國立台灣大學 應用力學研究所 實驗室晶片導論

微混合器與微反應器之研發與應用

Micro-mixers and Micro-reactors

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中華民國 一百零二 年 三 月 十二 日

Biomicrofluidics and Lab-on-a-Chip

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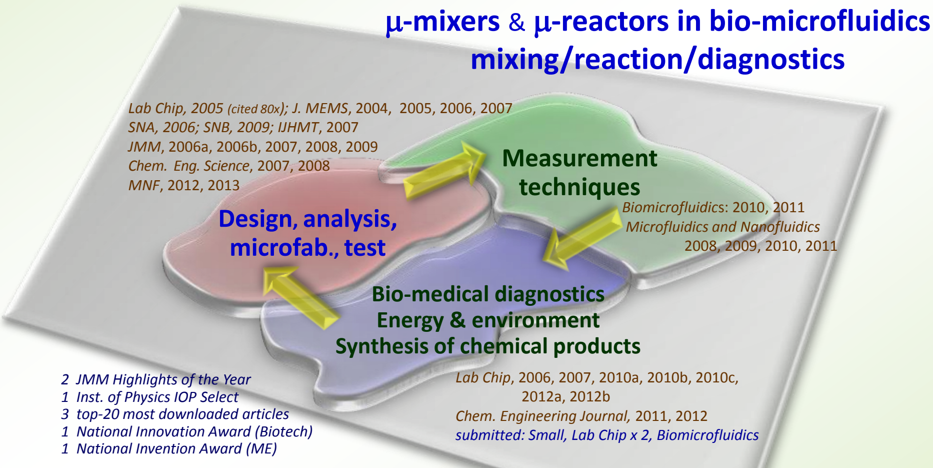
PhD candidate	PhD candidate	碩二	碩一	碩一	碩一	碩一	碩0.5

Research Frame of Micro-systems



- continuous flow
- droplets-based chips

Jing-Tang Yang
Beam Lab, NTU

3

What is mixing ?

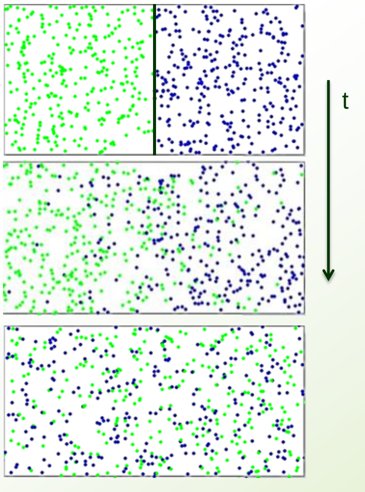
混合：

將兩種(or 兩種以上)不同的物、人或事摻雜在一起的行為。 *~from Wikipedia*

Ex.

物質中的混合。
音樂中的混合。
人類中的混合。
社會中的混合。
其他中的混合。

藉由**某些手段**讓系統中的物質更均勻分布於系統中
Ex. Diffusion (Brownian Motion), convection, turbulence, stir, etc.



Mixing phenomena in our daily life

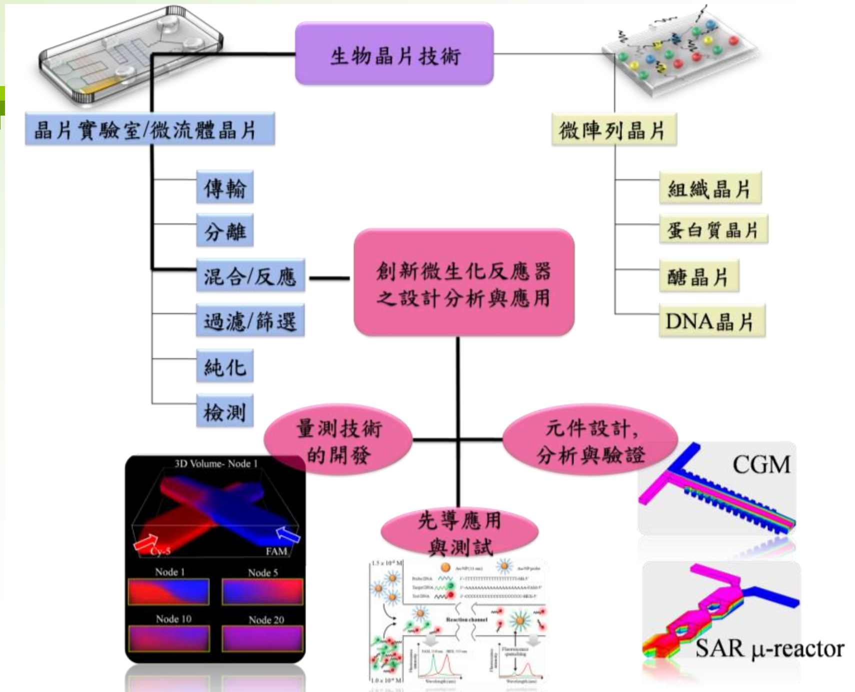
http://tw.aboluowang.com/life/2011/0316/%E5%92%96%E5%95%A1%E4%B8%8D%E7%82%BA%E4%BA%BA%E7%9F%A5%E7%9A%84%E5%A5%BD%E8%99%95-46561.html

Mixing is closely related to our daily life

Scientific Aspects

- **Miniaturization Approach** (1980s~mid-1990s)
  - silicon microfluidic devices:
  - size effect
  - power effect
- **Exploration of New Effects** (mid-1990s ~)
  - actuators with no moving parts and nonmechanical pumping principles
    - electrokinetic pumping, surface-tension-driven flows,
    - electromagnetic forces, acoustic streaming
    - new effects which mimic nature → nanotechnology
- **Application Development**
  - biomedical diagnostics, drug discovery, flow control, chemical analysis
  - distributed energy supply and thermal management
  - chemical production with microreactors

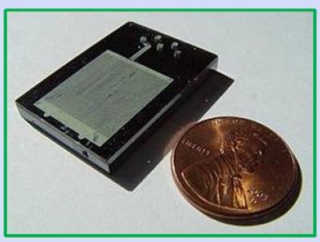
6



Micro-reactors

A microreactor is a reactor with characteristic dimensions in micrometers and reaction volumes in the nanoliter to microliter range.

- Types of Microreactor
  - Chip based
  - Capillary based



Karolin Geyer, Jeroen D. C., Codé, and Peter H. Seeberger. *Chem. Eur. J.* 2006, 12, 8434-8442.

http://www.chem.utoronto.ca/staff/RAB/pdf/Greg2008.pdf

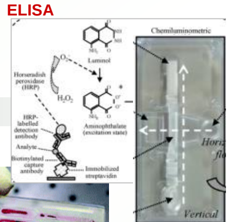
Advantages of Microreactors

- **More uniform mixing and heating**
  (a large ratio of surface to volume within the microstructure)
- **Economy**
  (through decreased consumption of source materials and reagents)
- **Ease of modulation**
- **Safe operation**
  (no need to store and to transport potentially hazardous materials)
- **Environmentally friendly**
  (as the process decreases consumption of most reagents).

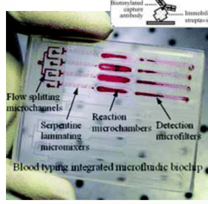
For the bio-medical reaction, the microreactor performs fast, continuous and sensitive detection of small amount of sample. For the chemical reaction, it also proceeds more rapidly, with decreased generation of side products, increased yield and improved conversion of reactants.

Applications

ELISA



Vijayendran *et al.*, *Langmuir*, 2003



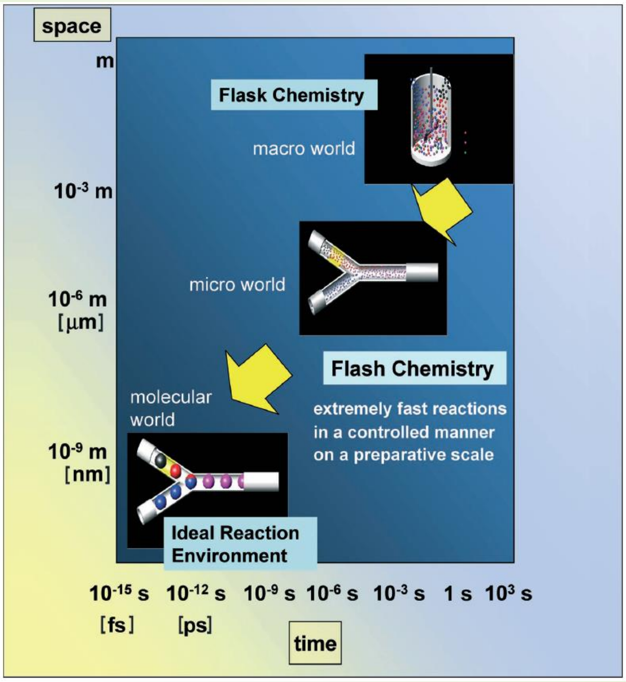
Kim *et al.*, *Lab Chip*, 2006

For Life Science

- **DNA analysis** (hybridization、PCR etc.)
- **Cell analysis** (drug reaction, cell interaction etc.)
- **Blood analysis** (typing)
- **Immunologic reaction**
- **Clinical diagnostics** (Detection of Potassium ion、iodine ion、Detection of DNA/ RNA Mutation)

For Chemistry

- **Organic synthesis**
- **Polymer synthesis**
- **Nanomaterial synthesis** (Au, CdS, CdSe, TiO_2 , Ag etc.)
- **Exothermic reaction、Competition reaction**
- **Catalyst reaction**

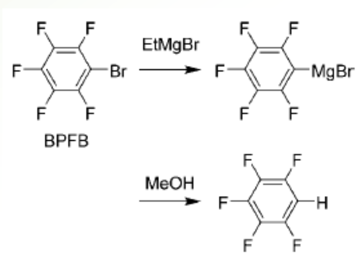


Yoshida et al., *Chem. Eur. J.*, 2008, 14, 7450-7459

Example: **Highly exothermic reactions that are difficult to control in conventional reactors.**

Halogen–magnesium exchange reaction of bromopentafluorobenzene (BPFB) and EtMgBr

- Slow addition is used to avoid a rapid increase in temperature.
- It takes a long time to complete the addition and the overall time efficiency is low.



residence time~ 5 s.
reaction temperature: 20 °C
14.7 kg /day (92%yield)

Figure 4. Picture of the pilot plant for the halogen-magnesium exchange reaction of BPFB and EtMgBr.

Wakami et al., *Org. Process Res. Dev.* 2005, 9, 787–791.

Example: Reactions in which a reactive intermediate easily decomposes in conventional reactors

Swern–Moffatt oxidation involves the formation of highly unstable intermediates, which undergo an inevitable Pummerer rearrangement at temperatures higher than -30 °C.

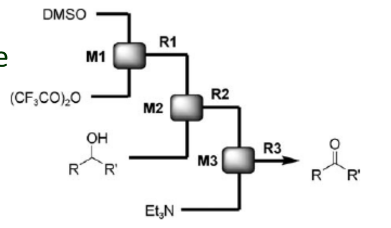


Figure 6. A microreactor system for room temperature Swern-Moffatt oxidation. **M1**, **M2**, **M3**: micromixers. **R1**, **R2**, **R3**: microtube reactors.

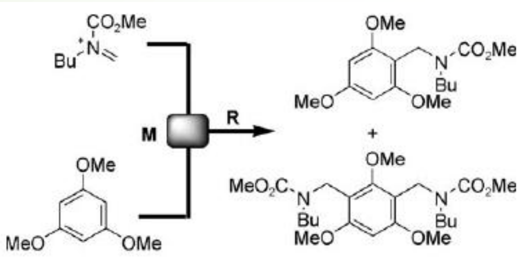
Table 1. Swern-Moffatt oxidation of cyclohexanol using a microreactor and a flask.

Method	Residence time t_{R1} [s]	T [°C]	Selectivity of cyclohexanone [%]
micro-reactor	2.4	−20	88
	0.01	0	89
	0.01	20	88
flask		−20	19
		−70	83

Kawaguchi et al., *Angew. Chem.*, 2005, 117, 2465–2468.

Example: Reactions in which undesired byproducts are produced in the subsequent reactions

Friedel–Crafts reaction



	monoalkylation product	dialkylation product
microreactor	92%	4%
flask	37%	32%

Figure 10. A microreactor system for selective Friedel-Crafts monoalkylation. **M**: micromixer. **R**: microtube reactor.

Suga *et al., Chem. Commun*. 2003, 354–355

Example: Reactions in which the products easily decompose in conventional reactors

The reactions should be quenched immediately after the formation of the products.

Acid-catalyzed dehydration of allylic alcohols

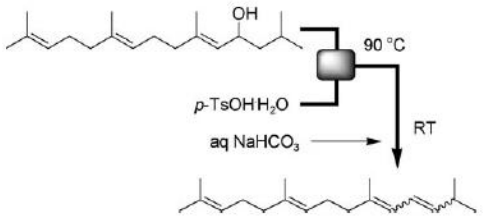


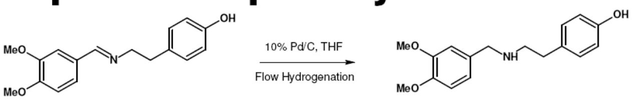
Figure 11. Acid-catalyzed dehydration of allylic alcohol using a microreactor system.

Tanaka et al., *Org. Lett*. 2007, 9, 299 –302.

47 s → quenched with a saturated $NaHCO_3$ solution. → 80% yield (diene).

Example:

Optimize quickly

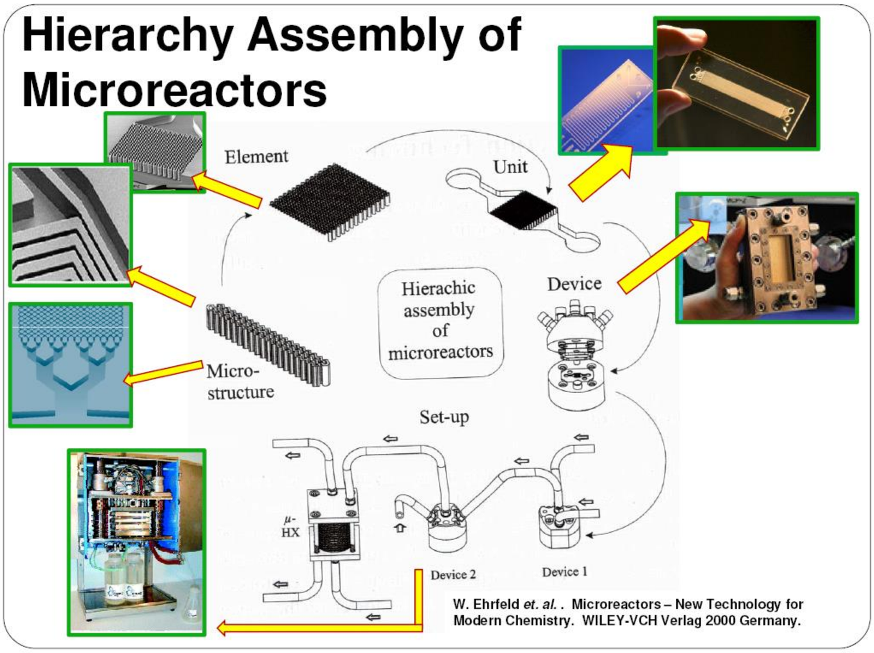


Run	Concentration M	Flow rate mL/min	Injection Volume (mL)	Pressure (bar)	Temp(C)	Conversion
1	0.5	1	5	20	25	17
2	0.1	1	5	20	25	85
3	0.05	1	5	20	25	100
4	0.025	1	5	20	25	100
5	0.5	2	5	20	25	4
6	0.1	2	5	20	25	70
7	0.05	2	5	20	25	85
8	0.025	2	5	20	25	100
9	0.5	1	5	20	60	33
10	0.5	1	5	40	25	33
11	0.5	1	5	40	60	33
12	0.05	1	70	20	25	95

Steven V. Ley *et. al.*, Chem. Commun., 2005, 2909-2911

http://www.chem.utoronto.ca/staff/RAB/pdf/Greg2008.pdf

Hierarchy Assembly of Microreactors



W. Ehrfeld *et. al.*. Microreactors – New Technology for Modern Chemistry. WILEY-VCH Verlag 2000 Germany.

http://www.chem.utoronto.ca/staff/RAB/pdf/Greg2008.pdf

Potential Benefits and Disadvantages

Advantages

- Precisely control various reaction parameters
- Applicable to combinatorial, multi-step, and industrial chemistry
- Safer and cleaner to operate
- Lower cost for transportation, materials and energy
- Faster transfer of research results into production
- Earlier start of production at lower costs
- Easier scale up of production capacity
- Smaller plant size for distributed production

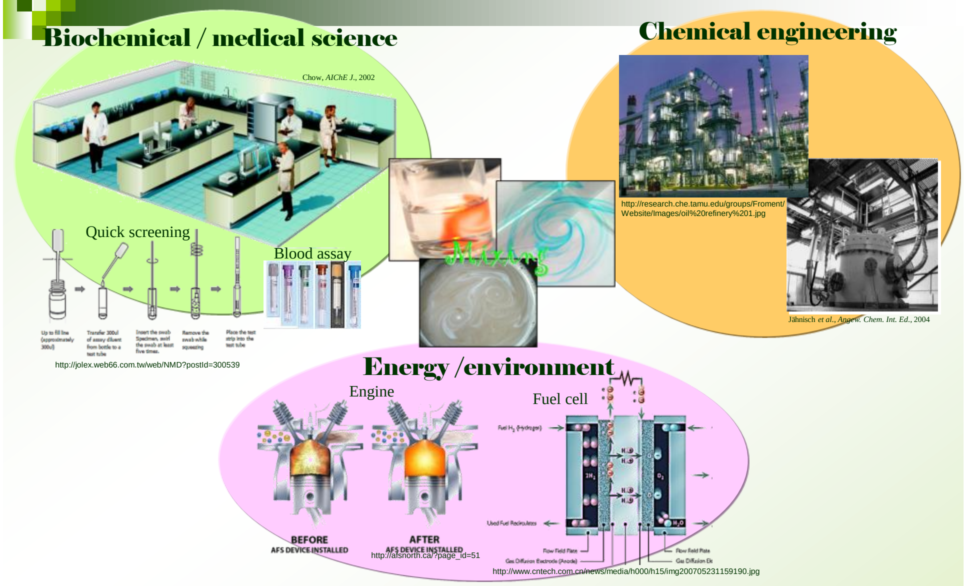
Disadvantages

- Can not be applied to all reactions.
- Microreactors are incompatible with solid reagents.
- Not as robust.
- Mainly useful for fast reactions.
- Technology is still expensive.
- Can be used for terrorist applications

W. Ehrfeld *et. al.*. *Microreactors* – New Technology for Modern Chemistry. WILEY-VCH Verlag 2000 Germany.

http://www.chem.utoronto.ca/staff/RAB/pdf/Greg2008.pdf

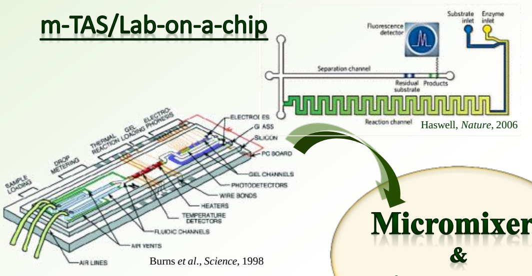
The importance of mixing



Reactions are crucially dominated by mixing

Merits of microfluidic mixing/reaction

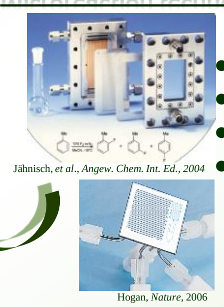
m-TAS/Lab-on-a-chip



- **Low sample/reagent consumption**
- **Parallel process**
- **Rapid detection**

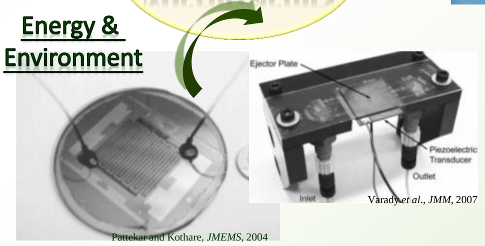
Micromixers & Microreactors

Microreaction technology



- High selectivity
- High safety
- Flash reaction
- Controllable

Energy & Environment



- **Green fabrication**
- **Eco-friendly usage**
- **Portable**

Deficiencies of microfluidic mixing

Low Reynolds number (Re < 1)

- Viscosity-driven system

$$Re = \rho V D_h / \mu$$

- Diffusion-driven mixing

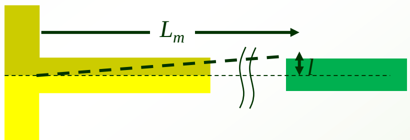
Fick's law

$$J = -D\nabla\phi \qquad J = -D\frac{\partial C}{\partial x}$$

$$\frac{\partial \phi}{\partial t} = D\nabla^2\phi \qquad \frac{\partial C}{\partial t} = D\frac{\partial^2 C}{\partial x^2}$$

$$n(x,t) = n(0)\,\mathrm{erfc}\left(\frac{x}{2\sqrt{Dt}}\right)$$ ***Diffusion length***

Ex. Mixing of fluids in a straight microchannel



$l \sim (Dt)^{0.5}$ $t = L_m / U$ Pe = Ul/D

$L_m \sim U \times (l^2/D)$

$L_m \sim \mathrm{Pe} \times l$

U = 1 mm/s, $D = 10^{-10}$ m²/s, l = 100 μm

L_m = 10 cm !!

Structural design of microchannels (i.e. micromixers) is urgently required.

State of the art for microreactors & micromixers

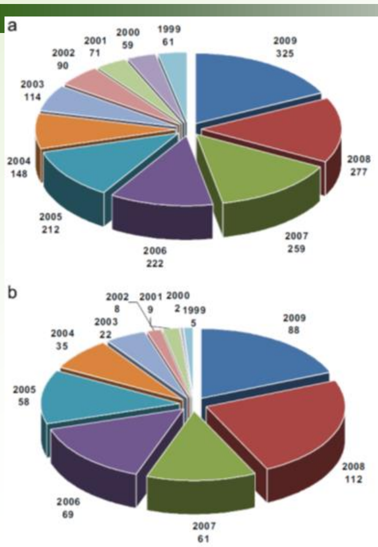


Fig. 1. Year-wise research articles published for (a) microreactors and (b) micromixers (year of publication, number of publications).

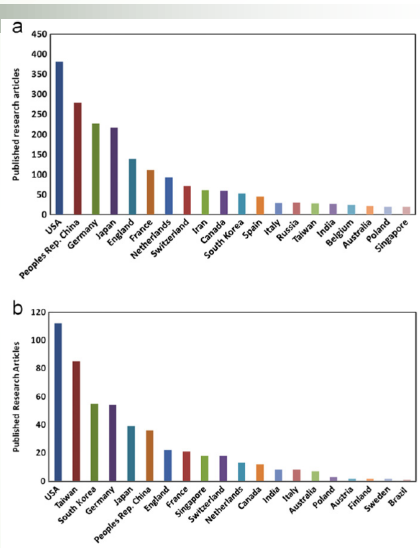
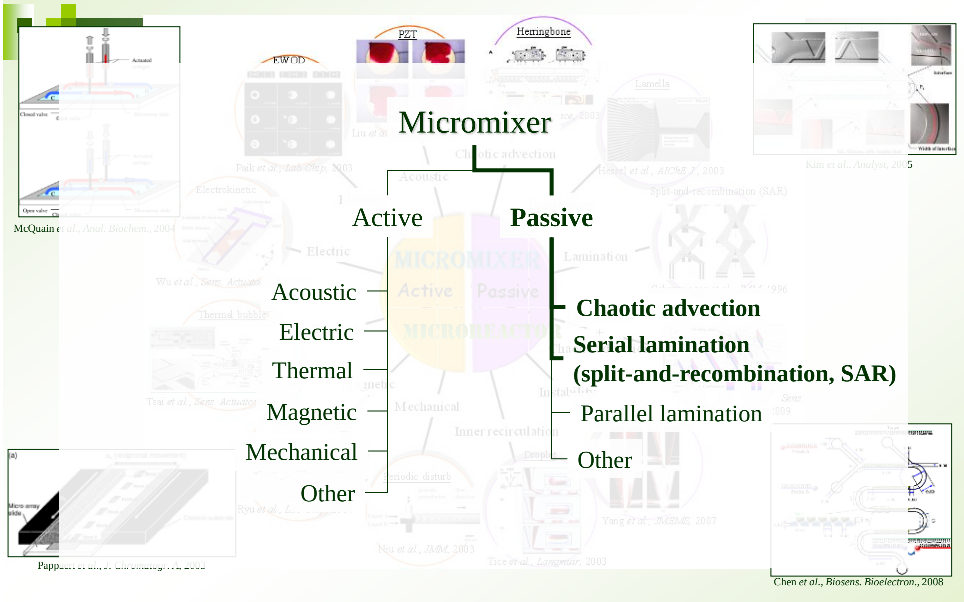


Fig. 2. Country-wise research articles published for (a) microreactors and (b) micromixers.

Kumar *et al.*, *CES*, 2011

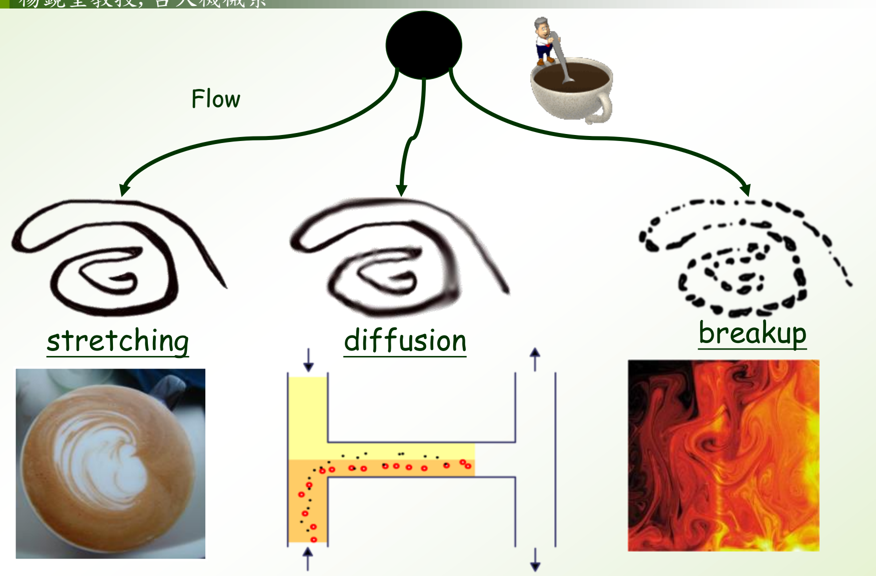
Framework of microfluidic mixing/reaction systems

Micromixers



How does mixing happen?

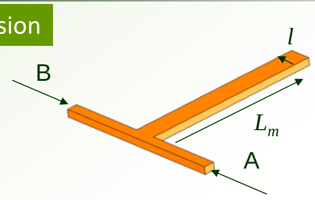
楊鏡堂教授, 台大機械系



Ref. :http://www.tj.xinhuanet.com/ztbd/2005-06/09/content_4420148_10.htm ; www.micronics.net ; http://physicsweb.org

Micromixers (chaotic advection)

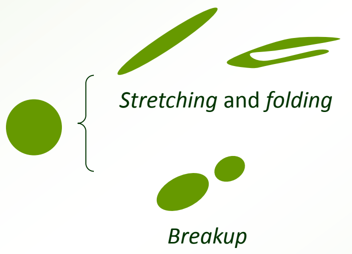
Molecular diffusion

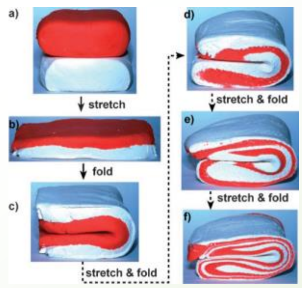


$L_m \sim U \times (l^2/D) = \mathrm{Pe} \times l$

$\mathrm{Pe} = Ul/D$

Chaotic advection





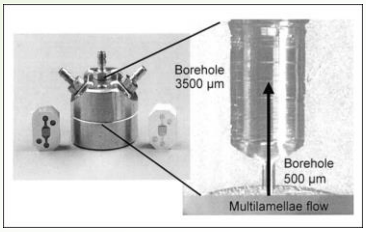
$L_m \sim \lambda \ln(\mathrm{Pe})$

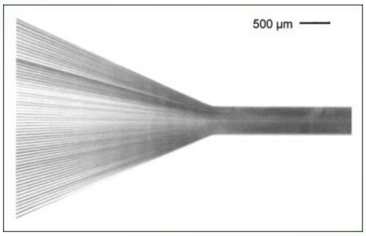
Ottino, J. M., 1989

Elongating the material interface

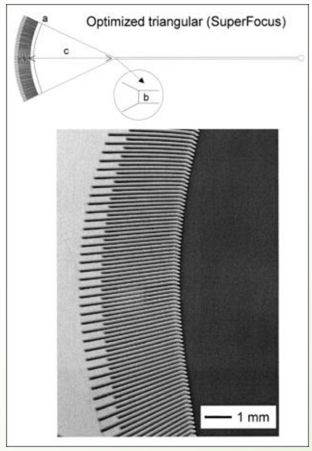
Micromixers (Lamination micromixers)

SuperFocus interdigital micromixer





Parallel lamination

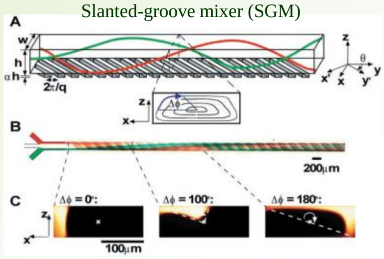


Hessel *et al.*, *AIChE J.*, 2003a,b

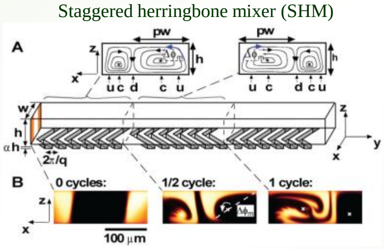
Times cited > 200

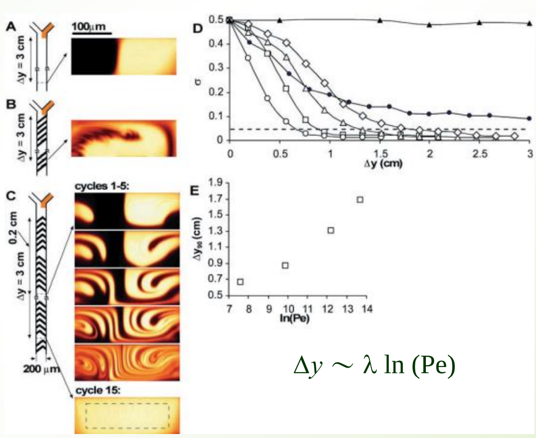
Micromixers (chaotic micromixers)

Slanted-groove mixer (SGM)



Staggered herringbone mixer (SHM)



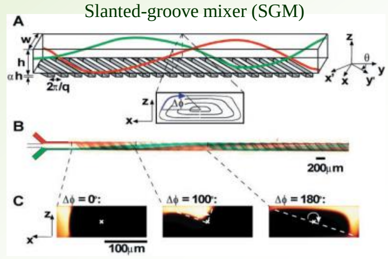


Stroock *et al.*, *Science*, 2002

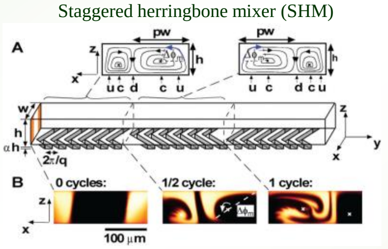
times cited > 1620

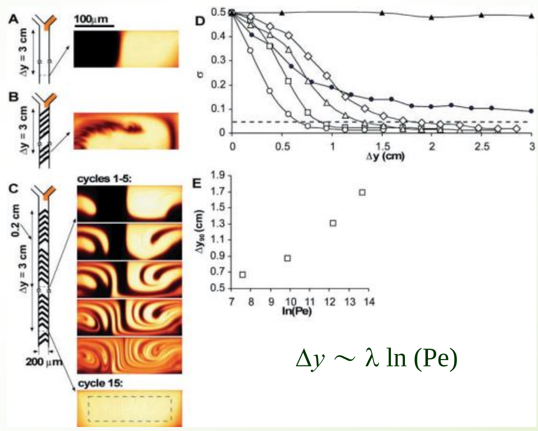
Micromixers (chaotic micromixers)

Slanted-groove mixer (SGM)



Staggered herringbone mixer (SHM)





$\Delta y \sim \lambda \ln(\mathrm{Pe})$

Stroock *et al.*, *Science*, 2002
Times cited > 1080

Micromixers (chaotic micromixers)

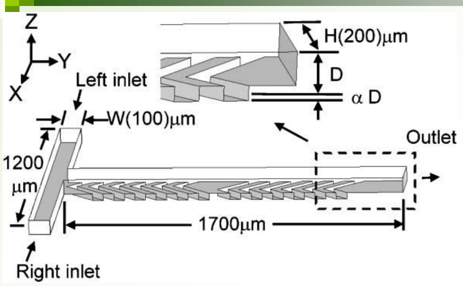
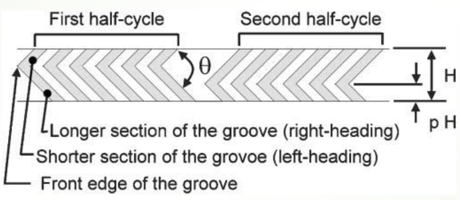


Table 1 Numerical values of geometric parameters

No.	Parameter	1	2	3
A	Asymmetry index (*p*)	0.21	0.33	0.45
B	Depth ratio of the groove (*α*)	0.07	0.13	0.18
C	Upstream to downstream channel width ratio (*W*/*H*)	0.5	1	1.5
D	Groove intersection angle (*θ*)	60°	90°	120°



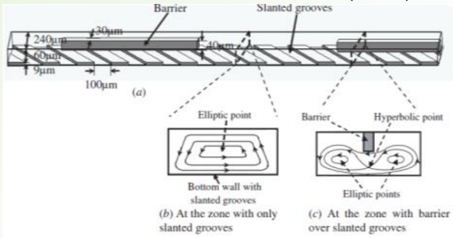
Geometric parameter analysis, based on both the simulation results and the *Taguchi method*, reveal the relative effectiveness as:

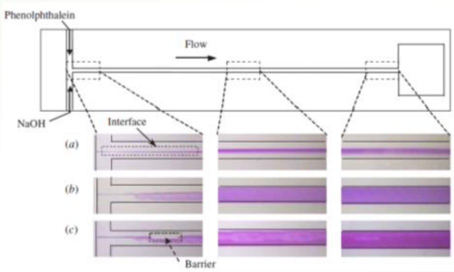
depth ratio of the groove ~ asymmetry index > groove intersection angle > Upstream to downstream channel width ratio.

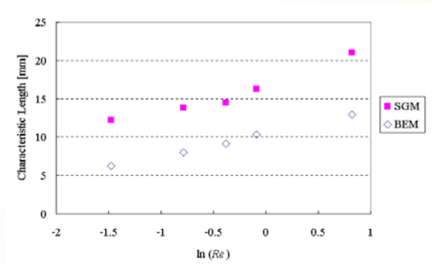
Yang *et al.*, *Lab* Chip, 2005
times cited > 80

Micromixers (chaotic micromixers)

Barrier embedded micromixer (BEM)



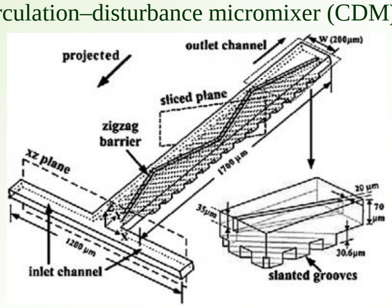


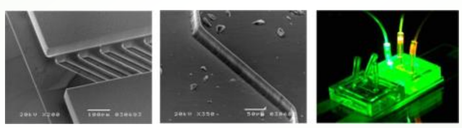


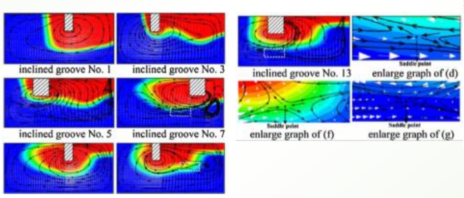
Kim *et al.*, *JMM*, 2004

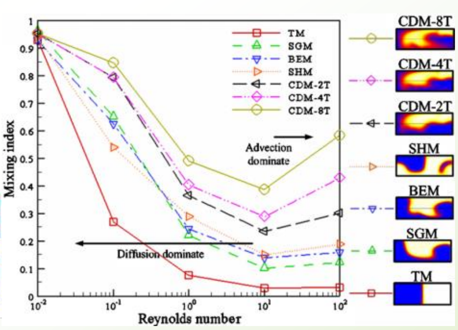
Micromixers (chaotic micromixers)

Circulation–disturbance micromixer (CDM)







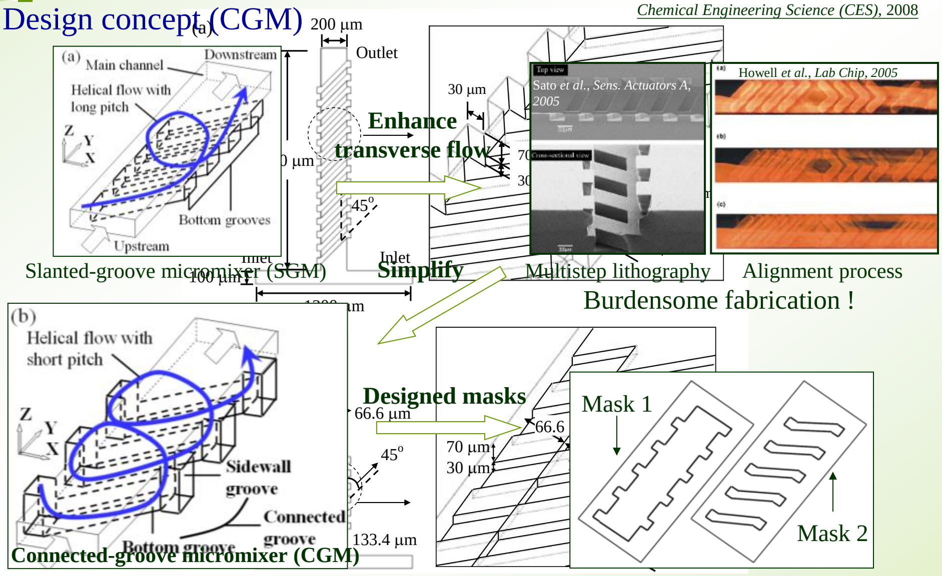


Yang *et al.*, *JMM*, 2007

Micromixers- Connected-groove micromixer (CGM)

Chemical Engineering Science (CES), 2008

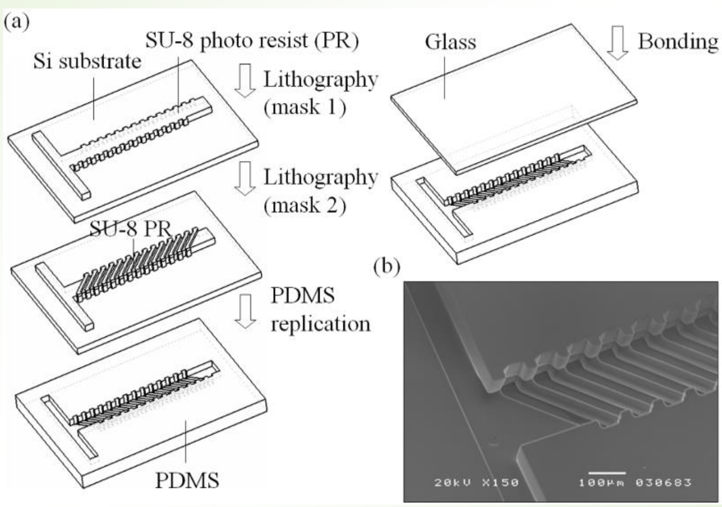
Design concept (CGM)



Micromixers- Connected-groove micromixer (CGM)

Chemical Engineering Science (CES), 2008

Simple fabrication

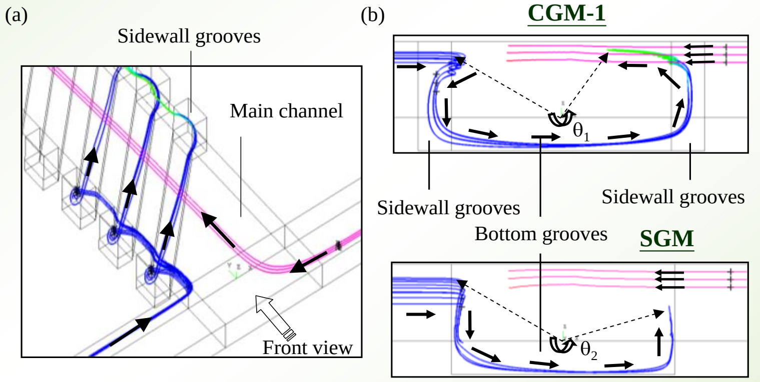


Micromixers- Connected-groove micromixer (CGM)

Chemical Engineering Science (CES), 2008

Flow field

CGM-1 *VS* SGM



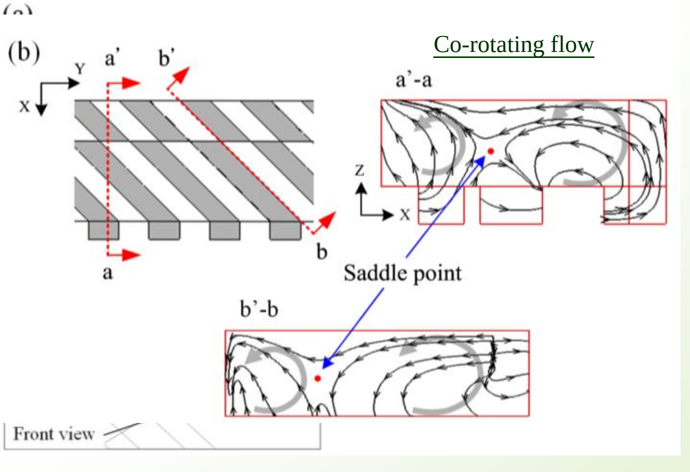
$\theta_1 > \theta_2$ → Greater helical flow in CGM-1

Micromixers- Connected-groove micromixer (CGM)

Chemical Engineering Science (CES), 2008

Flow field

CGM-2 *VS* SSGM

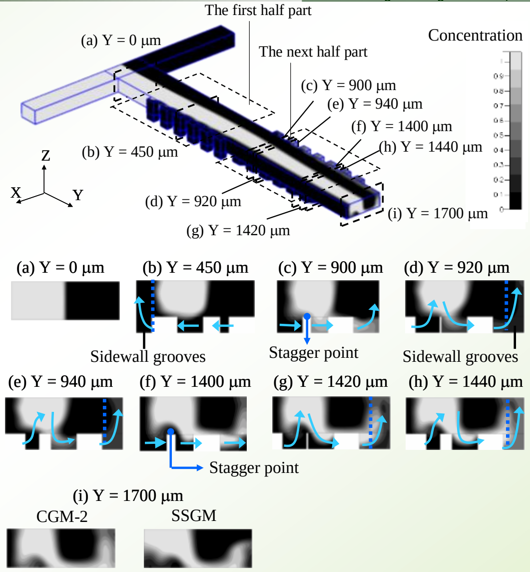


Micromixers- Connected-groove micromixer (CGM)

Chemical Engineering Science (CES), 2008

Concentration field

CGM-2 *VS* SSGM



Cutting and mixing of fluids near the stagger point

Micromixers- Connected-groove micromixer (CGM)

Chemical Engineering Science (CES), 2008

$$\sigma^2 = \frac{1}{n}\sum_{i=1}^{n}(c_i - c_\infty)^2$$

$$M_i = (1 - \frac{\int_A |c_i - c_\infty| dA}{\int_A |c_0 - c_\infty| dA})$$

c_i - concentration in element i of the cross section

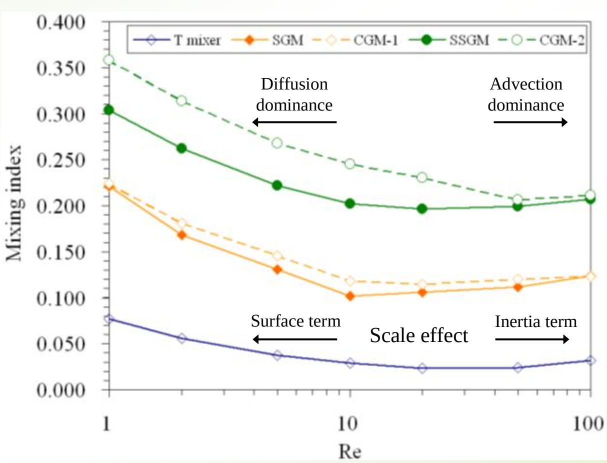
c_0 - the initial concentration at the entrance

c_∞ -the concentration at infinity

σ^2 -the coefficient of variation of concentration for each cross section

M_i -the mixing index, which equals unity to denote complete mixing

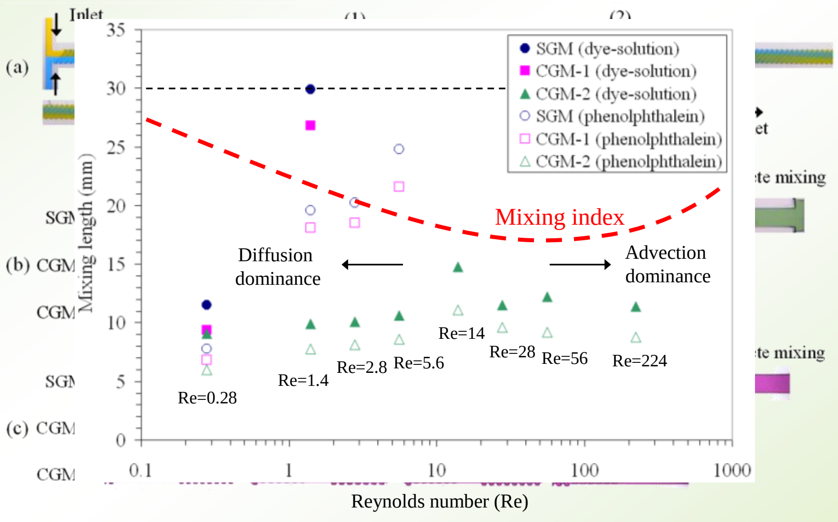
The concentration is normalized to unity for one inlet but zero for the other one.



Micromixers- Connected-groove micromixer (CGM)

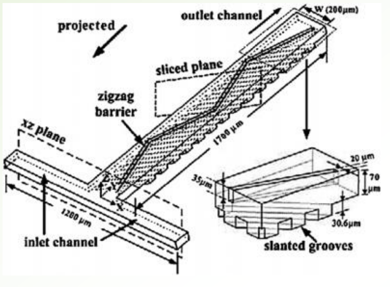
Mixing experiments

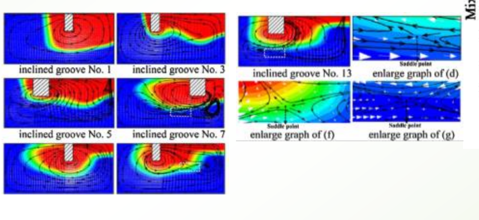
Chemical Engineering Science (CES), 2008

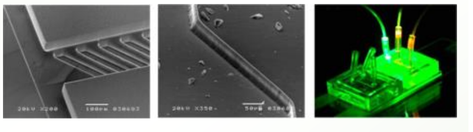


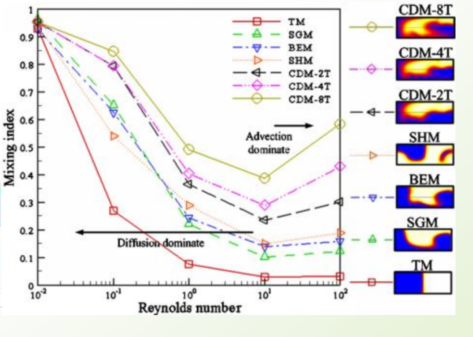
Micromixers (chaotic micromixers)

Circulation–disturbance micromixer (CDM)



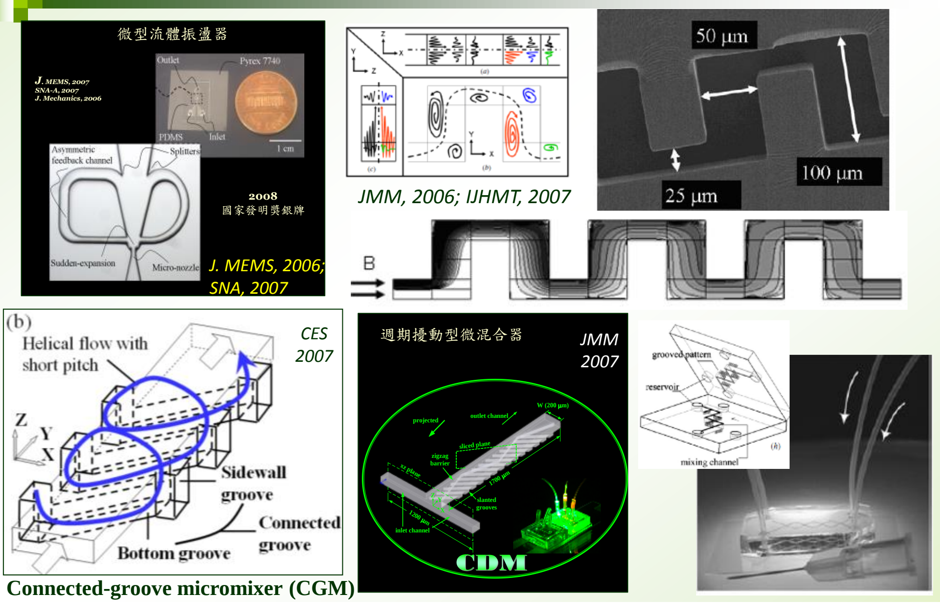






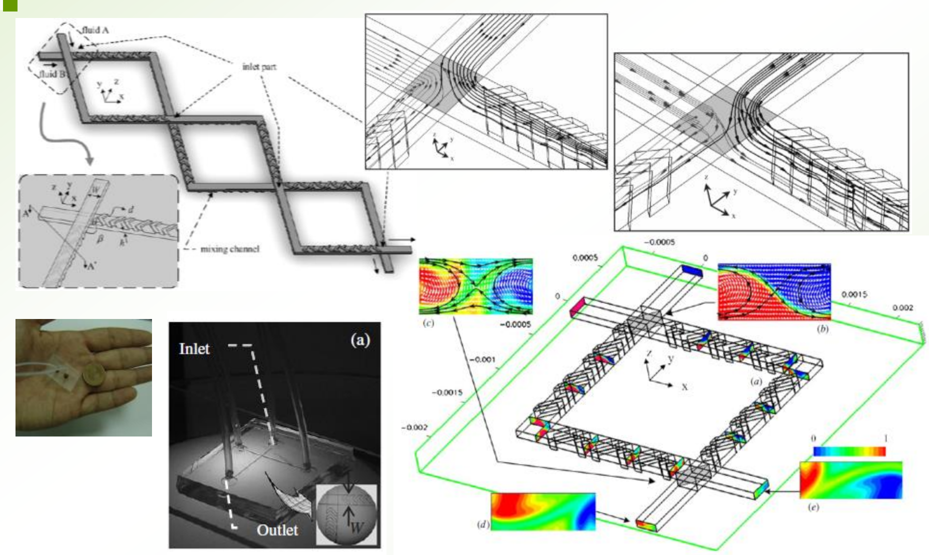
Yang *et al.*, *JMM*, 2007

Various Micromixers developed by Beam Lab.



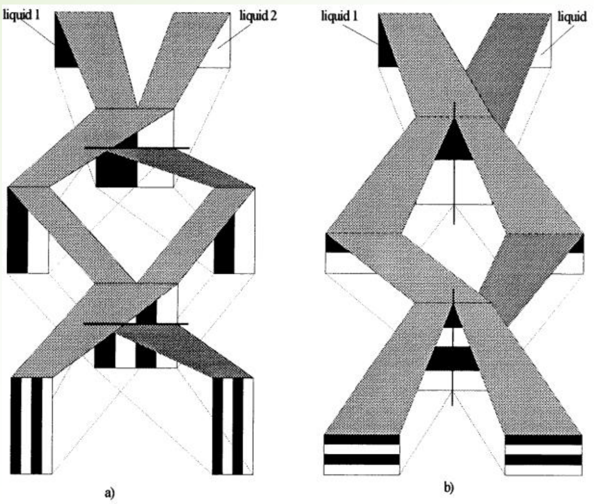
Overlapping Crisscross Micromixers

Wang & Yang, JMM Highlights of 2006, Chemical Engineering Science (CES), 2006



Micromixers (Lamination micromixers)

Serial lamination- split & recombination (SAR)



Exponential increase in contact interface

Suitable for melt polymer

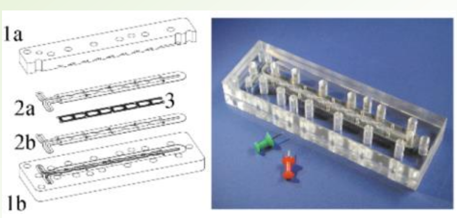
Multiform properties of biochemical solutions

Schwesinger *et al.*, *JMM*, 1996

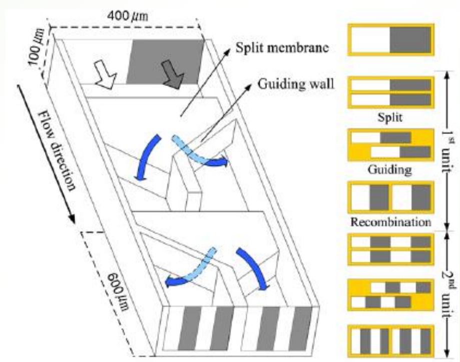
Times cited > 140

Micromixers (Lamination micromixers)

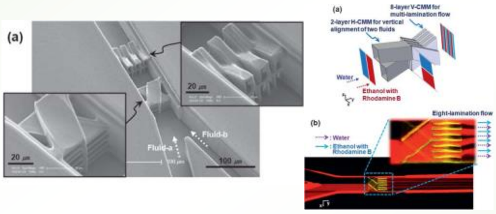
Serial lamination- split & recombination (SAR)



Schönfeld *et al.*, *Lab Chip*, 2004



Lee *et al.*, *JMM*, 2006



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

Intermediate layer

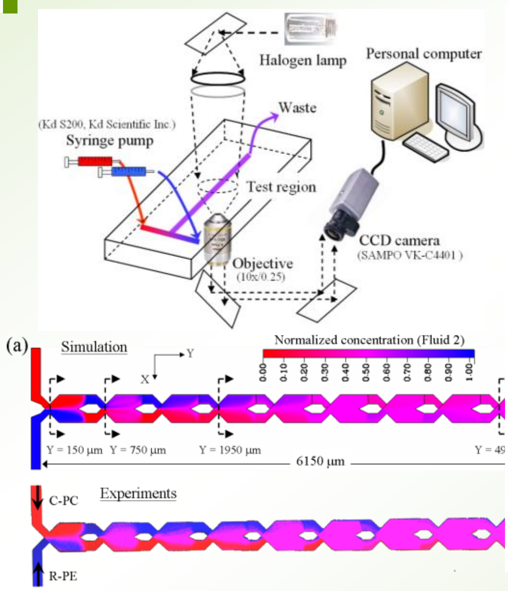
Separate channels

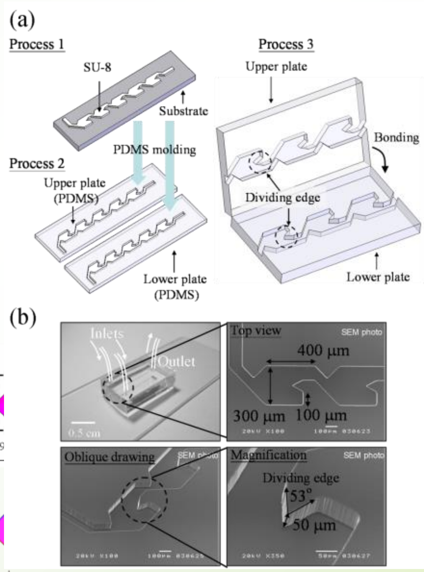
Confluent channels

A Novel Microreactor with 3D Rotating Flow

方偉峰 楊鏡堂, 2009

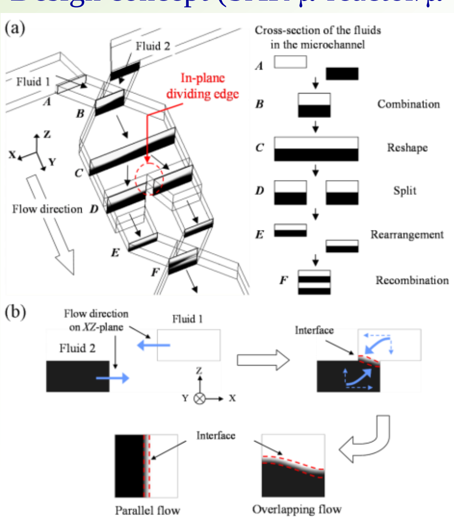
Sensors and Actuators B- Chemical, 2009

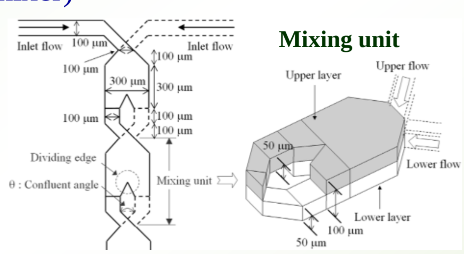




Micromixers- SAR μ-reactor/μ-mixer

Design concept (SAR μ-reactor/μ-mixer)





SAR + Chaotic advection

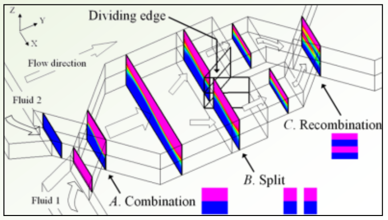
Strong transverse
advection and stretching

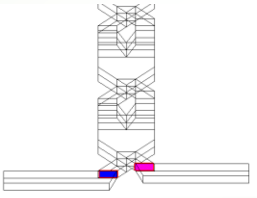
Fang & Yang, Sensors & Actuators B: Chemical, 2009

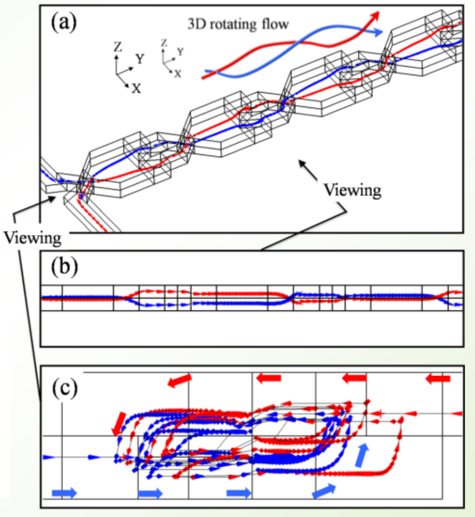
Micromixers- SAR μ-reactor/μ-mixer

Sensors & Actuators B: chemical, 2009

Flow field

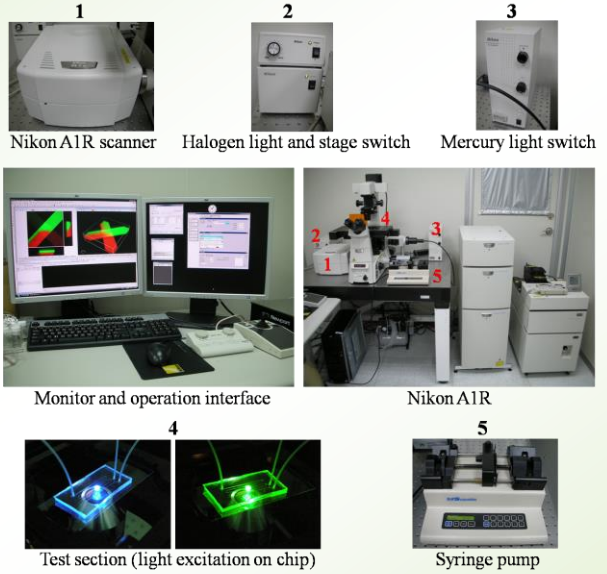






Confocal Microscope and Test Channels

Beam Lab., NTU



Nikon A1R scanner | Halogen light and stage switch | Mercury light switch

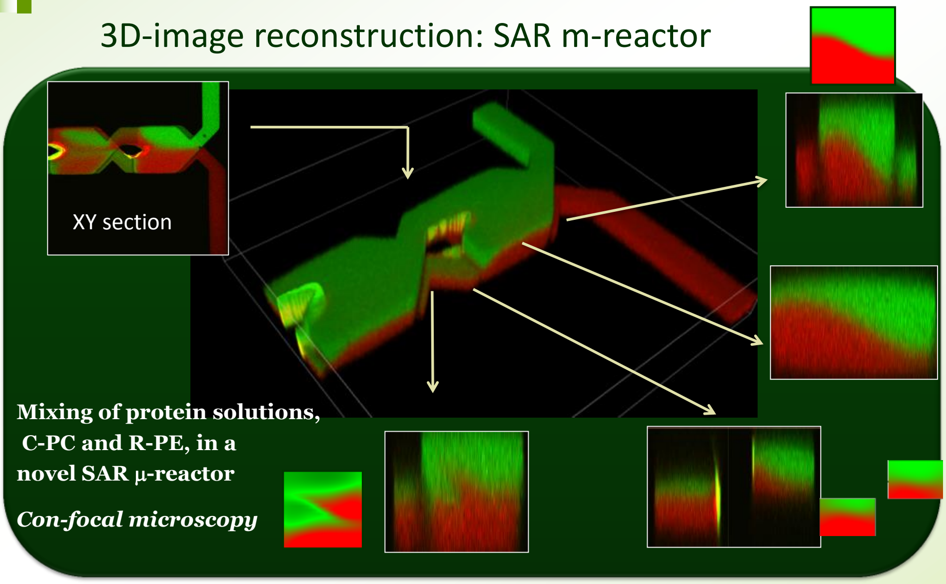
Monitor and operation interface | Nikon A1R

Test section (light excitation on chip) | Syringe pump

Performance Test of a SAR μ-Reactor

Fang & Yang, Sensors and Actuactors B, 2009

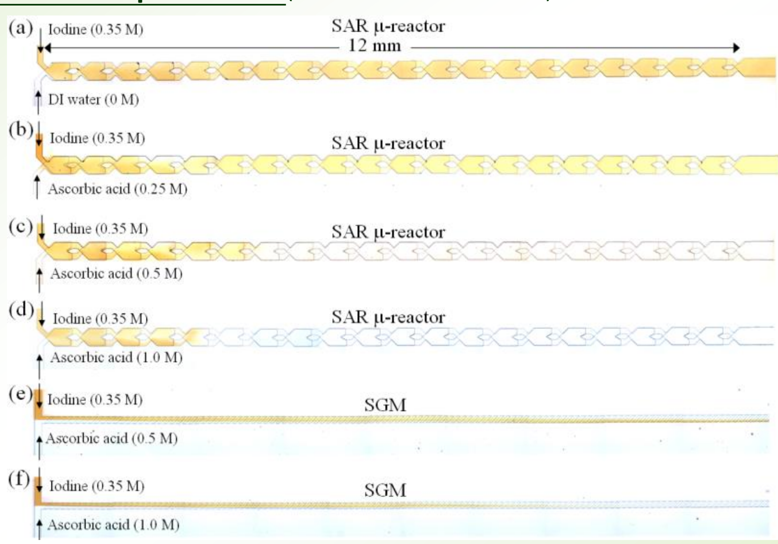
3D-image reconstruction: SAR m-reactor



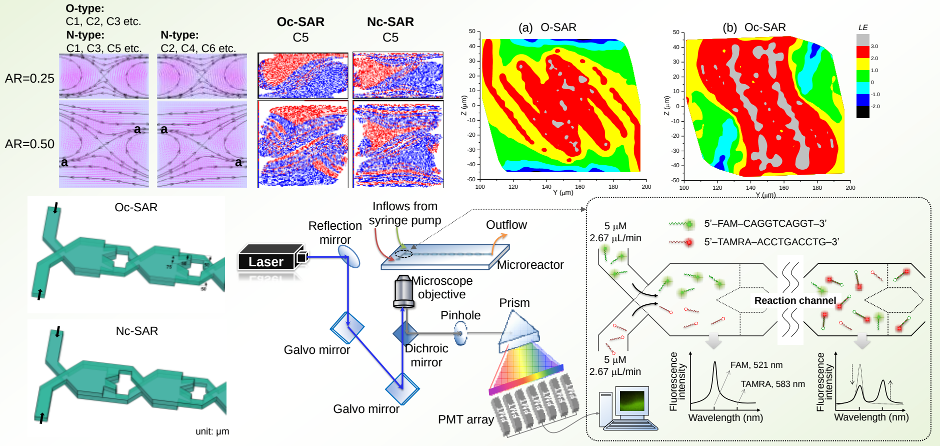
Micromixers- SAR μ-reactor/μ-mixer

Sensors & Actuators B: chemical, 2009

Reaction experiments (ascorbic acid and diiodine)



Analysis of chaos & FRET reaction in split-and-recombine microreactors, *Chen et al., Microfluidics and Nanofluidics, 2011*

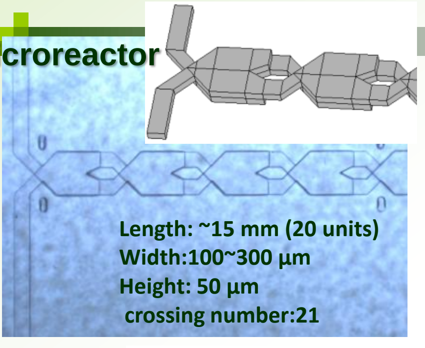


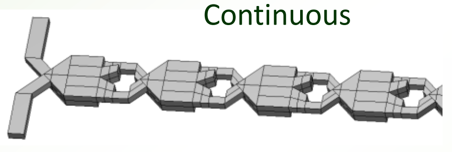
Through analysis of the chaos, we revealed numerically the dynamic mixing governed by multi-lamination and chaotic mechanisms in the devices. How the devices affected the rate of hybridization was thereby assessed, verifying that FRET is a technique capable of estimating the practical applicability of these devices.

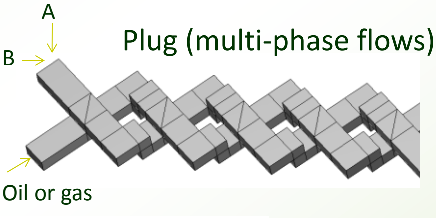
Beam Lab

Component

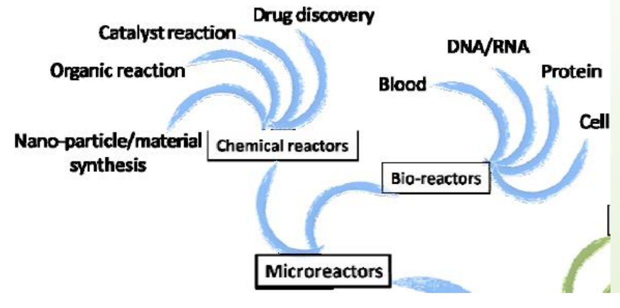
Microreactor





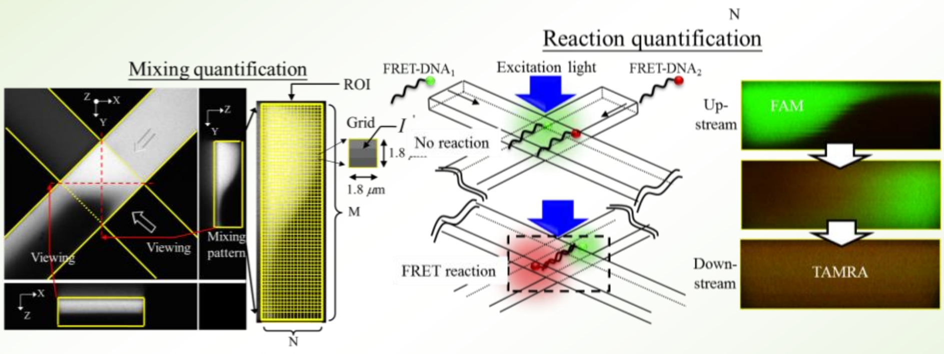


Reaction



Characterization of microfluidic mixing and reaction in microchannels *via* analysis of cross-sectional patterns

Fang *et al*., *Biomicrofluidics*, 2011

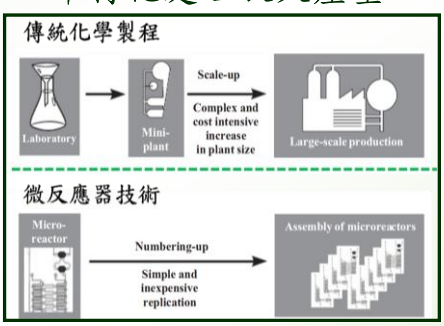


A quantification approach based on a confocal-fluorescence microscope is proposed to characterize fluid mixing precisely in microchannel devices. The approach is qualified for use to inspect microfluidic mixing, to disclose flow behavior, and to diagnose biochemical and chemical reactions in microfluidic devices.

微反應器的綠色特質

- 高表面積體積比
  - 表面張力、黏滯性
  - 擴散主導
- 高靈敏度、安全性
- 副產物少、減少汙染
- 產物轉換效率高
- 反應快速
- 試劑使用量小、減少資源浪費

平行化處理放大產量



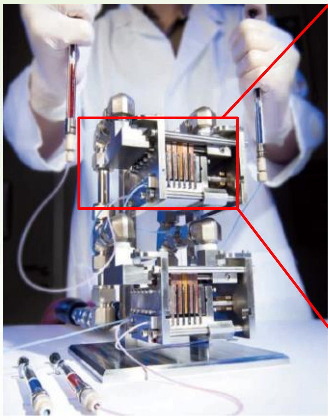
http://www.chem.utoronto.ca/staff/RAB/teachinglinks.html, extracted on 2012/07/12

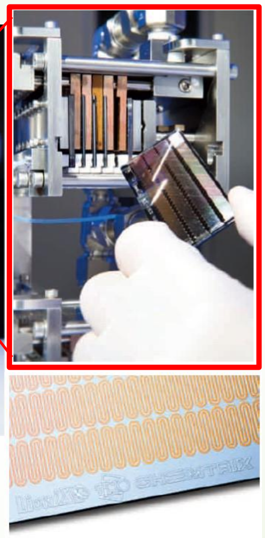
54

業界實例

TNO Science and Industry
研發的高產量微反應器裝置

微反應器晶片可以輕鬆替換



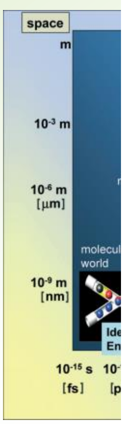


http://pubs.acs.org/cen/coverstory/87/8711cover4.html extracted on 20120810

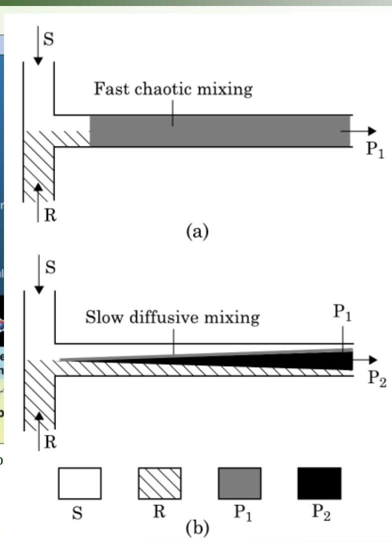
NicOx和DSM合作開發出微反應器晶片小製藥場

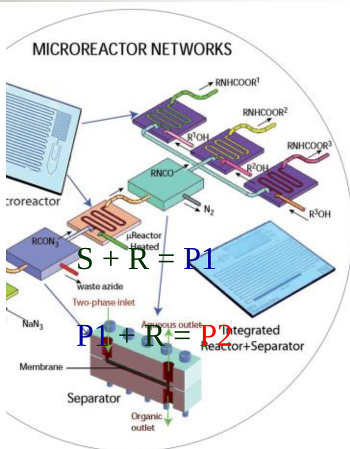
55 http://www.tno.nl/content.cfm?context=thema&content=prop_case&laag1=892&laag2=908&laag3=85&item_id=1020&Taal=2, extracted on 20120810

Microreactors



Yo





Sahoo *et al.*, *Angew. Chem. Int. Ed.*, 2007

Microreactors (oxidation reaction)

Swern-Moffatt oxidation of cyclohexanol in microreactors

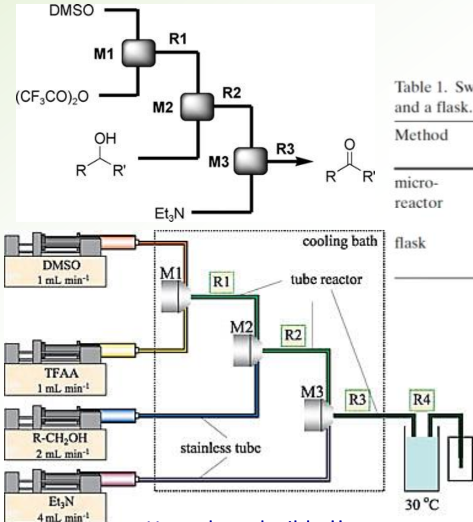


Table 1. Swern-Moffatt oxidation of cyclohexanol using a microreactor and a flask.

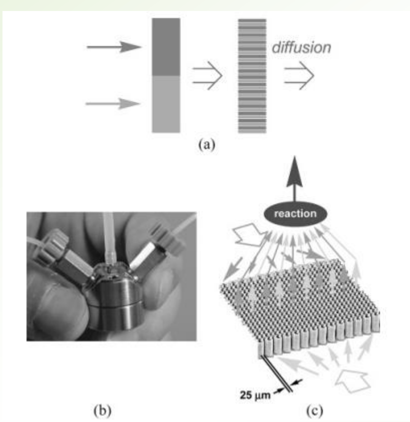
Method	Residence time t_{R1} [s]	T [°C]	Selectivity of cyclohexanone [%]
micro-reactor	2.4	−20	88
	0.01	0	89
	0.01	20	88
flask		−20	19
		−70	83

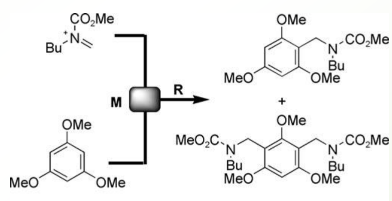
Hazard, explosible !!

Kawaguchi *et al.*, *Angew. Chem.*, 2005

Microreactors (Competitive Consecutive Reactions)

Friedel–Crafts reaction of cyclohexanol in microreactors

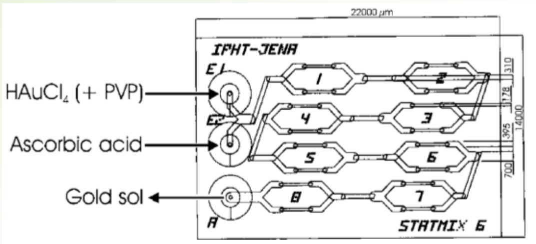


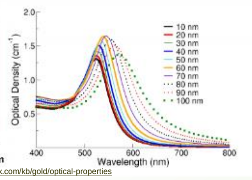


	monoalkylation product	dialkylation product
microreactor	92%	4%
flask	37%	32%

Nagak *et al.*, *JACS*, 2005

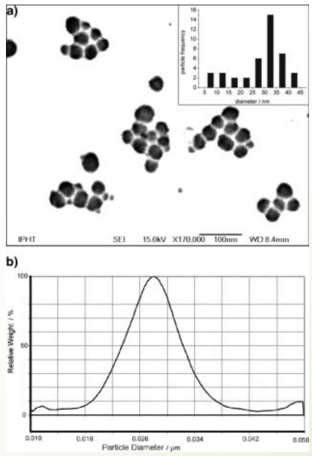
Microreactors (Synthesis of gold nanoparticles)





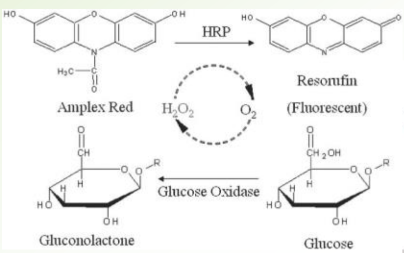
http://www.nanocomposix.com/kb/gold/optical-properties

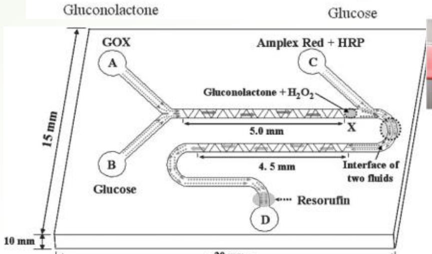
http://www.malvern.com/LabEng/industry/nanotechnology/gold_silver_nanoparticles.htm

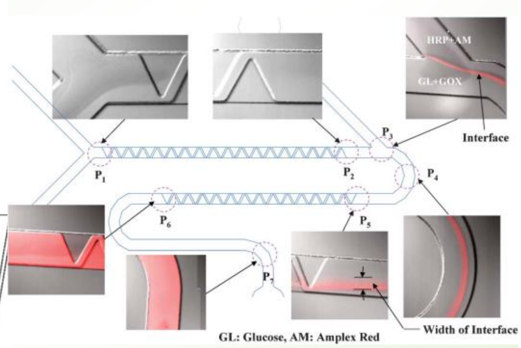


Wagner and Köhler, *Nano Lett*, 2005

Microreactors (Glucose-catalyst reactions)







Kim *et al.*, *Analyst*, 2005

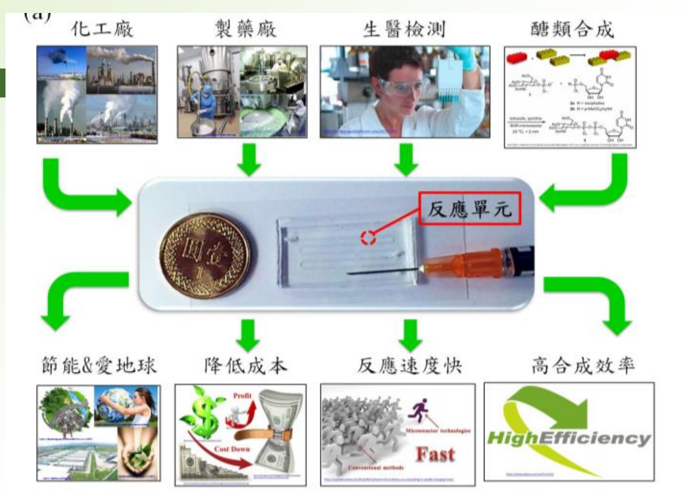
NSC Research Project

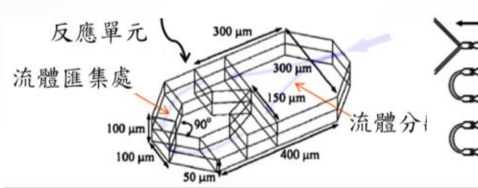
應用於生醫檢測之整合式微流體系統研發

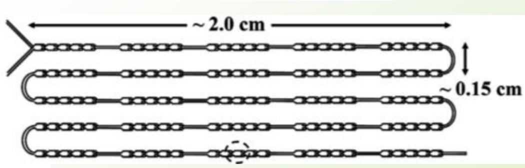
2011/08-2012/07, 約NTD 1,200,000

Prof. Jing-Tang Yang (楊 鏡 堂 教授)

Department of Mechanical Engineering
National Taiwan University







Objectives of the NSC Project

Beam Lab., NTU

-- 研發結合機械設計、流體力學、有機化學合成與生化分析整合之微全分析系統 (micro total analysis systems)

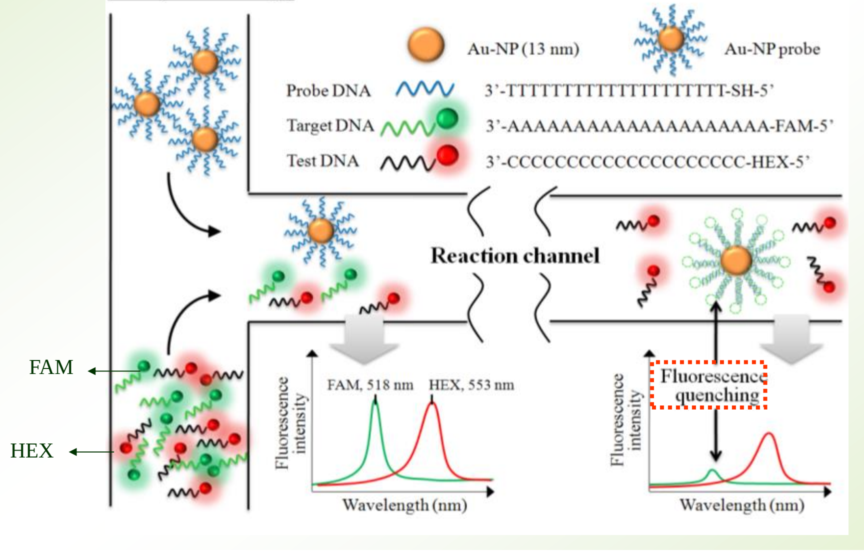
-- 突破傳統費時之檢測流程，主要研究包含微反應器設計分析、化學試劑與生醫流體混合、奈米粒子如奈米金球或磁珠與生醫流體待測物之鍵結、目標DNA之引入及分離篩選之訊號轉導量測技術研發，以達系統結合上的廣泛應用性及效率。

Enhanced Mobile Hybridization of Decorated Gold Nanoparticles with Oligonucleotide in Microchannel Devices

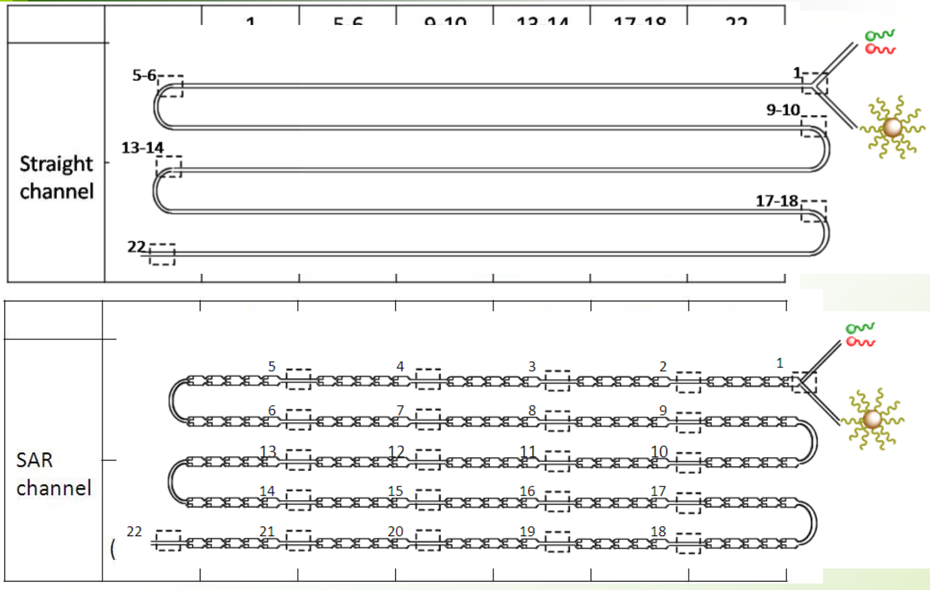
M. H. Hsu, W. F. Fang, Y. H. Lai, **J. T. Yang**,* T. L. Tsai, and D. B. Shieh

μTAS-2010, October 3-7, Groningen, Netherlands; *Lab on a Chip*, 10, 2583-2587, *2010*

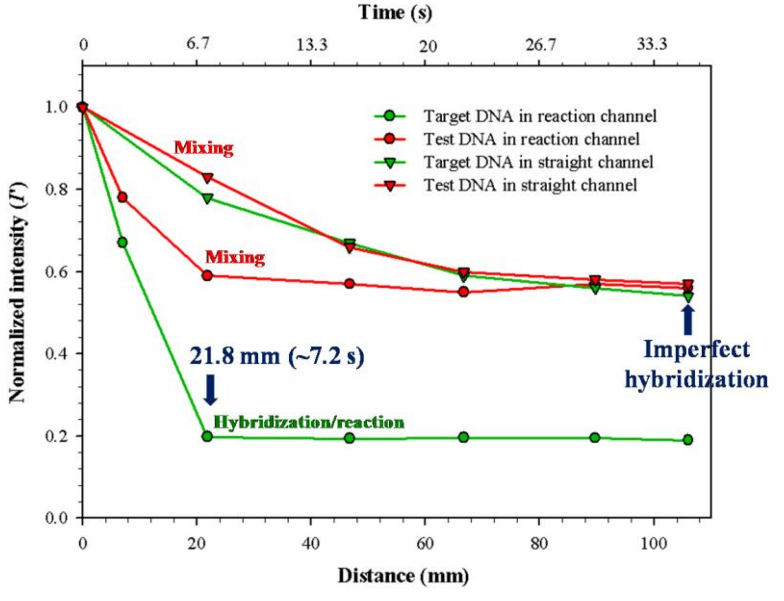
Analytic strategy



Mobile Conjugation in Two Microchannels



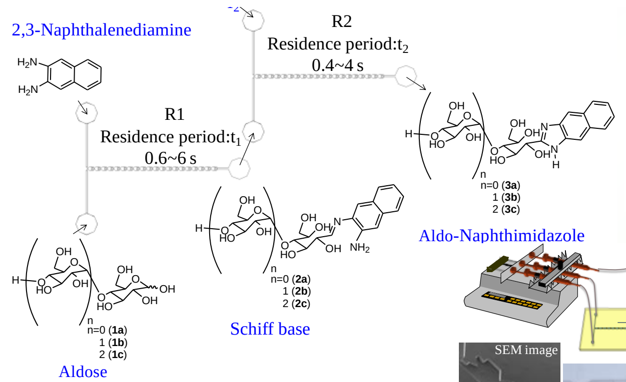
Reaction and Mixing Dsitance of Mobile conjugation in Various Microchannels



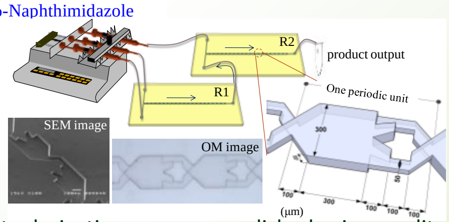
Flash synthesis of carbohydrate derivatives in split-and-recombine microreactors

Y. T. Chen, K. H. Chen, W. F. Fang, S. H. Tsai, J. M. Fang, and **J. T. Yang***

Chemical Engineering Journal, Vol. 174, pp. 421-424, 2011



The SAR-microreactor required just seconds (0.1 to 10 s), which was about 10^{-3}~10^{-6} the duration for the macro flask.

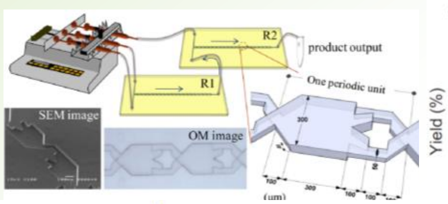


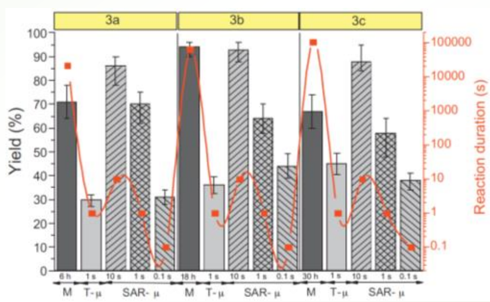
An efficient and rapid synthesis of carbohydrate derivatives was accomplished using a split-and-recombine (SAR) microreactor. Using two steps reaction process in SAR-microreactors, the carbohydrate derivatives, aldo-naphthimidazoles were generated by linkage of naphthalenediamine with mono-, di- or trialdoses in less than 10 s with satisfactory yield.

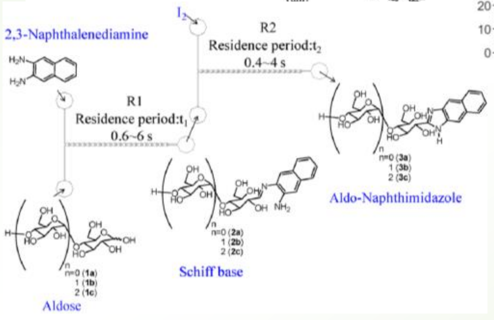
Microreactors (Flash synthesis of carbohydrate derivatives)

Chemical Engineering Journal (CEJ), 2011

Applications of SAR μ-reactor





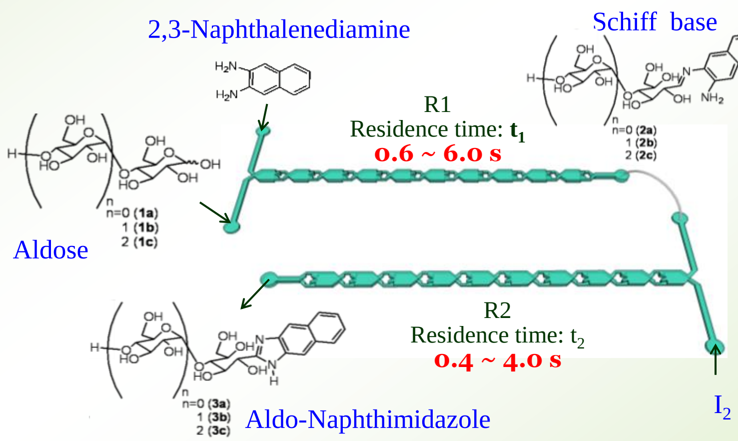


Macro flask:
- 6 h to 30 h
- Temp. above 100

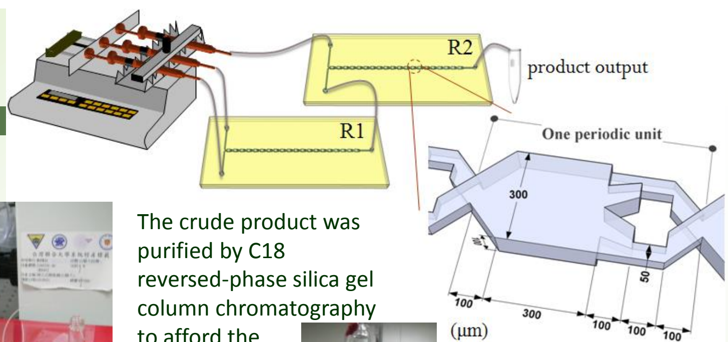
SAR μ-reactor :
- 0.1 ~ 10 s
- Temp. RT

Highly Efficient Synthesis of Carbohydrate Derivatives using Split-and-Recombine Microreactors

An efficient direct synthesis of carbohydrate was accomplished using a SAR-microreactor. The process requiring just seconds, **10^{-4}** duration less than for the macro flask. The yield of the product was also much enhanced relative to a T-shaped microreactor.

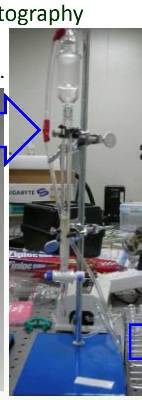


Setup



The crude product was purified by C18 reversed-phase silica gel column chromatography to afford the desired product.

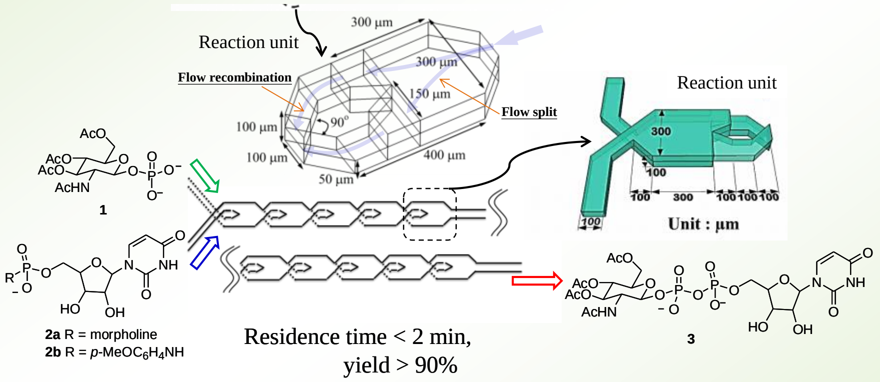

concentration


Column chromatography


concentration

Microflow Synthesis of Saccharide Nucleoside Diphosphate with Cross-coupling Reactions of Monophosphate Components

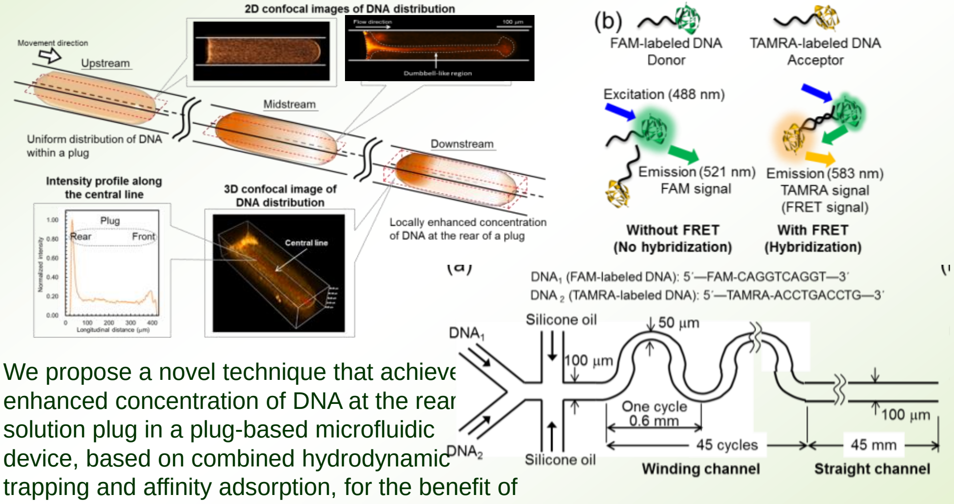
K. H. Chen, W. F. Fang, Y. T. Chen, J. M. Fang,* and **J. T. Yang***
Chemical Engineering Journal, Vol. 198, pp. 33-37, 2012



With this microreactor possessing the SAR mechanism that dramatically enlarges the material interface to promote the fluidic mixing, 85 % conversion of a cross-coupling reaction (GlcNAc monophosphate reacting with UMP-morpholidate) to the diphosphate (acetylated UDP-GlcNAc) was achieved in 10 s, which is a small fraction of the two days for 80 % conversion with a conventional batch reactor; the duration of reaction is hence decreased 10^5 fold.

Locally Enhanced Concentration and Detection of Oligonucleotides in a Plug-Based Microfluidic Device

W. F. Fang, S. C. Ting, C. W. Hsu, Y. T. Chen, and **J. T. Yang,***
mTAS-2011, October 2-8, Seattle**;** ***Lab on a Chip***, Vol. 12 (5), pp. 923–931, 2012



We propose a novel technique that achieve enhanced concentration of DNA at the rear solution plug in a plug-based microfluidic device, based on combined hydrodynamic trapping and affinity adsorption, for the benefit of detection of DNA at a small concentration.

國科會開發型產學合作計畫（聚眾公司）

A Proposal for NSC Research Project

產製潔淨能源之微型化高通量反應元件及製程技術開發

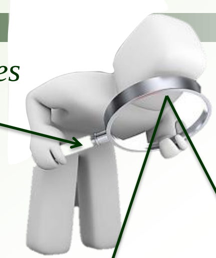
2013/06-2015/04

Prof. Jing-Tang Yang (楊鏡堂教授)

Department of Mechanical Engineering
National Taiwan University

Measurement Techniques

Measuring techniques



Magic !?

- ✓ To comprehend
- ✓ To verify
- ✓ To evolve

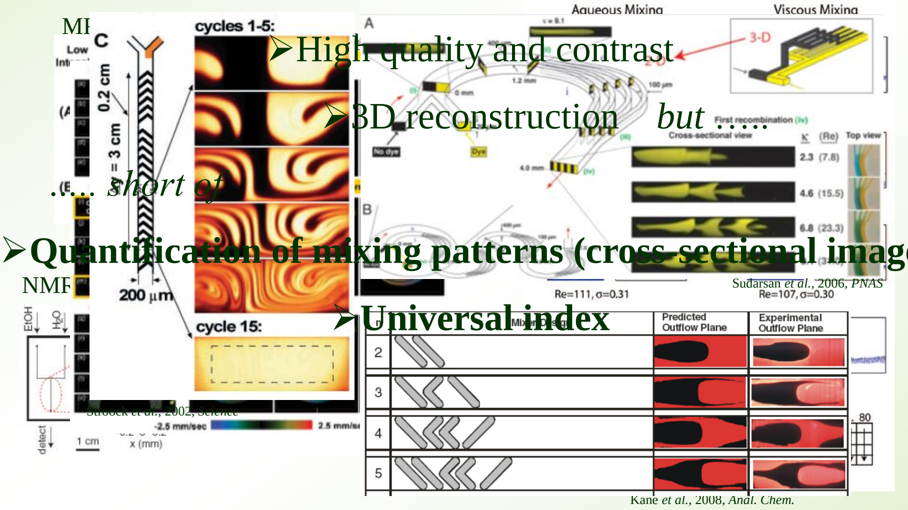
Measuring Techniques

Confocal microscopy

Synchrotron radiation circular dichroism, SRCD

MRI

NMR



- High quality and contrast
- 3D reconstruction *but .....*

... short of

- **Quantification of mixing patterns (cross-sectional images)**
- **Universal index**

Stroock *et al.*, 2002, *Science*

Sudarsan *et al.*, 2006, *PNAS*

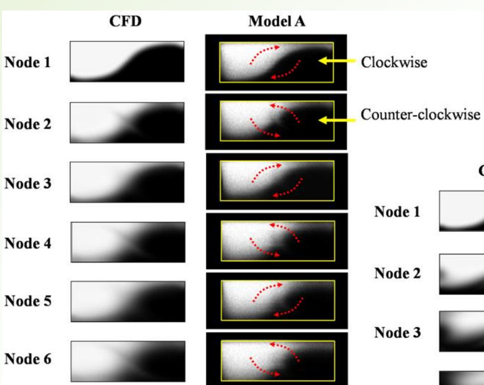
Kane *et al.*, 2008, *Anal. Chem.*

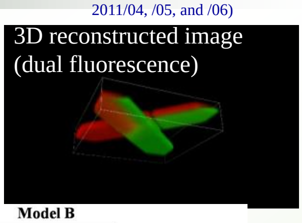
Howell *et al.*, 2008, *JMM*

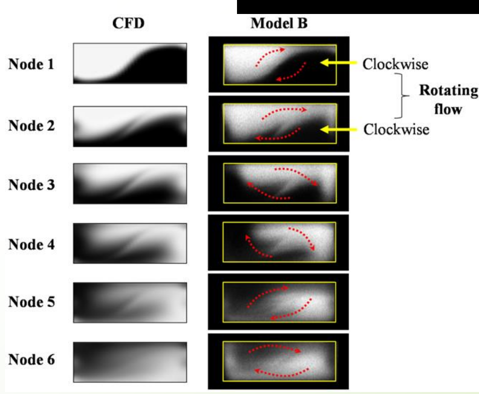
Measuring Techniques (Universal index)

Biomicrofluidics, 2011
(top 20 most downloaded articles, 2011/04, /05, and /06)

Mixing patterns





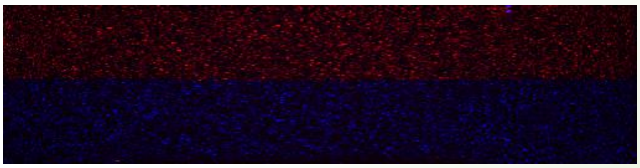


Measuring Techniques (simultaneous measurement)

Is it possible to achieve the simultaneous measurement of species velocities & concentrations in microdevices ?

Mass transfer & momentum transfer ? All in one ?

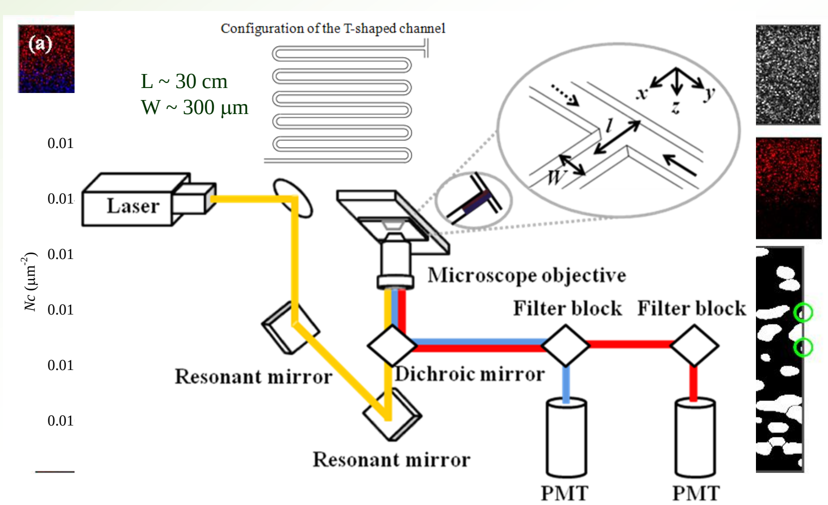
~ absolutely yes !



Measuring Techniques (simultaneous measurement)

Biomicrofluidics, 2010
(Top 20 most downloaded articles, 2010/04, and /06)

Simultaneous measurement (micro-PIV & particle counting method)

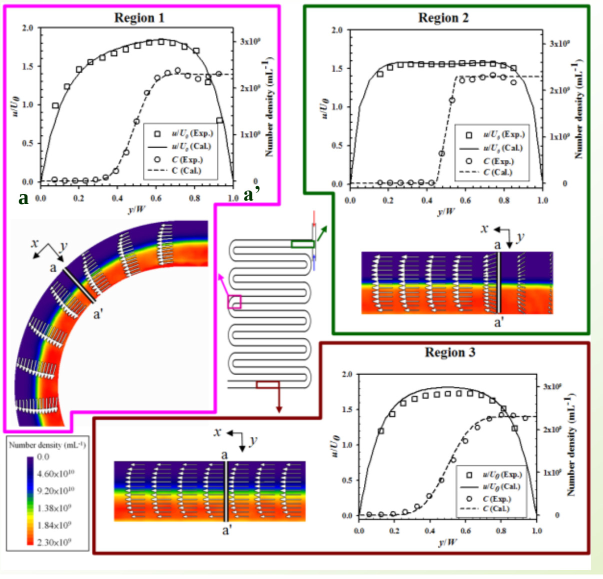


Measuring Techniques (simultaneous measurement)

Biomicrofluidics, 2010
(Top 20 most downloaded articles, 2010/04, and /06)

Simultaneous diagnosis of velocity and concentration fields

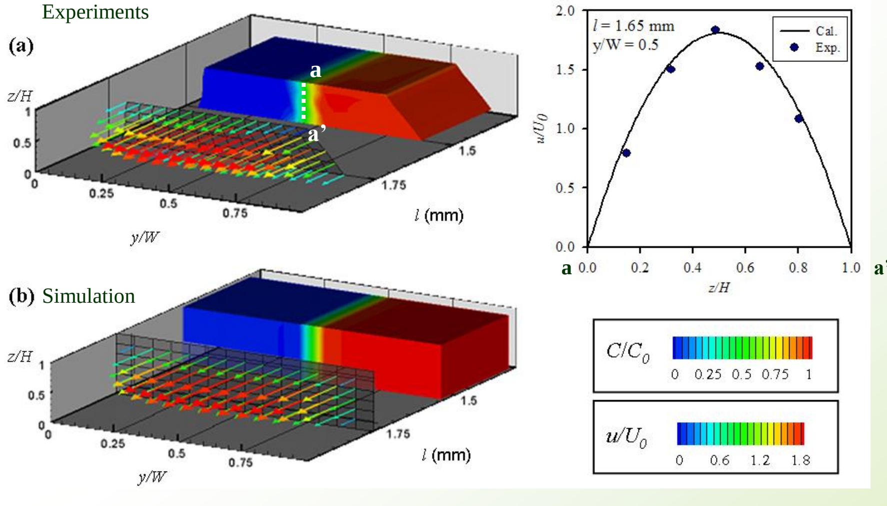
The maximum relative errors for both velocity and concentration fields between experimental and numerical results are about 5 %



Measuring Techniques (simultaneous measurement)

Biomicrofluidics, 2010
(Top 20 most downloaded articles, 2010/04, and /06)

3D velocity and concentration fields



快速均勻混合、加熱及冷卻

↓

精確控制反應參數

↓

提高資源和能量的使用效率、提高單位體積的生產能力

↓

體積小、操作簡單快速

↓

可提高提供準確數據給大型反應器參考、節省投資成本

↓

設備易於直接放大、安全性高、易控制

↓

可實現連續、整合、分散式及柔性生產 (按時、按地、按需生產)

↓

實現化工過程強化、微性化、綠色化!

未來展望

- 綠色製程取代高耗能高汙染傳統製造
- 目前正嘗試應用於環境檢測與生質能化學製造

http://futurewewant.org/portfolio/floating-cities-of-the-future/

Green Tech綠色製造

Acknowledgement: NSC projects

液珠型微流體反應器

Droplet-Based Micro-reactors

楊鏡堂 (Yang, Jing-Tang)

國立台灣大學 機械工程學系 終身特聘教授
國立台灣大學 生物技術研究中心 合聘研究員
國科會 熱流學門暨航太學門 召集人
jtyang@ntu.edu.tw

中華民國 一百零二 年 三 月 十九 日