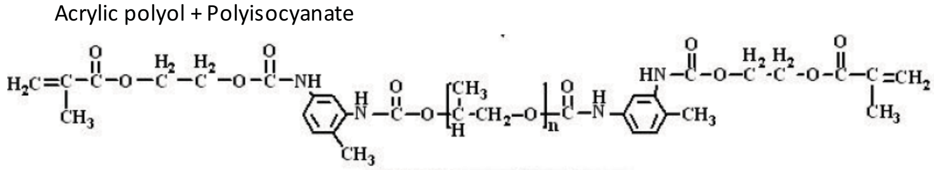
# Introduction to Microfluidics
and the Problem of Mixing

Sang-Gook Kim

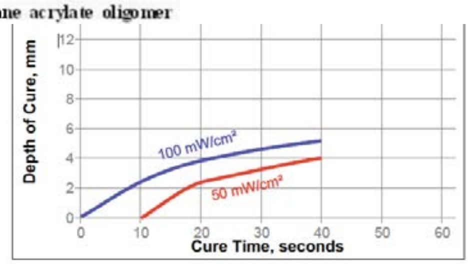
## Photoresist

Loctite® 3108™ is an acrylic, low hardness, rubbery, UV cure adhesive for potting and sealing of plastic, glass, and metal. Very flexible and resilient.

Acrylic polyol + Polyisocyanate

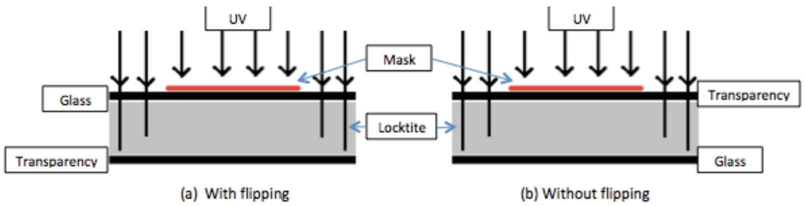


Polyurethane acrylate oligomer




EA-160 UV lamp, 365 nm, 820 $\mu W/cm^2$

# Bond Strength

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Xie, 2014

# Degassing of PDMS

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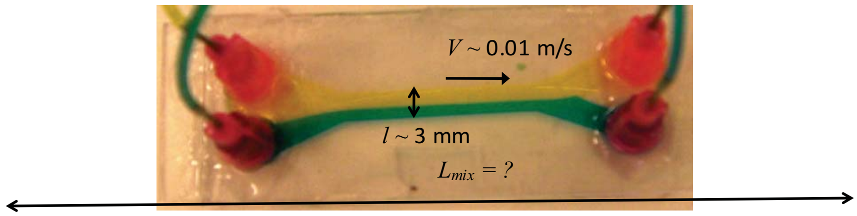
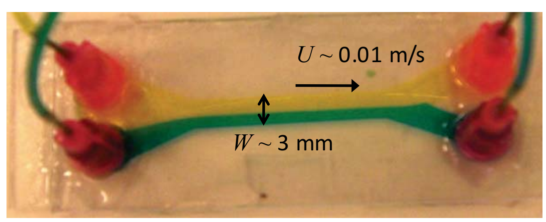
# Mixing

- Need better methods for mixing!!!




# Mixing in our millifluidic device

Why didn't we see much mixing???




$$\frac{\textit{timescale for diffusion across channel width}}{\textit{timescale for advection along channel length}} \sim \frac{W^2/D}{L/U} = Pe\left(\frac{W}{L}\right)^2 = \frac{W^2 U}{LD}$$

What designs actually worked?

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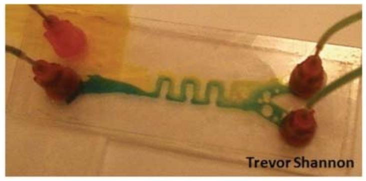
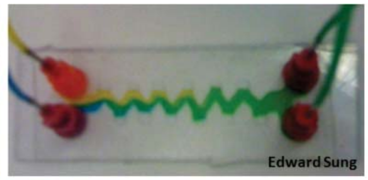
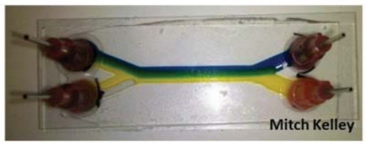
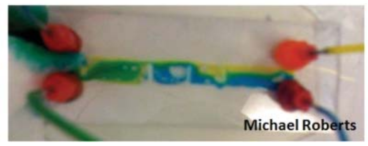
## Mixers that 'worked'! (last years)




- Turns
- Constrictions
- Long channels
- Bubbles

## Why did they work?

- Turns
  - Inertial effects (more in Lab 3)
- Constrictions or narrow channels
  - Smaller length for diffusion, slower velocity, inertial effects, 'twisting' of flow due to uneven channel walls
- Long, narrow channels
  - Slower velocity, smaller length for diffusion
- Bubbles
  - Surface-driven flows, e.g. see Marangoni effect, 'twisting' of flow

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## Two rivers meet near Geneve

- Rhone river meets Arve river

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Please see http://i2.asntown.net/15/river-in-geneva-switzerland-01.jpg.

Aiko Nakano, MIT, Class 2009

## Mixing

- What is "mixing"?

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Please see http://www.thewrendesign.com/wp-content/uploads/2012/08/mixing-black-dye1.jpg.

Mixing is the process by which uniformity of concentration is achieved
- May refer to particular component or set of components

thewrendesign.com

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Please see https://icecreamjournal.turkeyhill.com/blog/wp-content/uploads/2010/07/chocovanillacone.jpg.

Slide by R. Karnik

# Hard to Mix Compounds

- Banbury Mixer
  - Charles Goodyear, vulcanization

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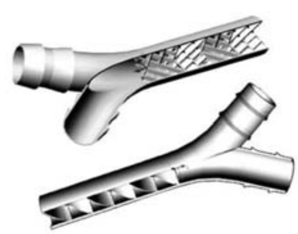
This image has been removed due to copyright restrictions. Please see https://tirenews4u.files.wordpress.com/2010/08/rubberindustrymanual-rev2.jpg.

# What makes microfluidic mixing so interesting? (or why is it a problem?)

- Low Reynolds number
  - Turbulence is almost always absent



- Fabrication capabilities
  - Cannot easily fabricate complicated stirrers and mixers!

Bertsch, et al, Lab Chip 1999

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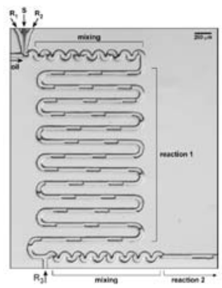
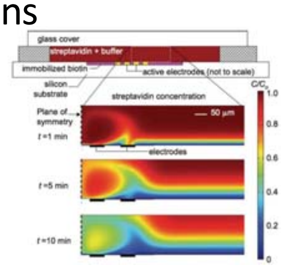
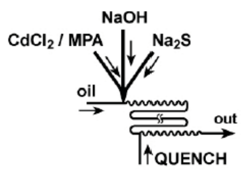
# Why is mixing important?

## Chemical reactions

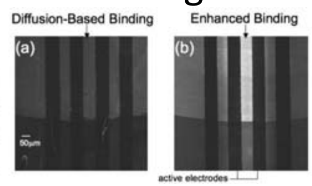



Shestopalov et. al
*Lab Chip* 2004




## Biosensing




Feldman et. al *Lab Chip* 2007

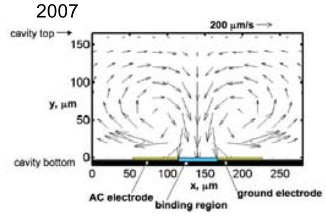



Fig. 2 Numerical model of electrothermal velocity. Two long, parallel electrodes on cavity bottom are driven at 200 kHz; 10 $V_{rms}$. Maximum electrothermal velocity generated is 1.1 mm $s^{-1}$, near the inside edges of the electrodes. Cavity sides extend well beyond plotted region.

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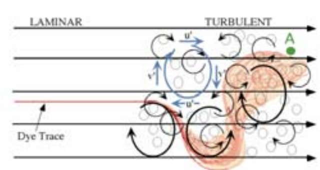
# Scale effect in mixing

- Flow through micro channels
- Reynolds number
- Turbulent Flow vs. Laminar Flow
- Diffusion

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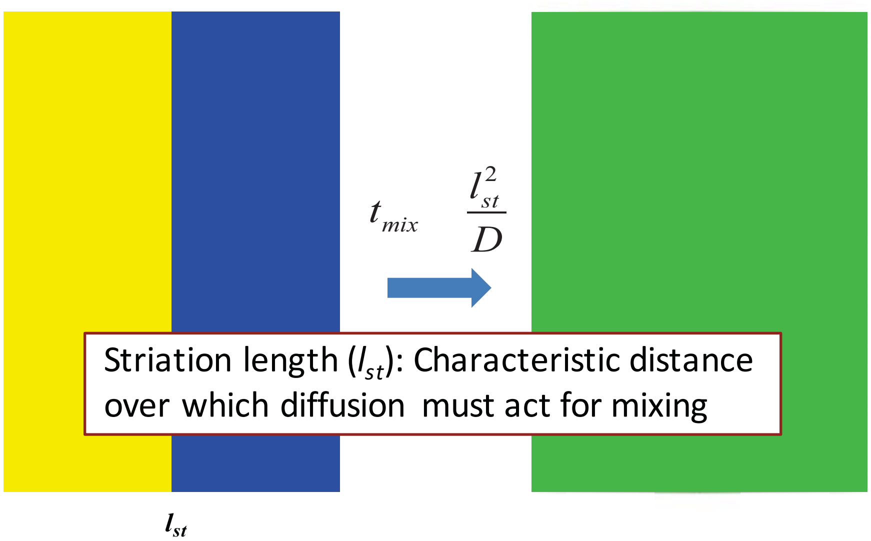
$$Re = \frac{\rho \cdot v \cdot d}{\mu}$$

https://www.youtube.com/watch?v=FZYnewBWUoc

## Transition

## How does mixing by diffusion occur?



# Brownian Motion

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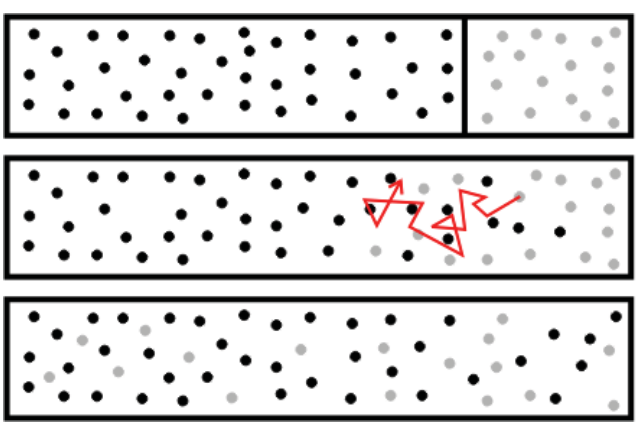
# Understanding diffusion



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en.wikipedia.org/wiki/Molecular_diffusion

## Understanding diffusion

- Macroscopic diffusion 'results' from random motion of individual molecules
- When a large number of molecules is observed, diffusion seems to be a smooth, continuous process with no indication of underlying randomness

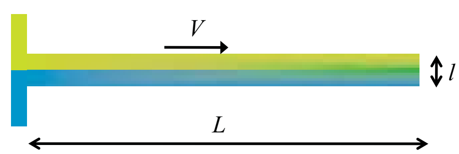
Observe random motion of microspheres in the lab!

## Mixing in flowing systems- Péclet number

- Péclet number: Compares transport due to advection to transport due to diffusion

$$t_{adv} \sim \frac{l}{V}$$

$$t_{diff} \sim \frac{l^2}{D}$$




$$Pe = \frac{t_{diff}}{t_{adv}} = \frac{lV}{D}$$

$$L_{mix} \sim Vt_{diff} = V\frac{l^2}{D} = lPe$$

# How can mixing be enhanced?

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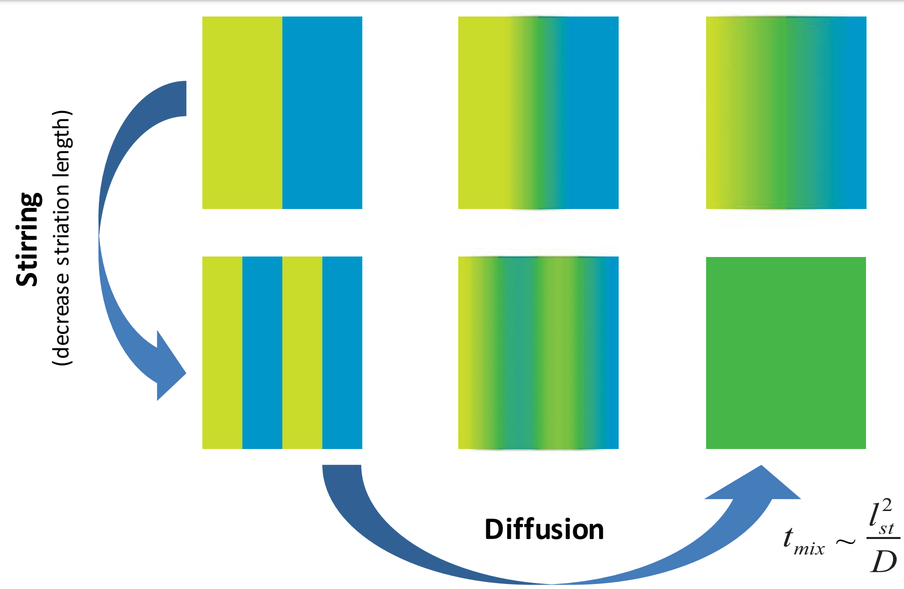
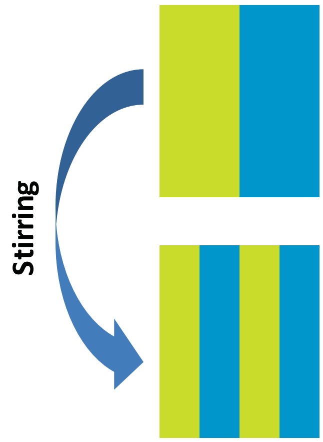
# The role of stirring

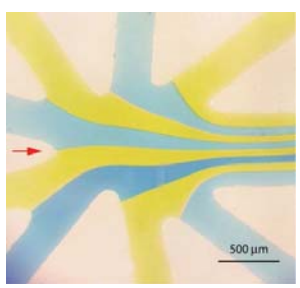


# Strategies for mixing

- Start off with small striation length
- Decrease striation length
  - Cannot be done in steady, two-dimensional flows
  - Use weak inertial effects
  - Use 3D geometries or time-varying flows (only option at very low Re)




# Laminated flow

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A.P. Sundarsan, Ph.D. Thesis, Texas AM, 2006

# Parallel Lamination Mixers

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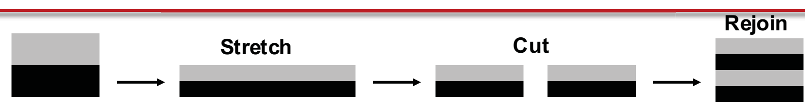
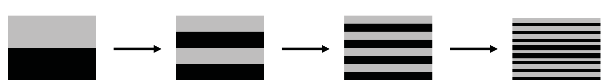
Please see Figure 3 in http://link.springer.com/chapter/10.1007%2F128_2011_150.

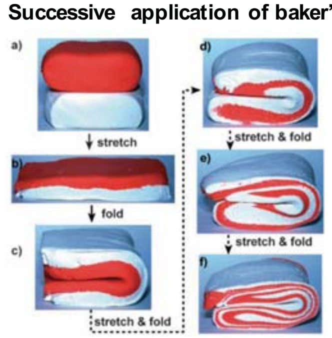
# Baker's transformation




**Baker's transformation**



**Successive application of baker's transformation**




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

Each cycle decreases the striation length by a factor of two!
After $n$ cycles:

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# Sequential

Split and Recombine (SAR) mixers

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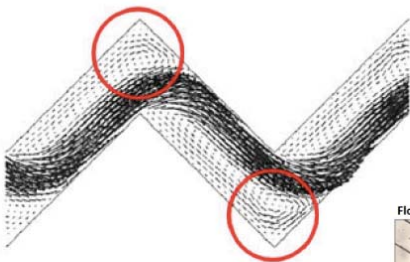
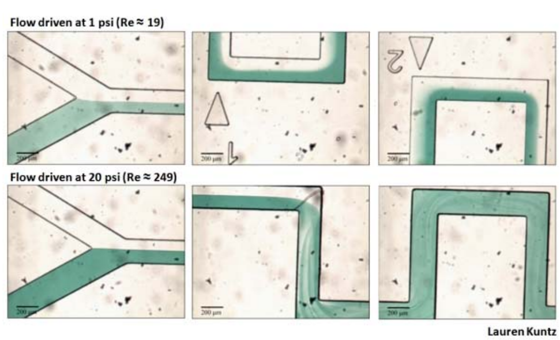
# Zig-Zagging



Inertial Effect

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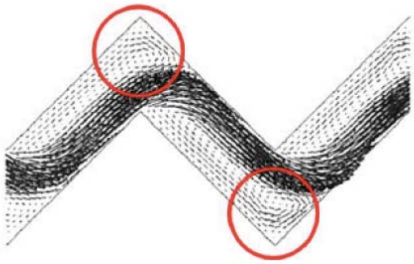
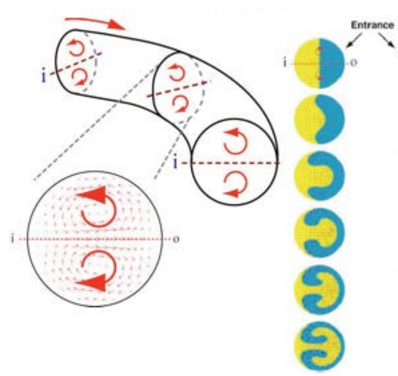
2.674, 2013

# Zig-Zagging



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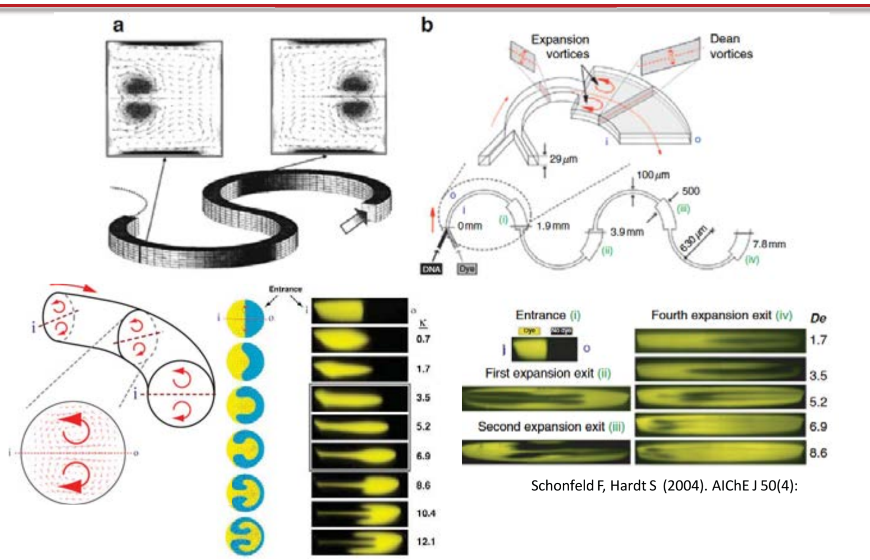
# Dean Vortices




Schonfeld F, Hardt S (2004). AIChE J 50(4):

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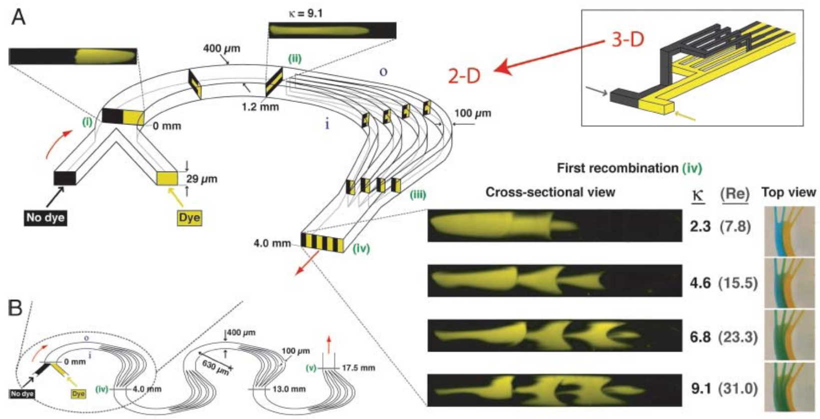
# Mixers employing baker's transform: Dean flow



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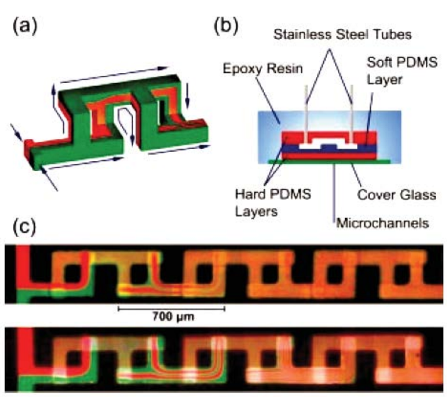
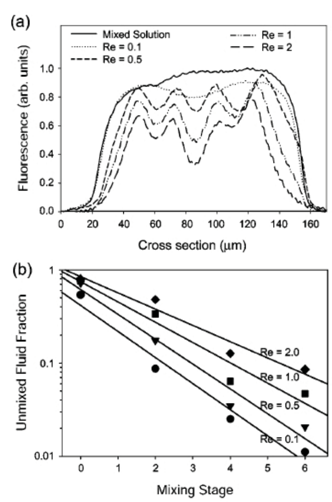
Dean number : $\kappa = \mathrm{Re}\sqrt{D/2R}$ (R is radius of curvature of channel)
D is diameter of the pipe.

Sudarsan and Ugaz, PNAS 103, 7228 (2006)

# Mixers employing baker's transform

Topologic Mixing





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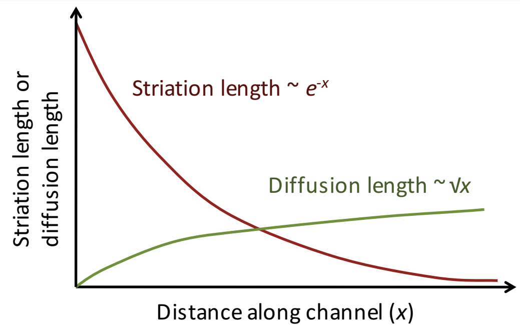
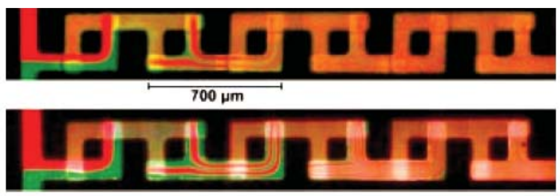
Chen and Meiners, Applied Phys. Lett. (2004)

# Timescale for mixing




Mixing length ~ log (Pe)
i.e. $L_{mix}$ ~ log($lV/D$)

→ Much shorter channels suffice

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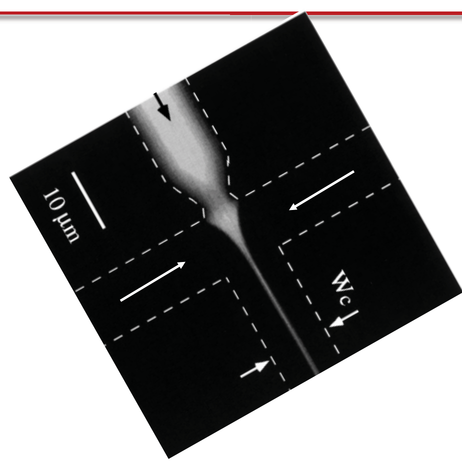
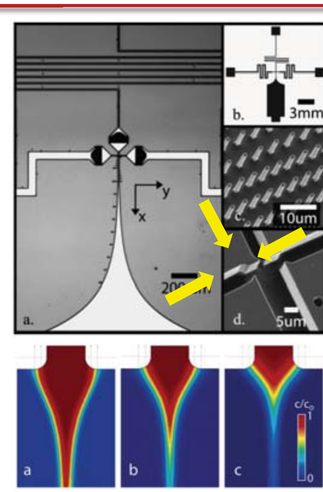
# Flow focusing




Hertzog et al., Analytical Chem. (2004)
Knight et al., Phys. Rev. Lett. (1998)

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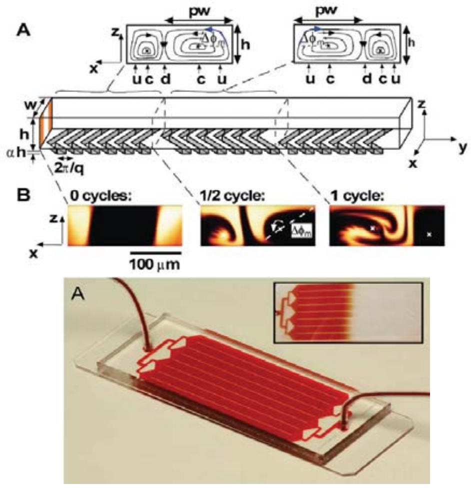
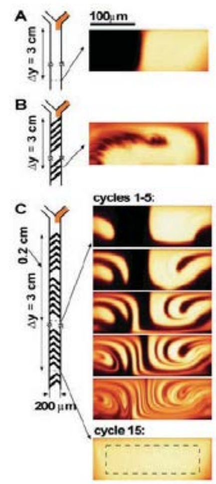
# Staggered Herringbone Mixer

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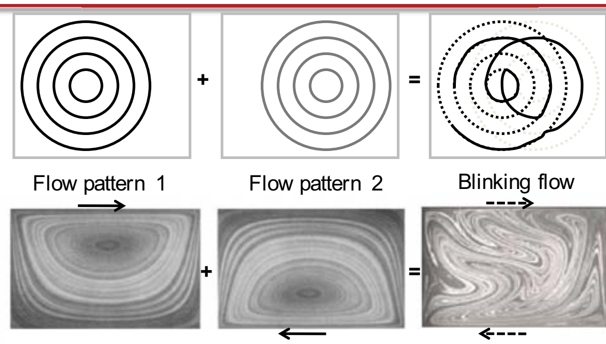
Toner et al., *PNAS* (2010)

Stroock et al., *Science* (2002)

# Blinking vortex flow




**Chaotic advection in blinking flows**

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Chaotic advection: Sensitive dependence on initial conditions in deterministic systems; typically used for low Re flows

# Passive vs. active mixers

- Passive mixers
  - No work input
  - T- unction, Flow focusing, Parallel lamination, Serial Lamination, Chaotic Advection, Droplet micromixing
- Active mixers
  - Work input apart from that used for driving flow

# "Wet" labs in 2.674

- Lab 1: Benchtop lithography
- Lab 2: PDMS micromolding
- Lab 3: Microfluidics device assembly and mixing/diffusion
- Lab 4: Droplet microfluidics
- Lab 5: Electrokinetics

Microfluidics (Labs 3–5)

- Lab 6: Surface engineering using soft lithography

# What is Microfluidics?

"... the science and technology of systems that process or manipulate small amounts of fluids, using channels with dimensions of tens to hundreds of micrometres."

-George Whitesides

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# Micromolding in PDMS

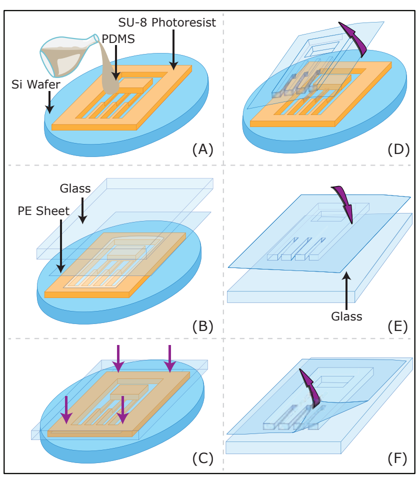


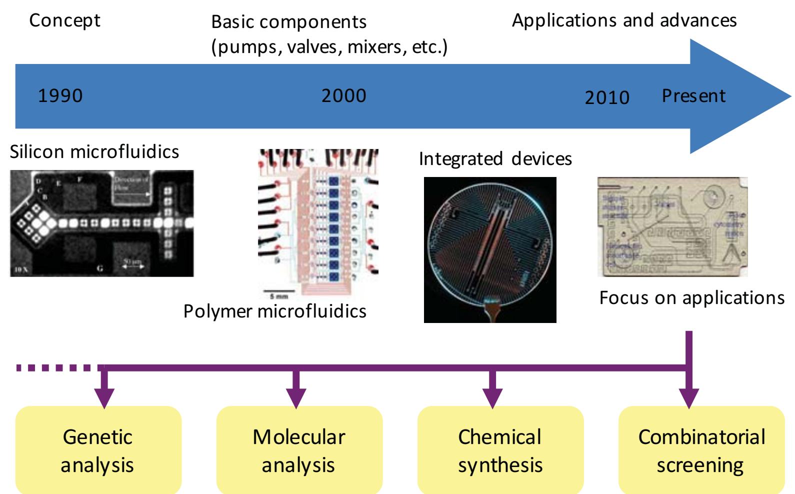

Image by MIT OpenCourseWare.

PDMS molding process
Courtesy Folch lab

Most popular material for prototyping of microfluidics devices in the lab

- Easy to use in lab
- Low cost
- Doesn't need clean room
- Permeable to oxygen
- Good transparency
- Versatile- can make flexible pumps, valves, multilayer components easily
- Disposable

# The evolution of microfluidics

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# Driving Applications

**Chemical and biological analysis**
-DNA analysis and sequencing
-Cell separation and analysis
-Biosensing and diagnostics
-Detection of chemicals
-Preparation for mass-spec

**Tissue engineering**
-Cell culture
-Patterning of cells
-Analysis of cellular response

**Others**
-Drug screening
-Chip cooling
-Propulsion

**Laboratory research**
-Experiments with cells and small organisms
-Study of fluid mechanics, biology, cells, …

**Chemical synthesis**
-Nanoparticles and quantum dots
-Emulsions

## Advantages of Microfluidics

- Small sample consumption
- Faster analysis
- Manipulation of small volumes
- Access to microscale phenomena
- Process integration
- Portability

- Disadvantages
  - System integration and robustness
  - High complexity

## Chemical Analysis

**Microfluidics can trace its origins to miniaturization of chromatography**

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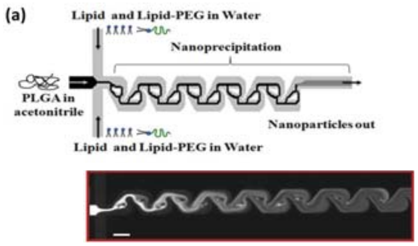
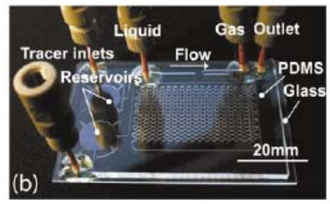
# Chemical Synthesis

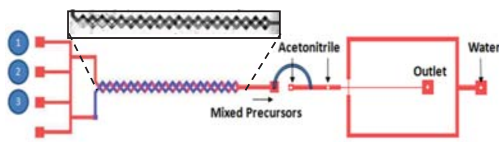
**Synthesis of nanoparticles for drug delivery**

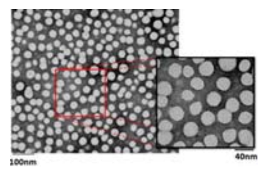



**Synthesis of colloids**




Jensen group, MIT



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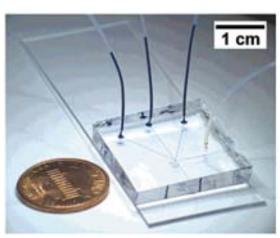
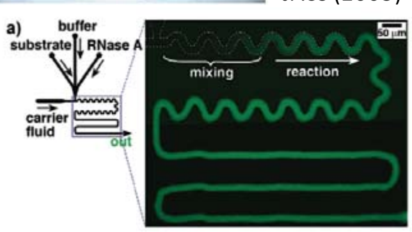
Karnik/Langer/Farokhzad groups, MIT & Harvard

# Laboratory Research Tool

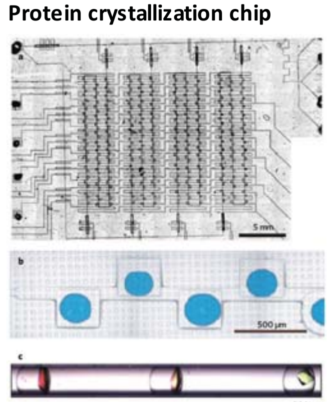
**Measurement of fast reaction kinetics**




Song & Ismagilov, JACS (2003)




**Protein crystallization chip**

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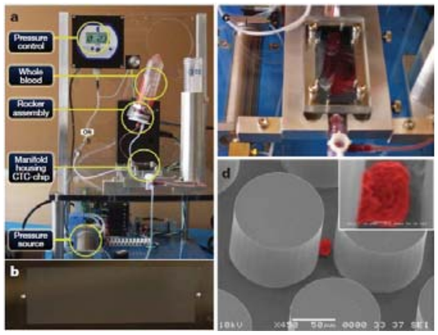
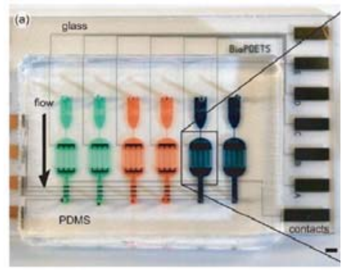
# Biological Applications

**Cancer cell detection chip**

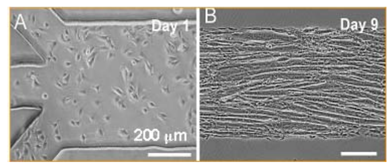



Toner group, MGH

**Cell culture and analysis**




Luke Lee group, UC Berkeley




Folch group, U Wash.

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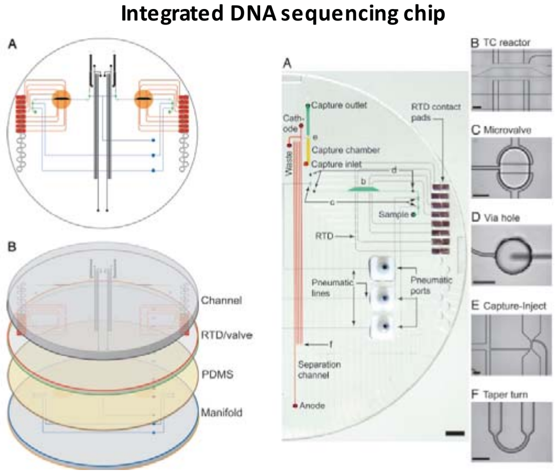
# Biological Applications

**Integrated DNA sequencing chip**

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Mathies group, UC Berkeley

## Device fabrication challenges

- Integration of diverse materials
  - Polymers, glass, biomolecules, surface coatings
- Process compatibility

**→ Focus on low-cost polymer devices**

**→ New versatile fabrication techniques compatible with different materials including biomolecules and cells**

ctor

- Cost issues
  - Computer processors- high volume, long life
  - Biological chip- Low volume, disposable

## Controlling Transport in Microfluidics

- Transport phenomena
  - Very important in micro/nano systems in general.
  - E.g. transport of charge (electrons/ions), thermal energy, mass (molecules/ions/protons), etc.
- Pumps
  - Pressure-driven, electrokinetic, others…
- Valves
- Mixers

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