# CH-413 Nanobiotechnology

## Microfluidics

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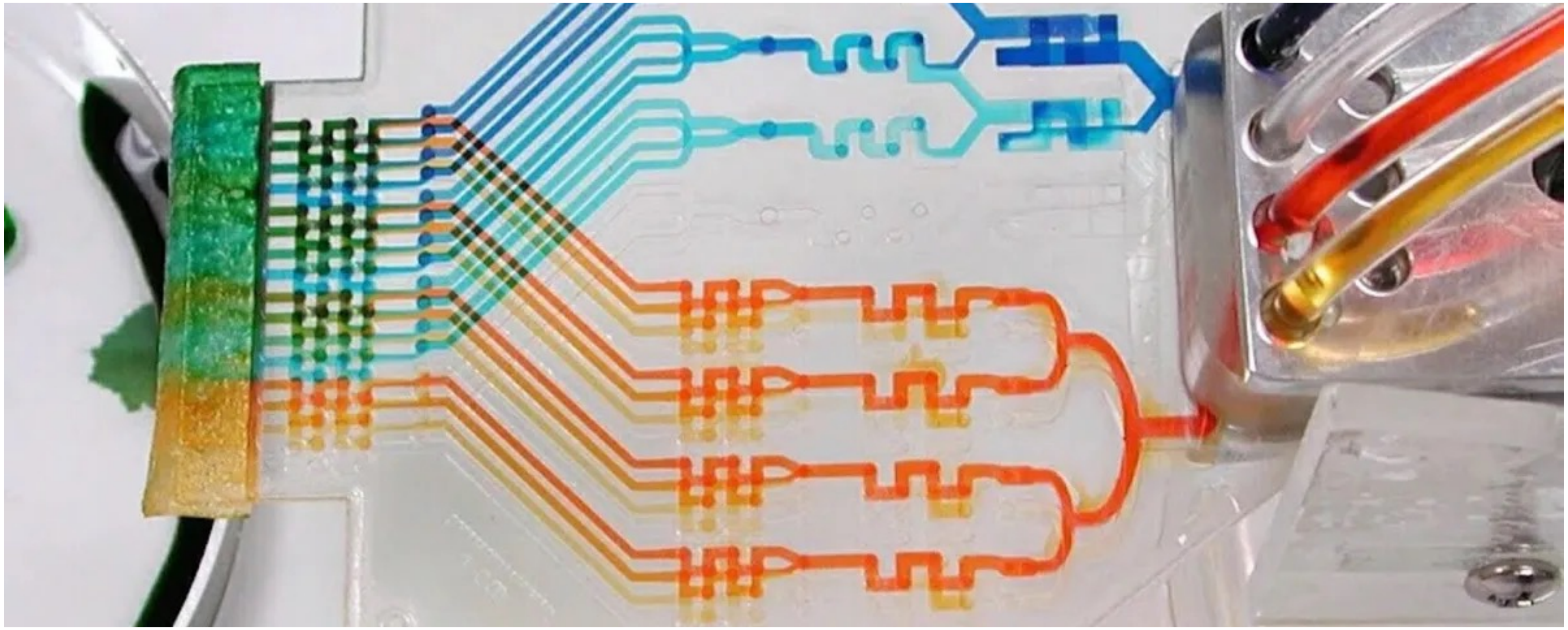
# Microfluidics

*A field of science and engineering that involves the study, design, and manipulation of fluids that are geometrically constrained to a small, typically sub-millimeter, scale. It focuses on the* ***behavior****,* ***precise control****, and* ***manipulation*** *of fluids that are constrained within small volumes, often down to the microliter or even picoliter level.*



https://www.the-scientist.com/microfluidics-biology-s-liquid-revolution-71667

# Warm-up: what's happening here?

- https://www.youtube.com/watch?v=p08_KlTKP50&ab_channel=UNMPhysicsandAstronomy

# Activity

1. Observe: what did you see?
2. Why is this unexpected? Describe what you would expect to happen under “normal” circumstances.
3. Discuss: what are the physical parameters that drive this behavior? How could you “mess up” the demonstration, meaning what could you change so that liquid unmixing would not be observed?
4. Why do you think this is relevant for microfluidics?

# Viscosity

Viscosity of a simple liquid:

Related to **intermolecular interactions**

Measure of fluid's resistance to deformation at a given rate, **"internal friction"**

Temperature-dependent

Unit: Poise (g $s^{-1}$ $cm^{-1}$)

Water

Viscosity: 1 cP at RT (1 cP = $10^{-2}$ P = $10^{-3}$ Pa·s = 1 mPa·s)

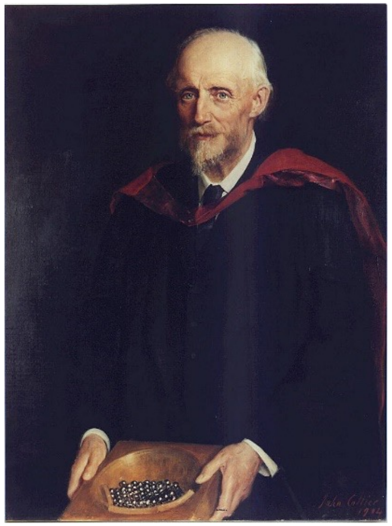
Pitch

230 billion times more viscous than water, one drop every 10 years

# Pitch drop experiment live

- http://thetenthwatch.com/feed/

# The Reynolds number



Osborne Reynolds (1842-1912)

**Reynolds number:**

$$Re = \frac{\rho u L}{\mu}$$

$\rho$: density
$u$: velocity
$\mu$: viscosity
$L$: characteristic length

$$Re = \frac{\text{Inertial forces}}{\text{viscous forces}}$$

Reynolds number: a dimensionless number that gives the ratio of **inertial forces (characterizing how much a particular fluid resists to motion)** to viscous forces.

- The Re-number is the most important dimensionless number in microfluidics
- **<u>Low Re-numbers, i.e. viscous forces, dominate in microfluidics</u>**

# Inertial vs. viscous forces


Image Source:
https://en.wikipedia.org/wiki/Francis_Scott_Key_Bridge_collapse#/media/File:Francis_Scott_Key_Bridge_and_Cargo_Ship_Dali_NTSB_view_(cropped).jpg

# Laminar vs. turbulent flow

- https://www.youtube.com/watch?v=9A-uUG0WR0w&t=29s

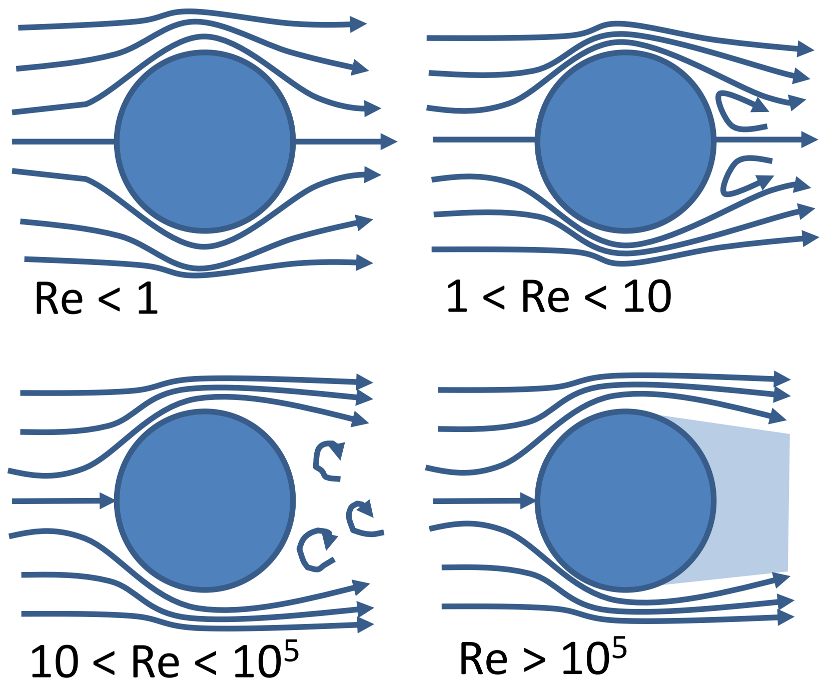
# Laminar vs. turbulent flow

**Reynolds number:** $$Re = \frac{\rho u L}{\mu}$$

Proportional to **length**, **velocity**, **density**
Inversely proportional to **viscosity**

*Re* < 2000 → **laminar flow**
2000 < *Re* < 40000 → transitional flow
*Re* > 4000 → turbulent flow (Eddy currents)

***Re* rarely exceed 0.1 in microsystems** with flow rates not faster that 1 cm/sec and mm-sized channels

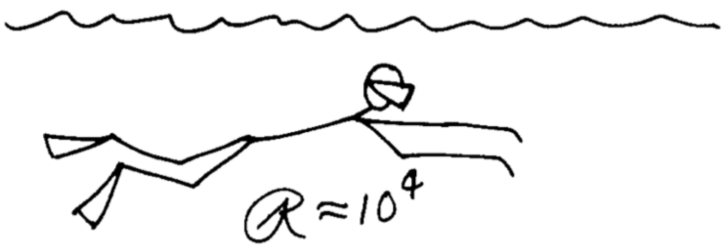


# The Reynolds number

Reynolds number: $$Re = \frac{\rho u L}{\mu}$$

## Life at low Reynolds number

E. M. Purcell
*Lyman Laboratory, Harvard University, Cambridge, Massachusetts 02138*
(Received 12 June 1976)




It helps to imagine under what conditions a man would be swimming at, say, the same Reynolds number as his own sperm. Well, you put him in a swimming pool that is full of molasses, and then you forbid him to move any part of his body faster than 1 cm/min. Now imagine yourself in that condition: you're under the swimming pool in molasses, and now you can only move like the hands of a clock. If under those ground rules you are able to move a few meters in a couple of weeks, you may qualify as a low Reynolds number swimmer.

# The scallop theorem

At low Reynolds number, any reciprocal motion (i.e., time-reversible motion) produces no net displacement.

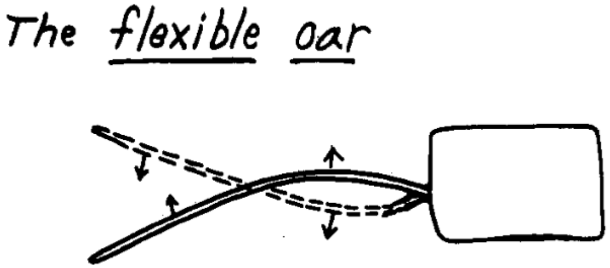
**Why? The Physics**

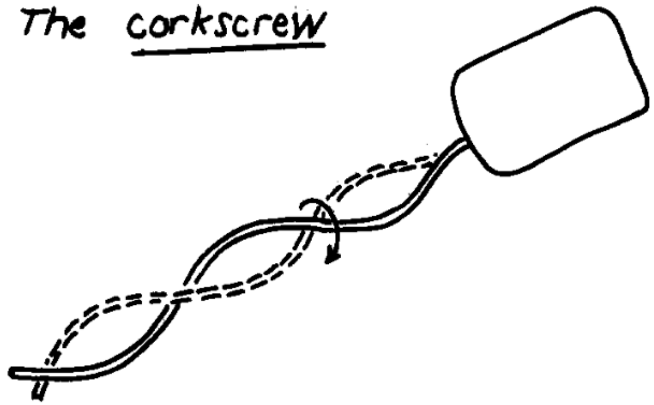
The Navier–Stokes equations simplify dramatically at low Re:

$$\mu \nabla^2 v = \nabla p$$

- No inertial terms (no $\rho \frac{dv}{dt}$)—the fluid is governed only by viscous and pressure forces.
- The equations are **linear** and **time-reversible**. That means:
    - If you reverse the motion of the swimmer, the flow also reverses.
    - So: any sequence of shapes that is the same when reversed in time **cannot create net movement**.

# So how do microorganisms swim at low Re?



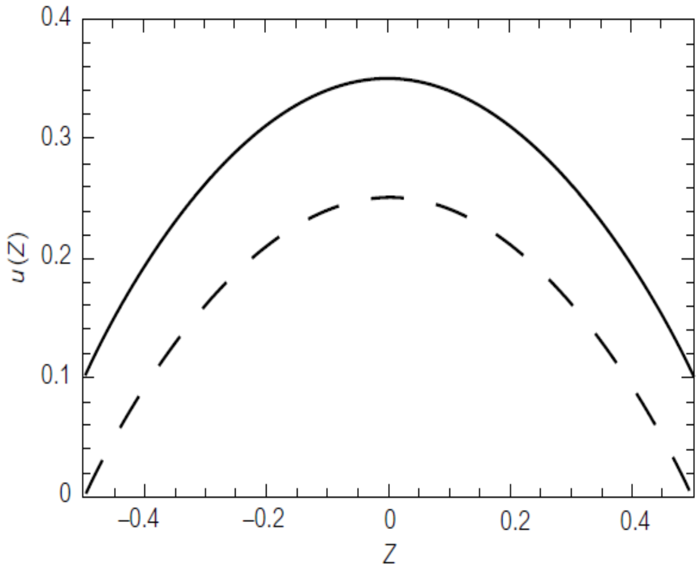

They break time-reversal symmetry by using non-reciprocal motion:

- **Flexible oar: Eukaryotic cells** (e.g., sperm) use **traveling waves** along cilia or flagella
- **Corkscrew: Bacteria** use rotating flagella (not a back-and-forth stroke).
- Artificial microswimmers use **shape cycles** (e.g., three-bead swimmers with coordinated motions).

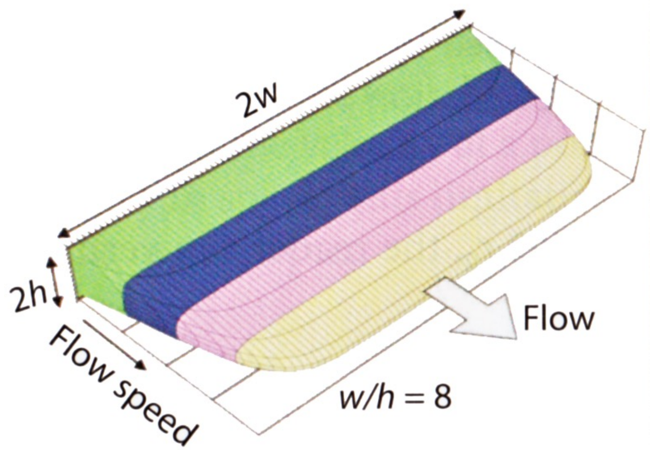
These motions have a **geometric phase**—the sequence of shapes traces a loop in configuration space, **not a straight line**, so the net effect is movement.

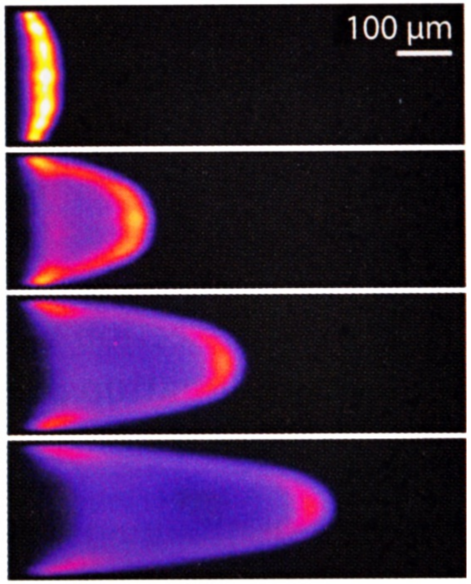
# Laminar flow

The most important properties of laminar flow:
- Non-turbulent
- Parabolic flow profile
- Velocity zero at wall



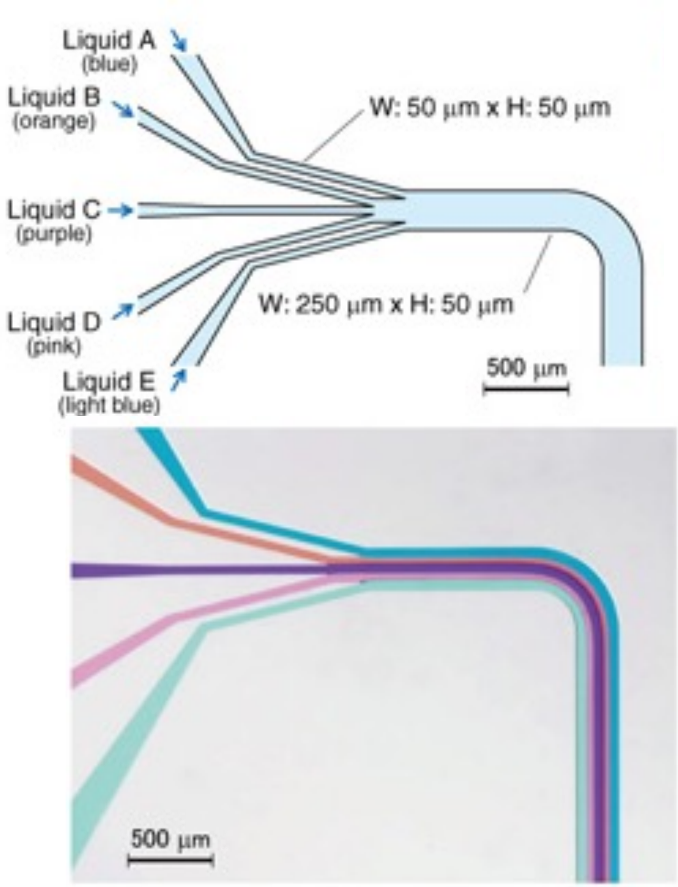

**No slip condition:**
Velocity zero at wall / boundary



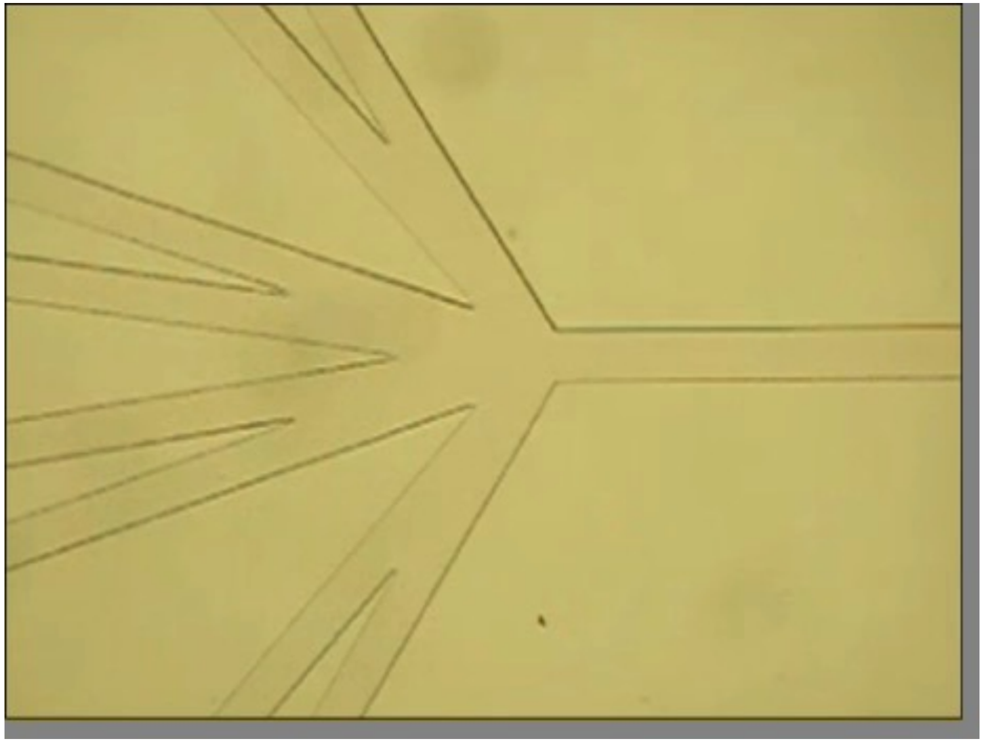




**Parabolic** flow profile

# Laminar flow, no mixing




*Nano Fusion Technologies, Inc.*
*Web site*



**Laminar flow:**
Side-by-side layers of liquid do not mix, no turbulence
Only mixing occurs at interface due to **diffusion**

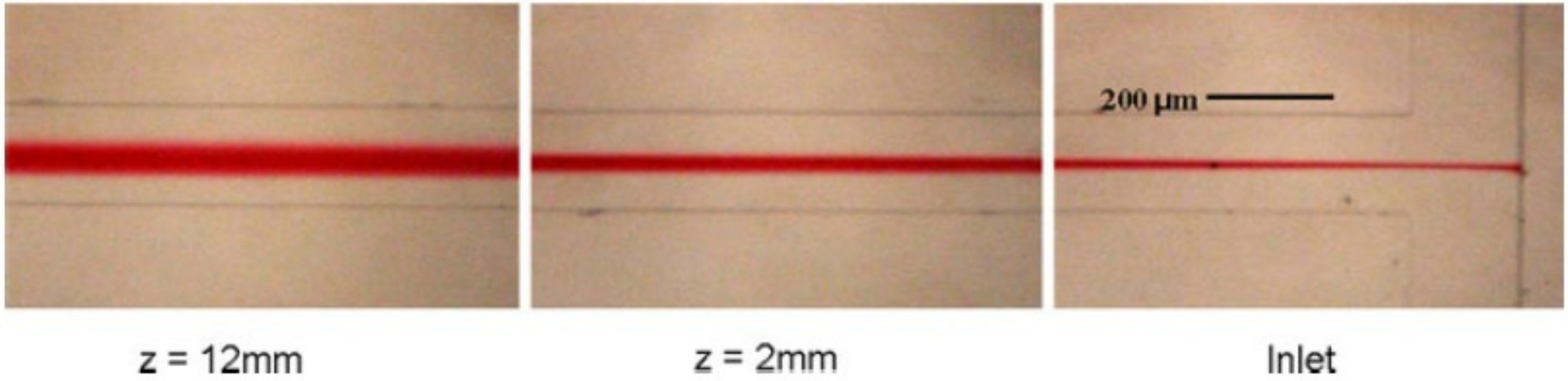
# Activity: simulate laminar flow

- https://learncheme.com/simulations/fluid-mechanics/laminar-flow/

Try to break the laminar flow.

# Mixing in microfluidics flows

# Mixing by diffusion




**T-channel mixer**
Red-dyed solvent is slowly mixing through diffusion over time

# Diffusion: Time dependence

$$D = \frac{kT}{f} = \frac{kT}{6\pi\eta r}$$

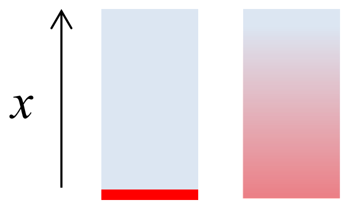
Boltzmann's constant, *k*
Temperature, *T*
(=kinetic energy)

Radius of particle

Viscosity
(solvent mobility)

Units: cm²/s

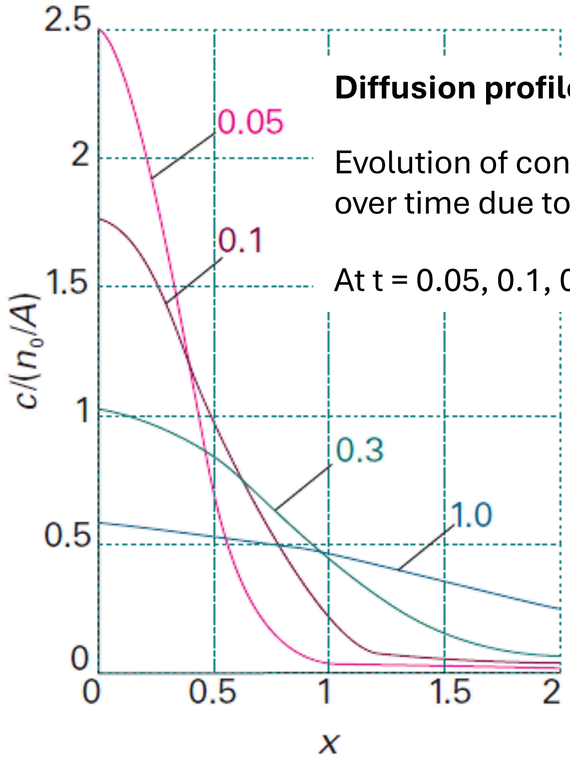
Fick's second law: $c(x,t) = \frac{n_0}{A(\pi\,\mathrm{Dt})^{1/2}} e^{-x^2/4Dt}$




Area $A$

$N_0$ particles, $n_0 = N_0/N_A$

Describes how concentration changes over time due to diffusion




**Diffusion profile over time:**

Evolution of concentration profile over time due to diffusion

At t = 0.05, 0.1, 0.3, and 1.0

**Derive**: $t_{diff} \sim x^2/D$

Diffusion is **very efficient** at short lengths for mixing

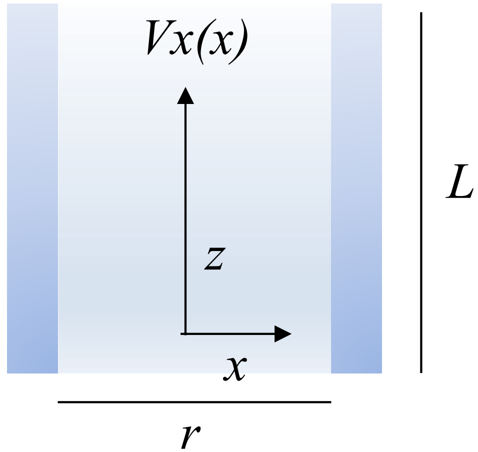
Diffusion is **extremely inefficient** for mixing over large length scales

# Resistance

**In microchannels**: large surface-to-volume ratio

Walls of channels exert high friction

Without pumping: fluid stops immediately




Resistance: $R = \frac{\Delta P}{Q}$

With resistance, $R$, flow rate, $Q$, and pressure difference $\Delta P$

For tubular channel: $R = \frac{8\eta L}{\pi r_0^4}$ L: length of channel

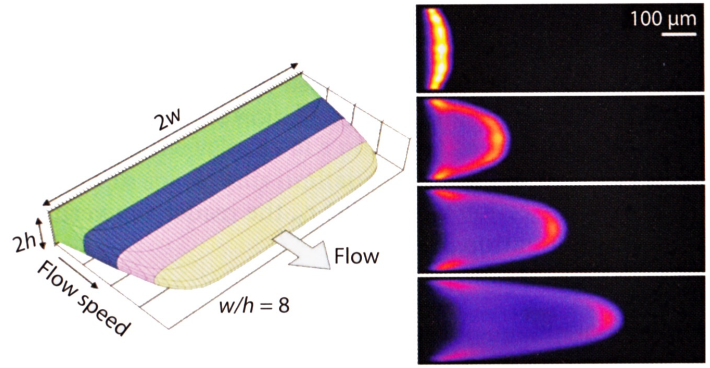
**R is a property of the channel/defined by the cross section and length channel!**

# Summary: Flow in microfluidic systems

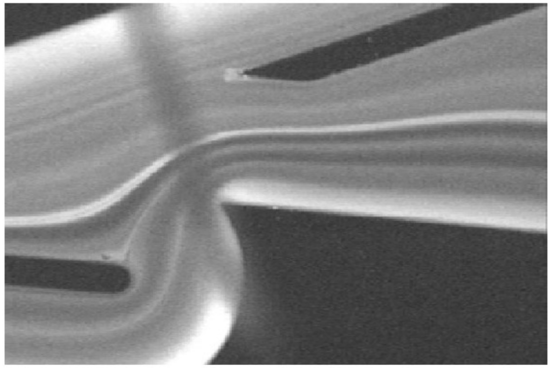
**Flow in microfluidic systems:**

- **Deterministic**: predictable and calculable flow behavior
- **Laminar**: smooth, parallel layers of fluid moving in orderly fashion, no cross-stream mixing
- **Reversible**: flow processes are theoretically time-reversible
- **Reciprocity**: the scallop doesn't move!

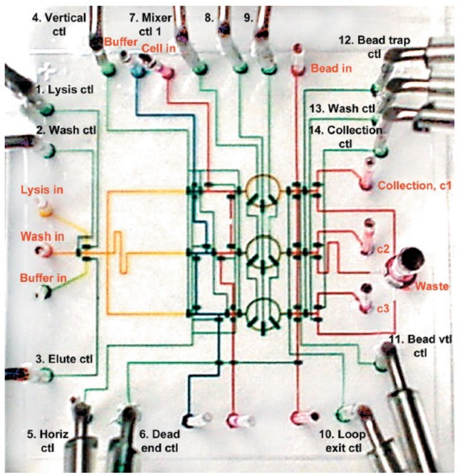
# Microfluidics




Small channels:
Laminar flow



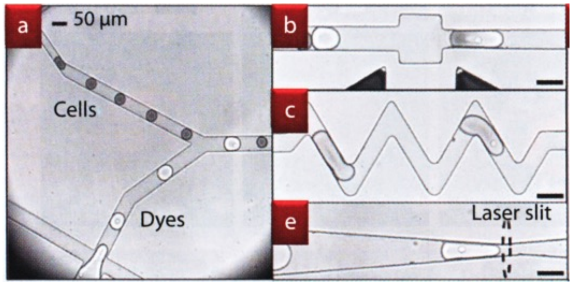
Determi-
nistic flow




High throughput

Small device
footprint
Little reagents/waste

Cheap fabrication /
cheap operation

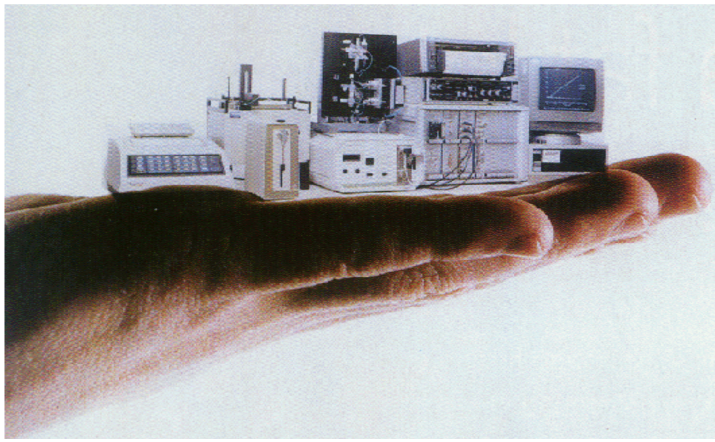



Cellular
scale

Micorvalves and
micropumps

# Why go small?

- Flow in microchannels is **laminar** and mathematically predictive
- Easy fabrication of **cellular scale** (or smaller) features → access to the cellular- or sub-cellular scale
- Integration of microvalves, micropumps, electronics etc.: **Fully automated control** at very high precision
- **Batch fabrication**: low cost per unit
- Parallel operation allows **high throughput**
- Low reagent consumption
- Low system footprint



*'Handheld Instrumentation': micro Total Analysis System*

# Case study

LETTERS

nature biotechnology

## A nanoliter-scale nucleic acid processor with parallel architecture

Jong Wook Hong[1,4], Vincent Studer[1,2,4], Giao Hang[1], W French Anderson[1,3] & Stephen R Quake[1]

# Aims of the paper's study

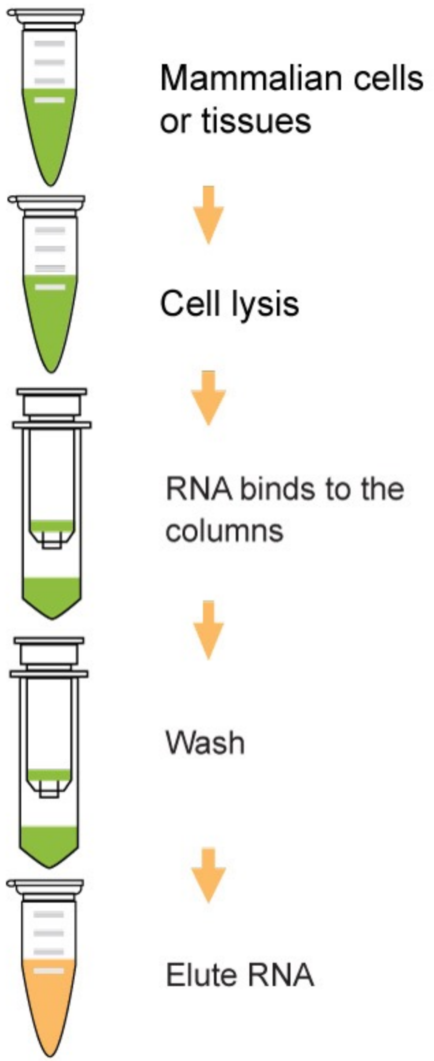
**Standard method for RNA and DNA extraction:**

**Lysis takes place in a bulk sample, followed by purification**

- Many modern applications require to get DNA (cDNA library) from few or even single cells
- This would allow to characterize
  - single-cell polymorphisms in a heterogenous population (cancer)
  - epigenetic variations

- **Solution:** Extract RNA or DNA from a single cell, all in one microfluidic chip

# Activity: design challenge




You've seen how mRNA is extracted using the spin column kit. Now imagine designing a fully integrated lab-on-a-chip that performs the same process.

What components would you need to replace the shown steps on-chip?

Jot down or sketch your component list (1-2 min).

Discuss with another person in class (2-3 min).

# Summary: Flow

- Re = intertial / viscous forces, in microfluidics Re is low
- Flow is laminar in microfluidics
- Diffusion is inefficient over long length scales
- Viscosity rules!

# Connections

https://connections.swellgarfo.com/game/-NwFiIRRYiVw3cIYhErE