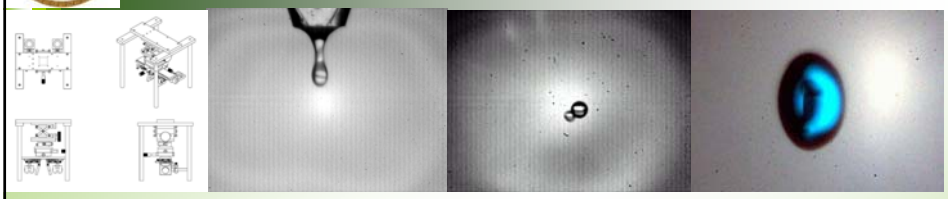
Hybridization-mediated growth of gold nanoparticle probes for visual and spectrophotometric screening of DNA mismatch



	Sequence (20 mer)
Probe DNA	5'-thiol-GAGCTGGTGGCGTAGGCAAG-3'
CDNA	5'-CTTGCCTACGCCACCAGCTC-3'
SMDNA	5'-CTTGCCTACTCCACCAGCTC-3'
TMDNA	5'-CTTGCCTACTTTACCAGCTC-3'
SixMDNA	5'-CTTGCCTTTTTTTCCAGCTC-3'
HMDNA	5'-CTTGCGGTTT TTTGGAGCTC-3'
20T_DNA	5'-TTTTTTTTTTTTTTTTTTTT-3'

A novel color approach to detect rapidly and conveniently DNA samples is proposed based on a concept of DNA hybridization-mediated growth of AuNP probes. With this method, one can not only evaluate semi-quantitatively the target DNA but also screen mismatches of DNA samples with a naked eye or simple spectrophotometer.

國立台灣大學 機械工程學系 碩士論文計畫書



雙組份液滴碰撞與燃燒現象之觀測與分析

The Investigation on Collision Behavior and Combustion Characteristics of Binary Droplet

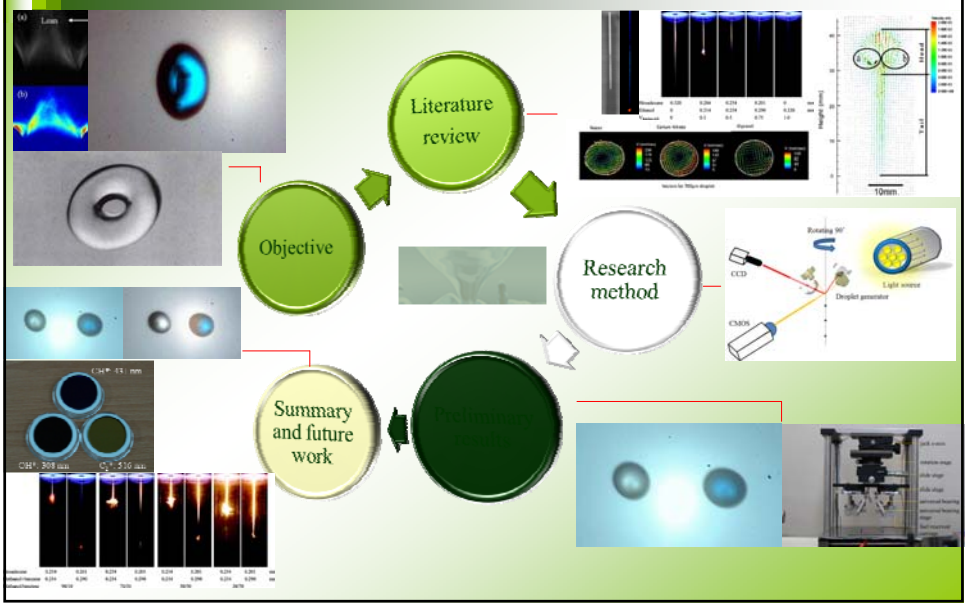
學生姓名: 莊宗穎 (Jhuang, Zong-Ying)

指導教授: 王興華 博士 (Dr. Wang, Ching-Hua)

楊鏡堂 博士 (Dr. Yang, Jing-Tang)

中華民國101 年12 月20 日

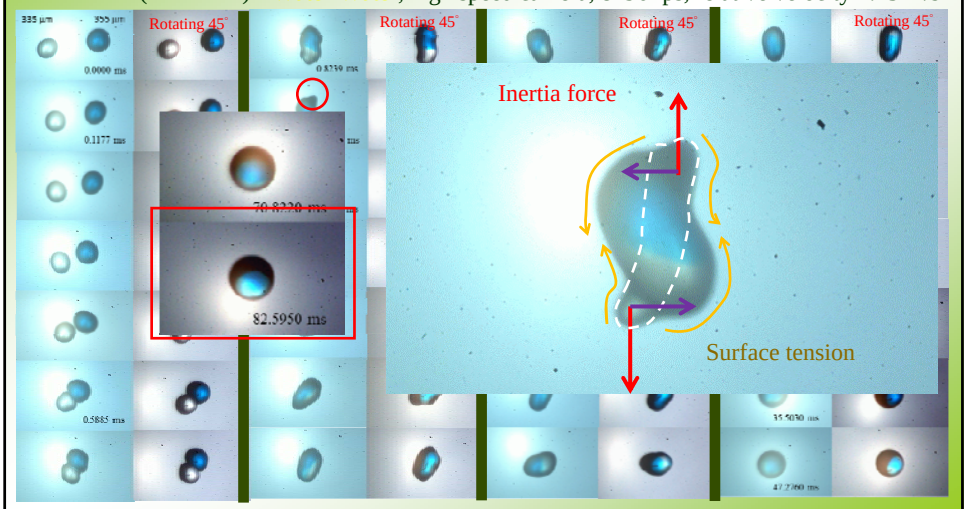
雙組份液滴碰撞與燃燒現象之觀測與分析



Droplets collision

Department of Mechanical Engineering,
National Taiwan University
[莊宗穎碩士論文計畫書]

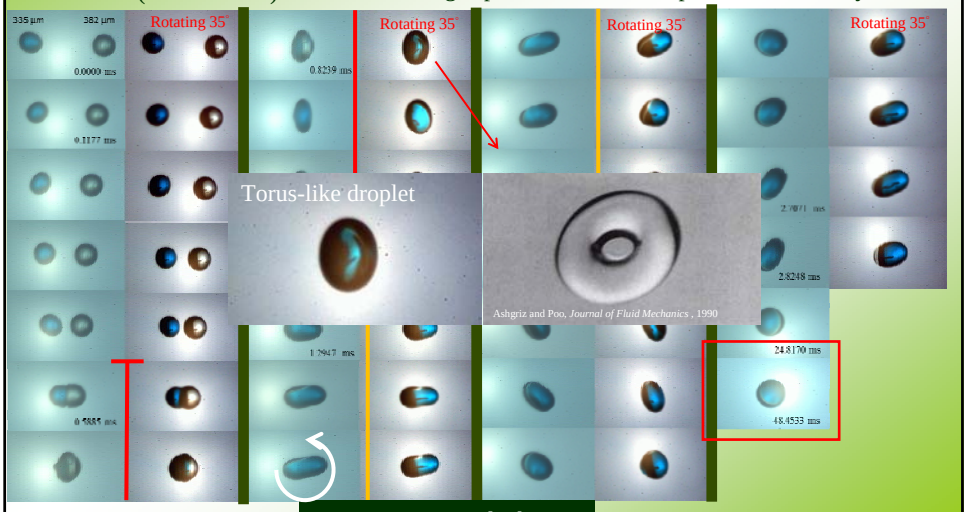
Coalescence (off-center) Water-Water, high speed camera, 8496 fps, relative velocity 1.13 m/s



Droplets collision

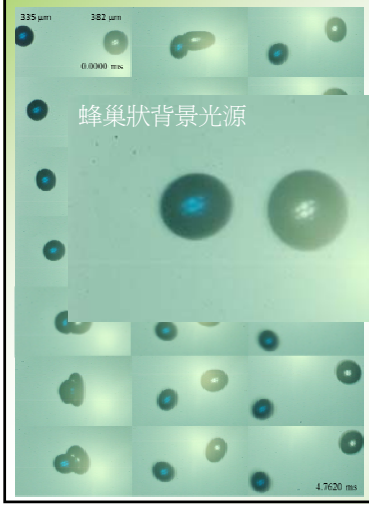
Department of Mechanical Engineering,
National Taiwan University
[莊宗穎碩士論文計畫書]

Coalescence (near head-on) Water-Diesel, high speed camera, 8496 fps, relative velocity 1.42 m/s

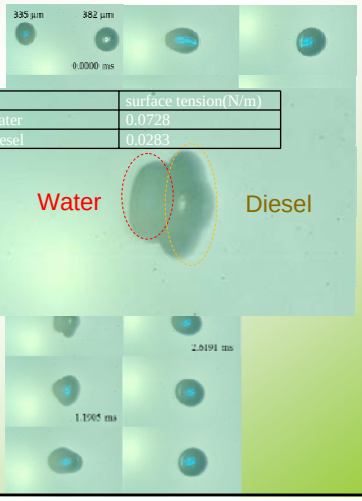


Droplets collision

Water-Diesel, high speed camera, 4200 fps
Bouncing (head on)

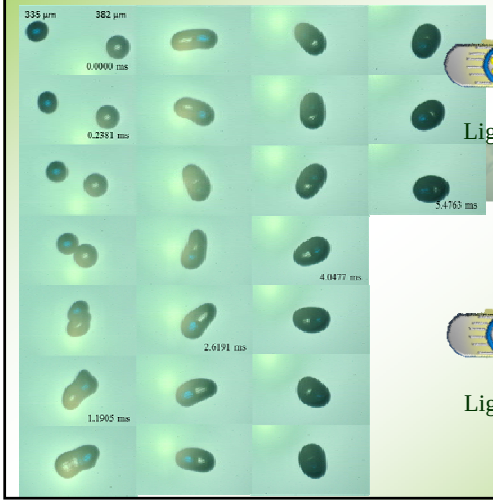


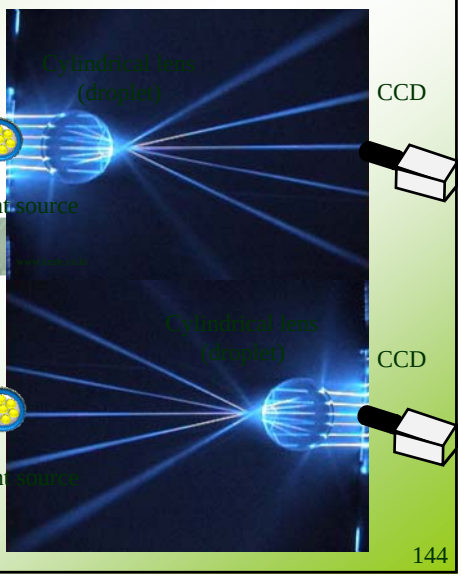
Water-Diesel, high speed camera, 4200 fps
Coalescence (head on)



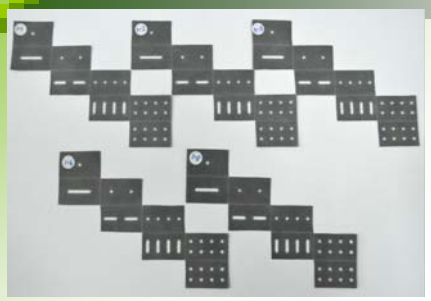
	surface tension(N/m)
Water	0.0728
Diesel	0.0283

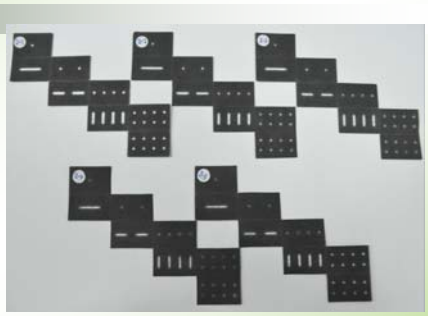
Water-Diesel, high speed camera, 4200 fps
Coalescence (off-center)

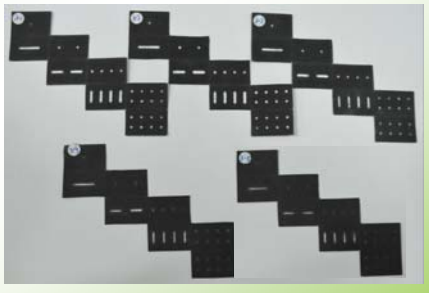




紙基底微流體電池



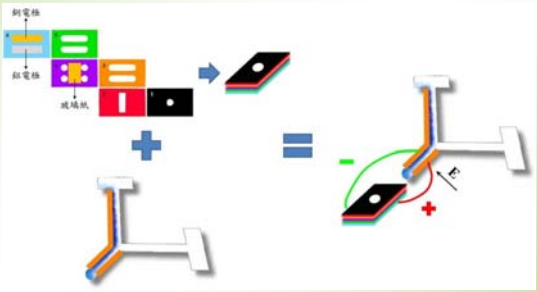




國立台灣大學 機械工程學系暨研究所 碩士論文計畫書

中華民國101年12月19日

紙基底之可攜式自驅動微流體電泳元件與流道閥

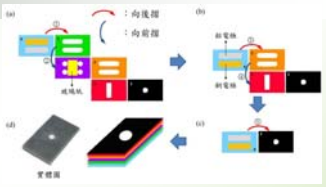


學生：陳崧昇 機械所熱流組

指導教授：楊鏡堂 博士 廖英志 博士

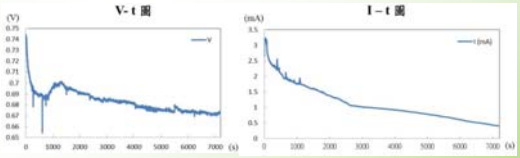
紙基底之可攜式自驅動微流體電泳元件與流道閥

(1) 兩道步驟即可完成紙基底流道，並以摺紙術迅速將流道由2-D摺疊成3-D

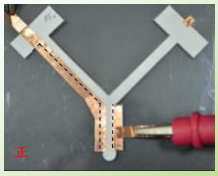


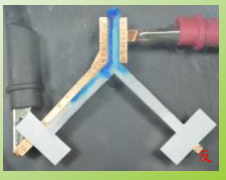
(2) 隔膜型紙基底電池(one cell)：

- 降低成本
- 穩定放電電壓 **0.69 V**
- 最大電流 **3.22 mA**
- 平均電流 **2.3 mA**



(3) 以紙濾紙電泳於紙基底流道中進行**分離與濃縮**





(4) 只需提供**15 V**，即可產生高壓電泳門檻**50 V/cm**的電場強度且具有不錯的分離效果

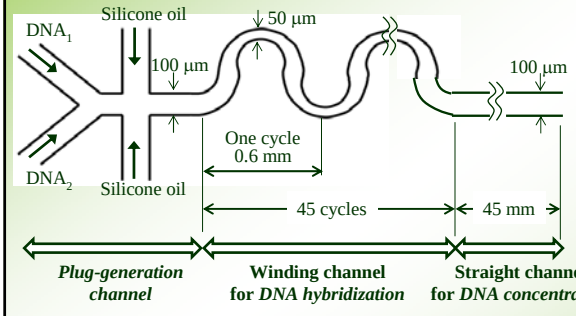
Locally enhanced concentration and detection of oligonucleotides in a plug-based microdevice

Lab Chip, in revision

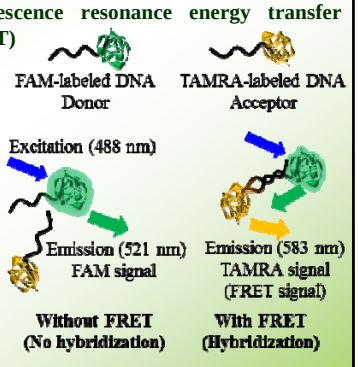
Hybridization test

DNA hybridization in a *designed device*

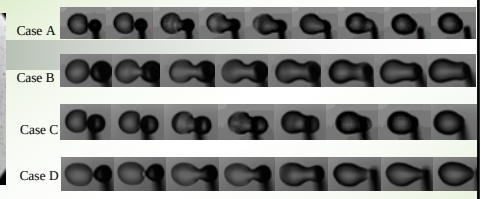
10-mer oligonucleotides



Fluorescence resonance energy transfer (FRET)

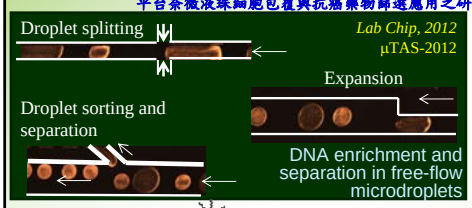


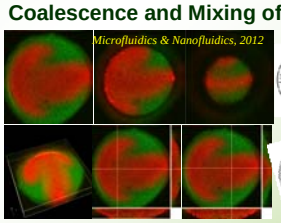
Progress of droplet-based microfluidics

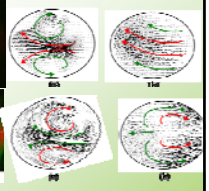


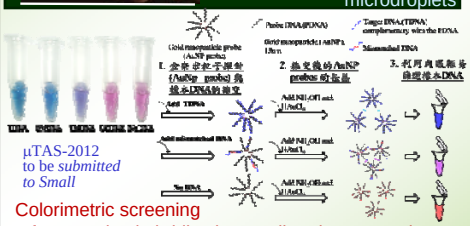
Fusion and fission of droplets → 研發糖尿病新藥篩檢的平台奈微液珠細胞包覆與抗癌藥物篩選應用之研究

Coalescence and Mixing of Colliding Droplets

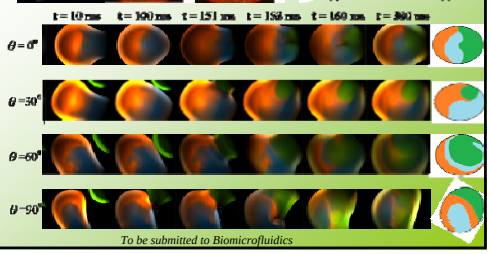








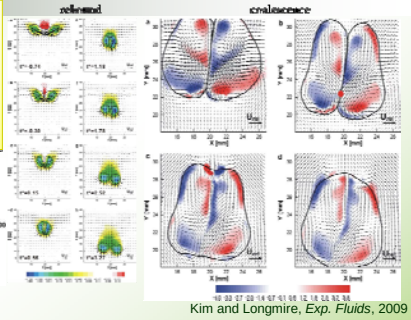
Colorimetric screening
of DNA using hybridization-mediated AuNP probes

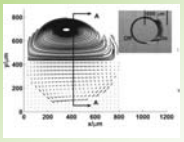


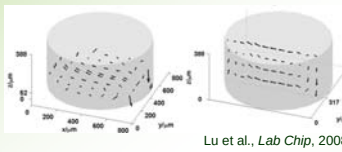
To be submitted to Biomicrofluidics

微液珠內部流場分析

早期的研究是使用micro-PIV觀察流道內液珠內部流場，並用以說明混合現像。近年來利用共軛焦顯微術的輔助，可得到液珠內部三維流場速度變化。

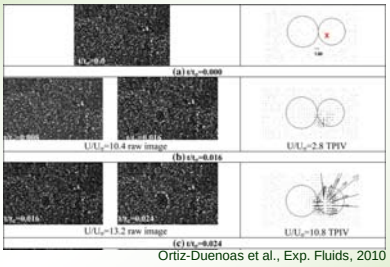




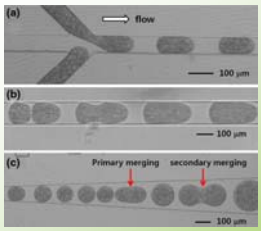


Lu et al., *Lab Chip*, 2008

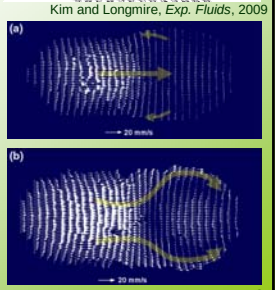
Kim and Longmire, *Exp. Fluids*, 2009



Ortiz-Duenoas et al., Exp. Fluids, 2010



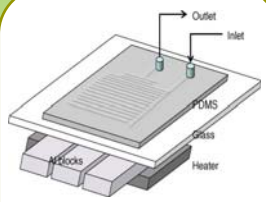
Jin and Joo, Exp. Fluids, 2012



加熱器構型

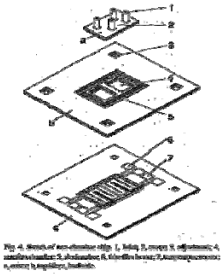
外加金屬塊熱源　蜿蜒狀　環狀　條狀　圍欄狀　陣列狀

1.外加金屬塊熱源

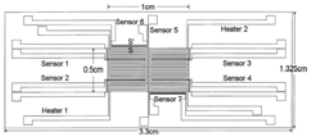


Kim *et al.*, *Biochemical Engineering Journal*, 2006

2. 蜿蜒狀(serpentine-type)

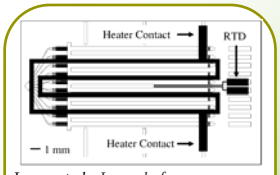


Poser *et al.*, *Sensors and Actuators A: Physical*, 1997

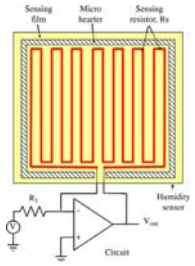


Lao *et al.*, *Sensors and Actuators A: Physical*, 2000

3.環狀



Losey *et al.*, *Journal of Microelectromechanical Systems*, 2002



Dai *et al.*, *Sensors and Actuators: B Chemical*, 2007

國 立 台 灣 大 學　機械工程學系暨研究所

網格式微反應器同步計數細胞並觀測溫度與細胞生長關係之研究

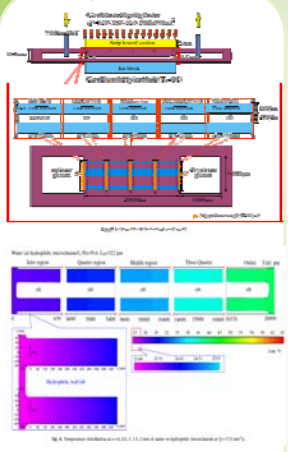
學生：俞又瑄

指導教授：楊鏡堂

日期：2012/11/08

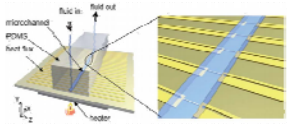
溫度量測

μLIF→螢光粒子
thermocouple

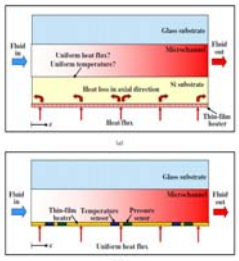


Hsieh *et al.*, *International Journal of Heat and Mass Transfer*, 2009

溫度感測器搭配溫控程式

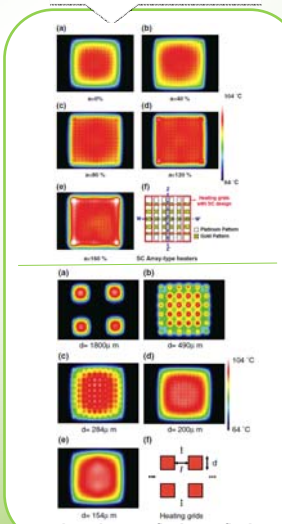


Hamadi *et al.*, *Lab Chip*, 2012



Lee *et al.*, *J.Micromech. Microeng.*, 2011

紅外線熱像儀



Hsieh *et al.*, *Microfluid Nanofluid*, 2009

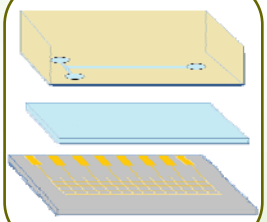
實驗架構

實驗儀器

電源供應器

PCI排線插槽

微加熱晶片



LABVIEW回授控制

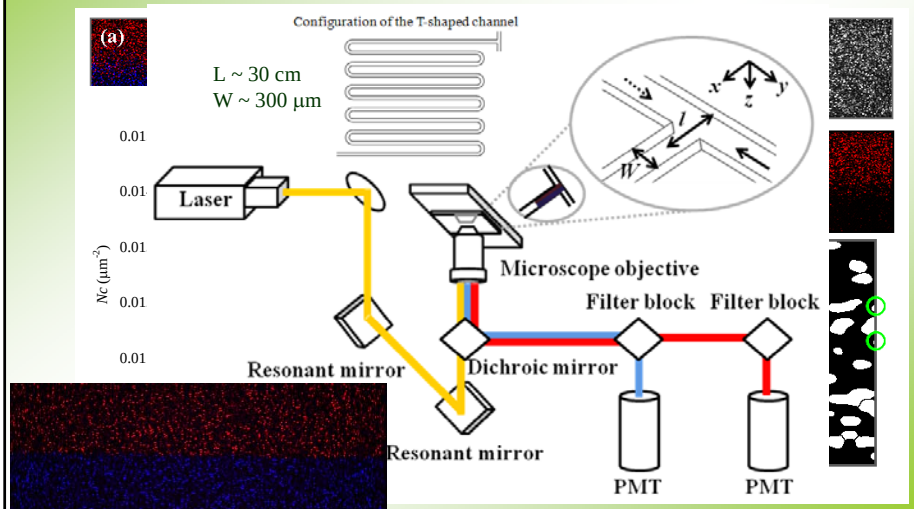
實驗量測

共軛焦顯微鏡

Multi-color Micro-PIV & Species Concentrations

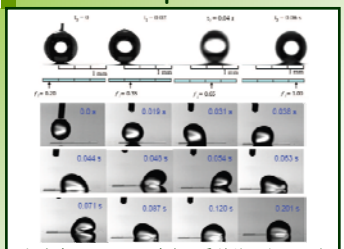
Beam Lab., NTU

Simultaneous measurement (micro-PIV & particle counting method)

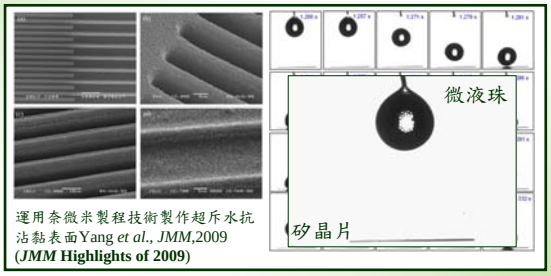


Droplet/plug-based microfluidics (open system)

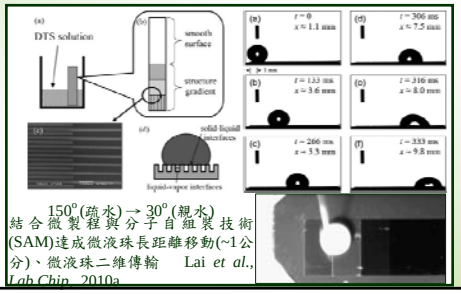
Droplet movement on textured/SAM surfaces



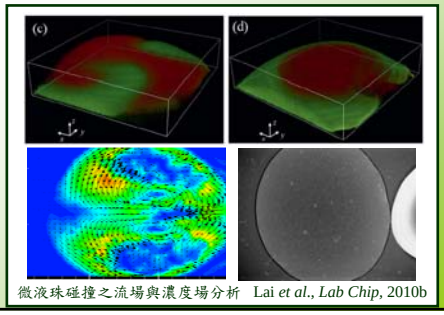
提出表面能階、能障與能量轉換的觀點，作為元件設計依據 Yang *et al.*, *Langmuir*, 2008



運用奈微米製程技術製作超斥水抗沾黏表面Yang *et al.*, *JMM*,2009 (***JMM* Highlights of 2009**)



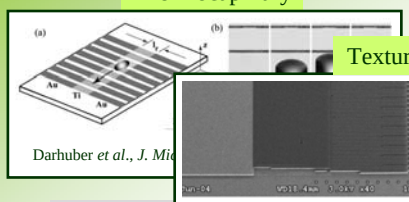
150°(疏水)→ 30°(親水)結合微製程與分子自組裝技術(SAM)達成微液珠長距離移動(~1公分)、微液珠二維傳輸 Lai *et al.*, *Lab Chip*, 2010a



微液珠碰撞之流場與濃度場分析 Lai *et al.*, *Lab Chip*, 2010b

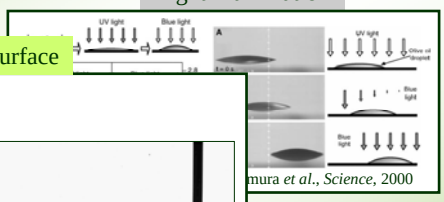
Droplet/plug-based microfluidics (open syste

Thermocapillary



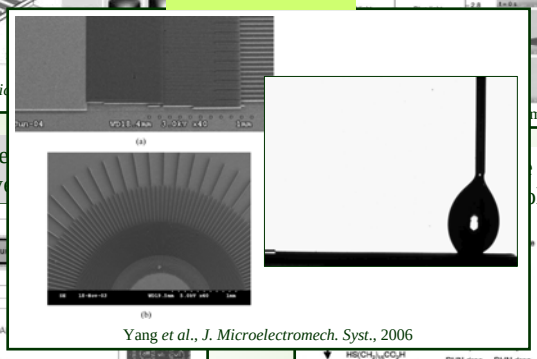
Darhuber *et al.*, *J. Mi*

Light illumination



mura *et al.*, *Science*, 2000

Textured surface

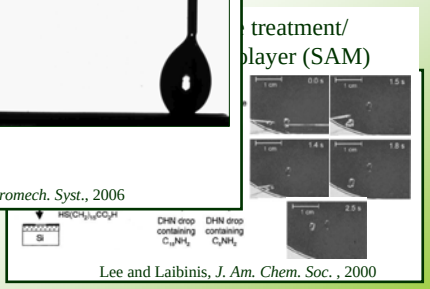


Yang *et al.*, *J. Microelectromech. Syst.*, 2006

Electrowe
lay

Cho *et al.*, *J. Microelectromech. Syst.*, 2003

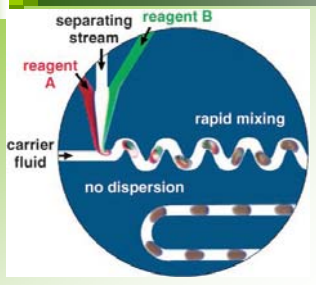
treatment/
layer (SAM)

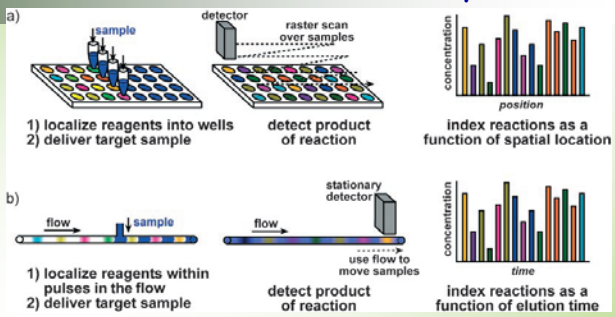


Lee and Laibinis, *J. Am. Chem. Soc.* , 2000

An external field might induce a dilemma!

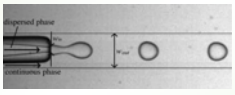
Droplet/plug-based microfluidics (closed system)



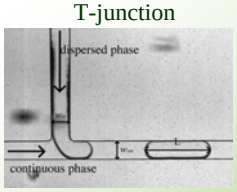


Song *et al.*, *Angew. Chem. Int. Ed.*, 2006

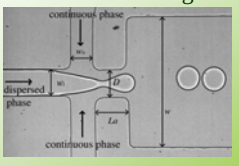
Co-flow



T-junction



Flow-focusing



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

Droplet/plug-based microfluidics (closed system)

Applications

Multi-emulsion & Janus particles | Biochemical reaction monitoring | Advanced materials