Microfluidics: Basics and Applications

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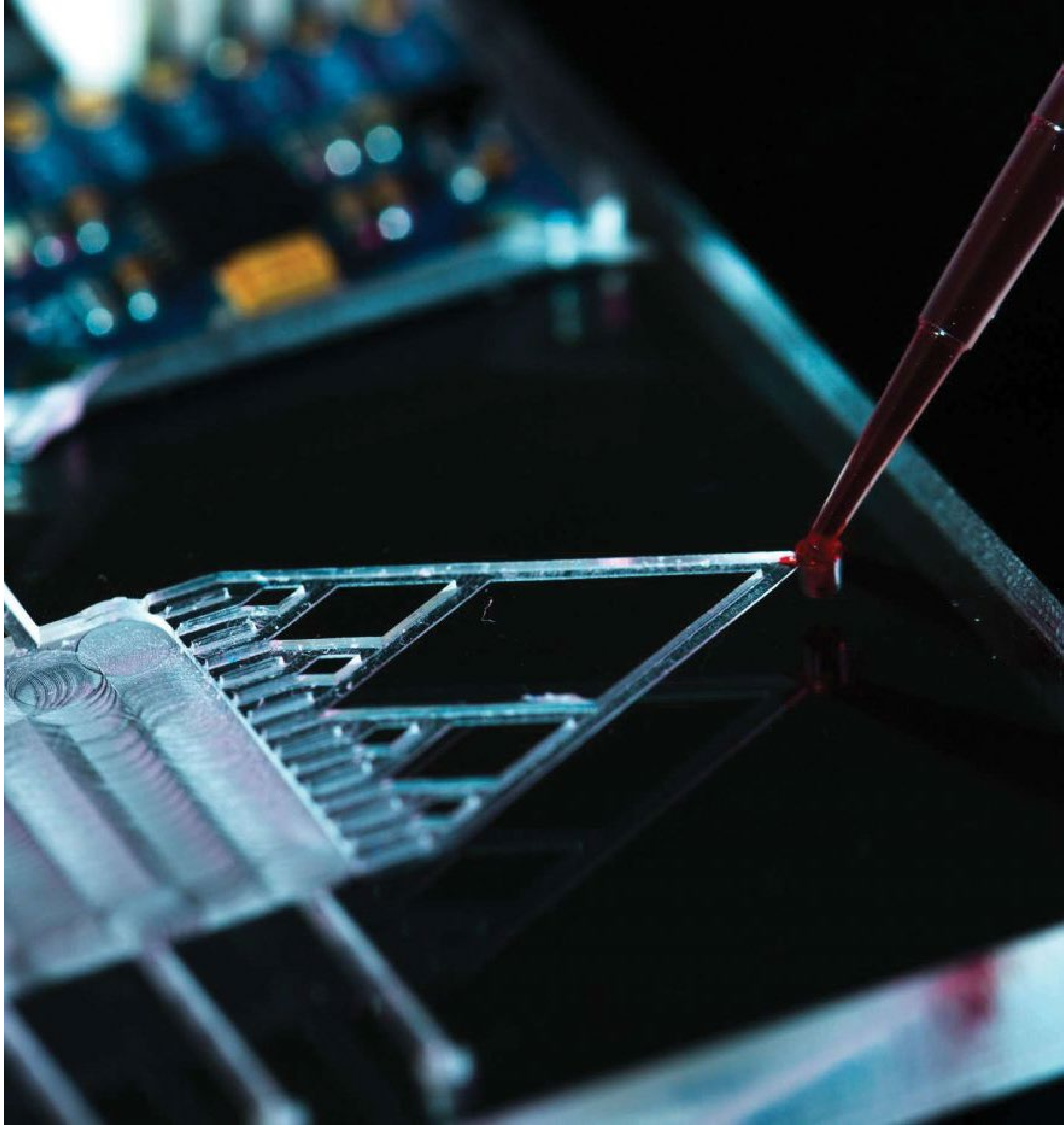
Cancer Engineering, October 14th, 2025

Memorial Sloan Kettering
Cancer Center



Course Outline

- What is microfluidics?
- Why microfluidics?
- Basics of fluid mechanics
- Special phenomena associated with the micro-scale:
  - Laminar flow
  - Diffusion and mixing
  - Capillary phenomena
  - Surface energy
- Microfluidics and lab-on-a-chip devices
- Challenges and barriers for commercialization

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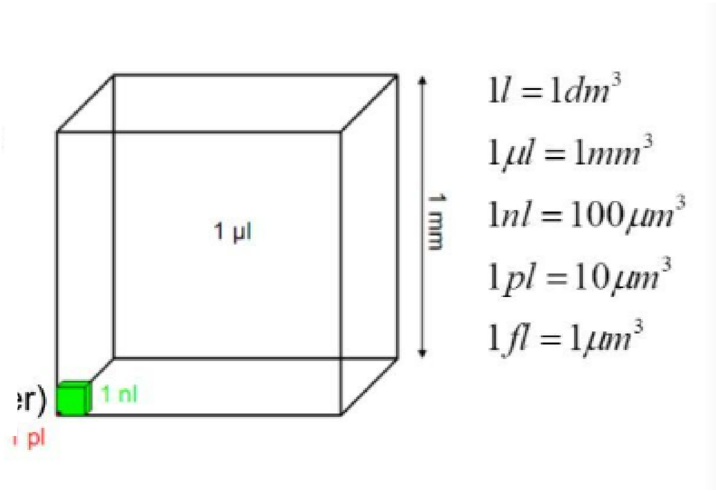
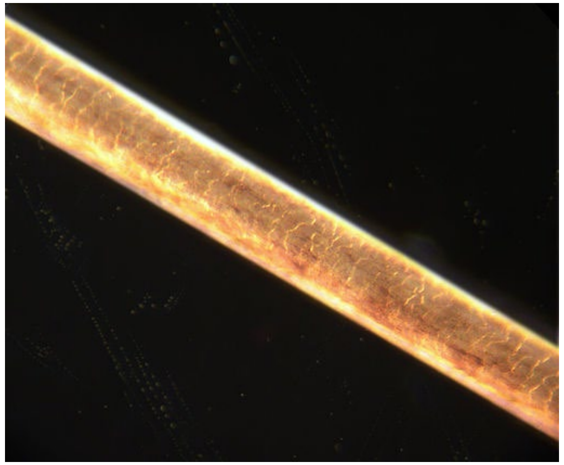
What is Microfluidics?

- **Fluidics:** The handling of liquids and/or gases
- **Micro:** Characterized by at least one of the following:
  - Small volumes (µl, nl, pl, fl)
  - Small size
  - Low energy consumption
  - Use of special phenomena





A microfluidic channel is about the same width as a human hair, ~70 µm.

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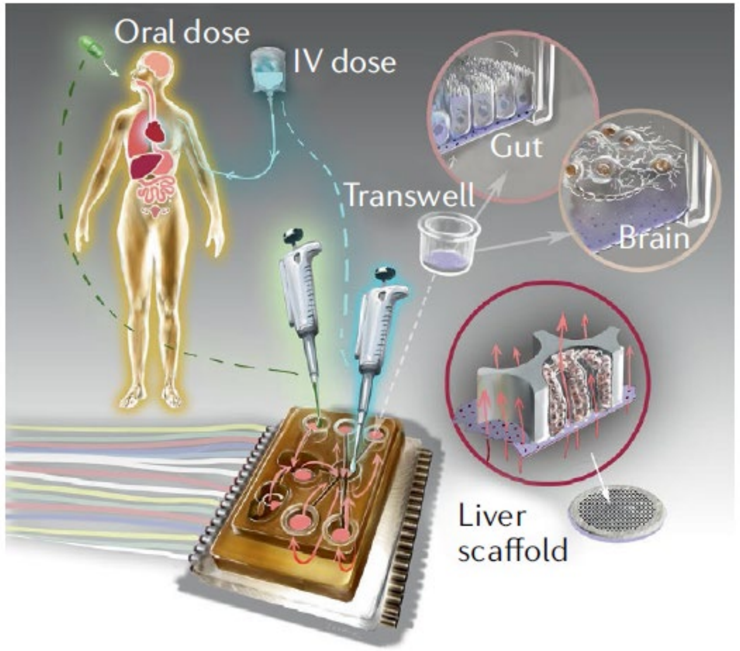
Why Microfluidics?

- Low sample and reagent consumption
- Small physical and economic footprint
- Parallelization and high-throughput experimentation
- Leverages unique physical phenomena at the micro-scale:
  - Laminar flow
  - Capillary forces
  - Diffusion

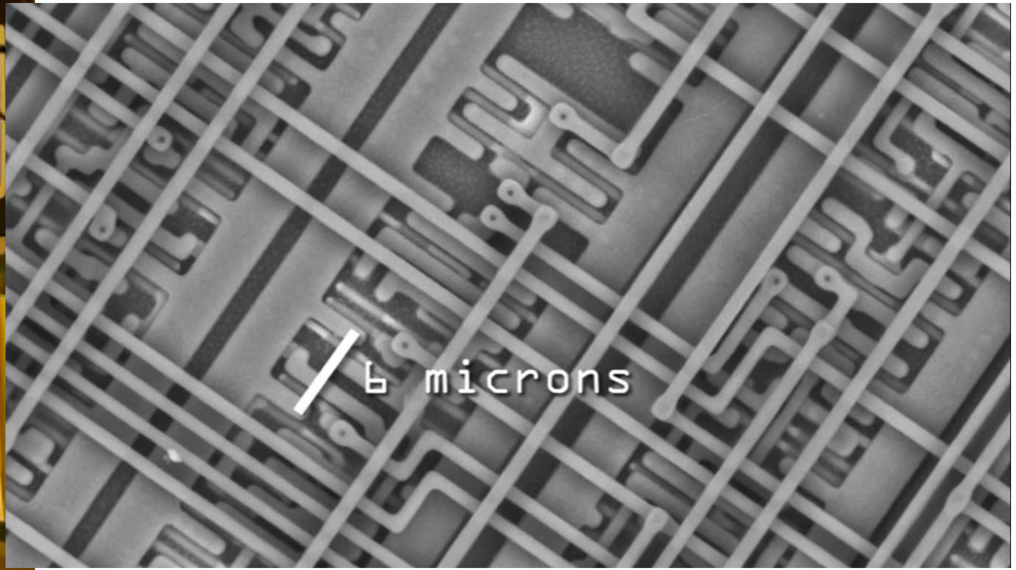


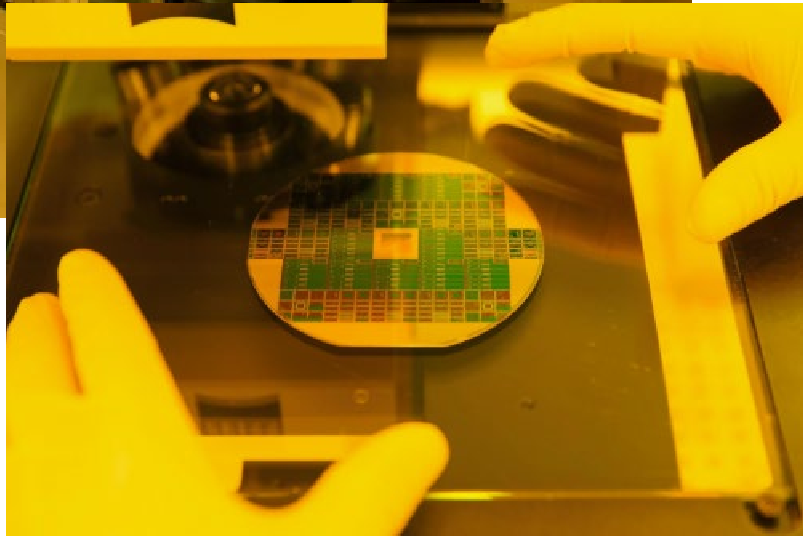
Reconfigurable multi-organ-on-a-chip (OoC): includes four, seven or ten different organ models that can interact with one another via microchannels

Leung et al., *Nature Reviews Methods Primers*, 2022

The first billion-dollar success of microfluidics

From the inkjet printer to bio-MEMS





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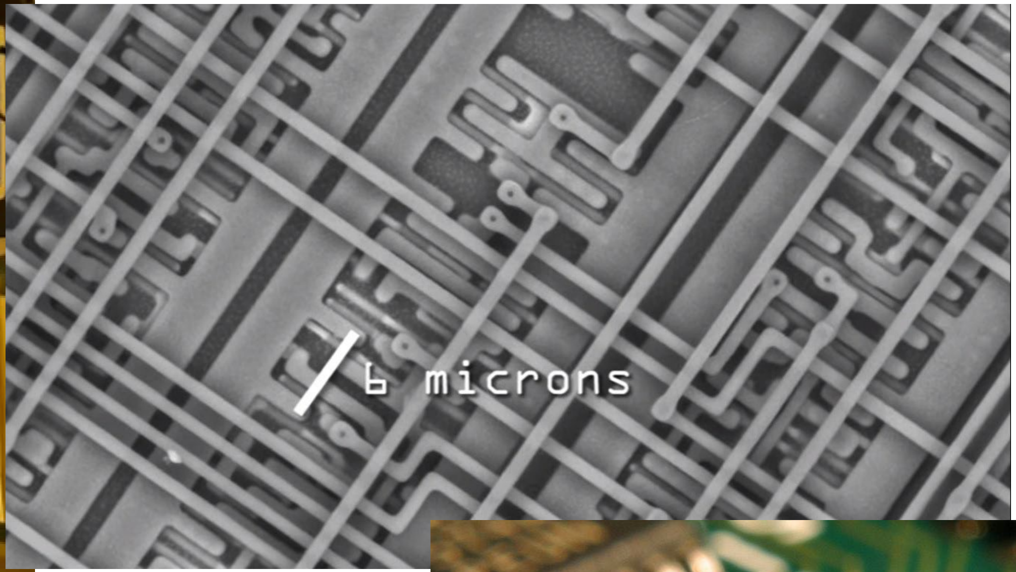

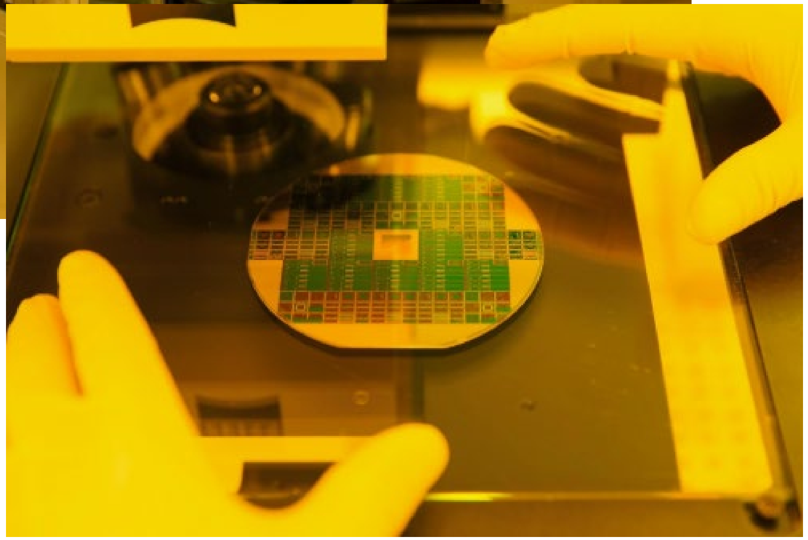

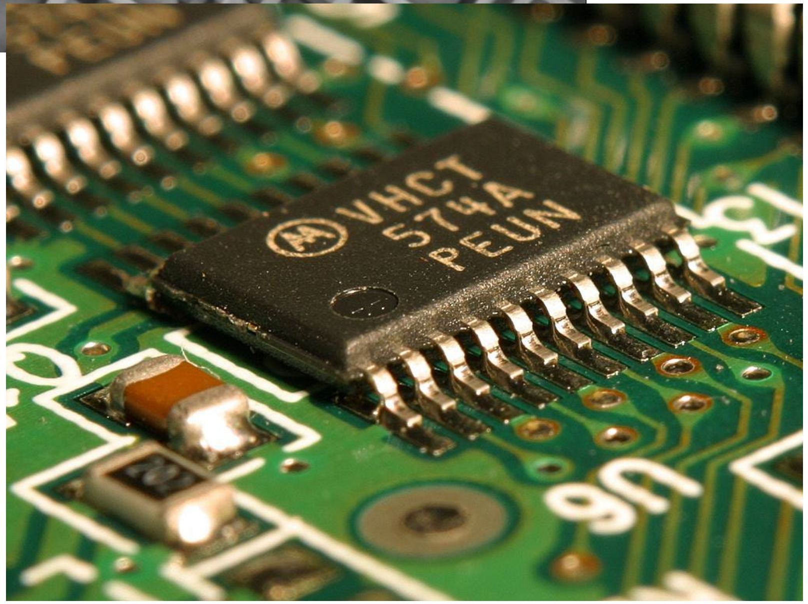

A Gas Chromatographic Air Analyzer Fabricated on a Silicon Wafer

STEPHEN C. TERRY, MEMBER, IEEE, JOHN H. JERMAN, AND JAMES B. ANGELL, FELLOW, IEEE

Abstract—A miniature gas analysis system has been built based on the principles of gas chromatography (GC). The major components are fabricated in silicon using photolithography and chemical etching techniques, which allows size reductions of nearly three orders of magnitude compared to conventional laboratory instruments. The chromatography system consists of a sample injection valve and a 1.5-m-long separating capillary column, which are fabricated on a substrate silicon wafer. The output thermal conductivity detector is separately batch fabricated and integrably mounted on the substrate wafer. The theory of gas chromatography has been used to optimize the performance of the sensor so that separations of gaseous hydrocarbon mixtures are performed in less than 10 s. The system is expected to find application in the areas of portable ambient air quality monitors, implanted biological experiments, and planetary probes.

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I. Introduction

THE VARIETY of transducers and sensors which have been fabricated in silicon has steadily increased as chemical etching and photolithographic techniques have been refined. This miniaturized gas analysis system has been developed as a result of the ability to fabricate complex three-dimensional structures in silicon, a process which has been labeled "micromachining." These micromachining techniques have been used to form a sample injection valve and separating capillary column on a single silicon substrate wafer. A thermal conductivity detector is separately batch fabricated using integrated circuit processing techniques, and is integrably mounted on the substrate wafer. The electrical output from the sensor is a result of both the gas chromatography process which takes place inside the etched silicon separating column and the action of the detector on the output gas stream.

Presently available miniature gas sensors lack the ability to

0018-9383/79/1200-1880$00.75

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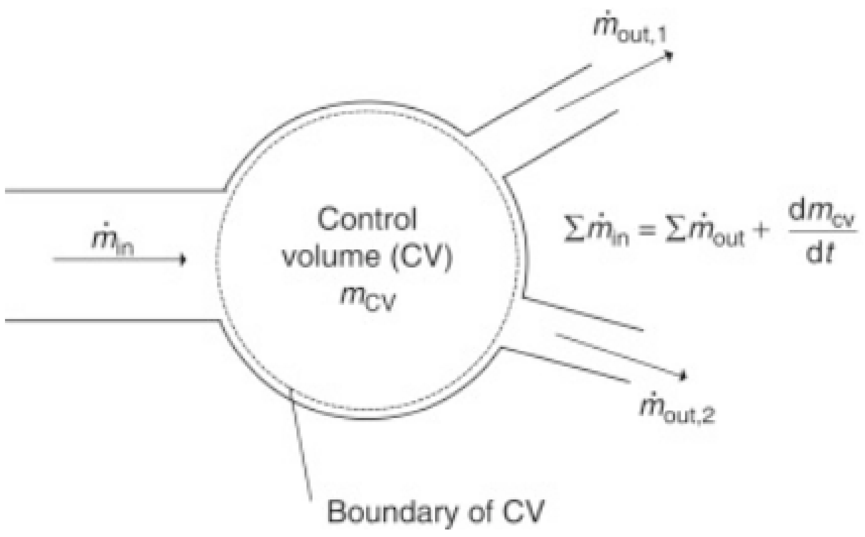
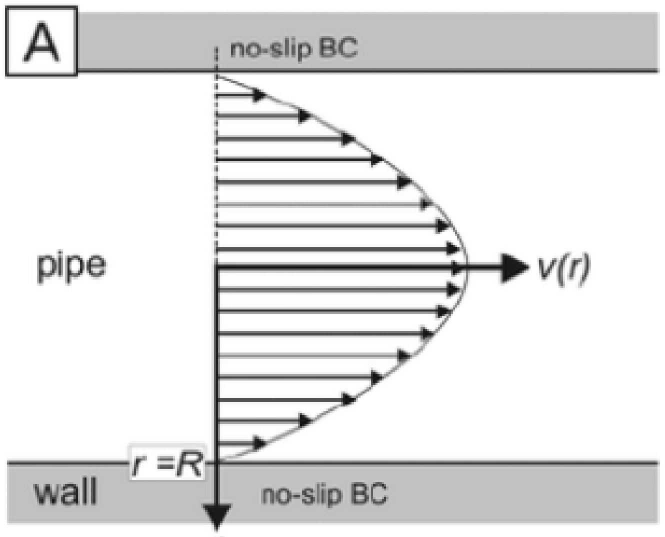
Basics of Fluid Mechanics

- Governing Laws:
  - Conservation of mass
  - Conservation of momentum



- Key Assumptions:
  - Incompressibility (for liquids)
  - No-slip boundary condition: The velocity of the fluid at a solid surface is zero.



No-slip Boundary Condition

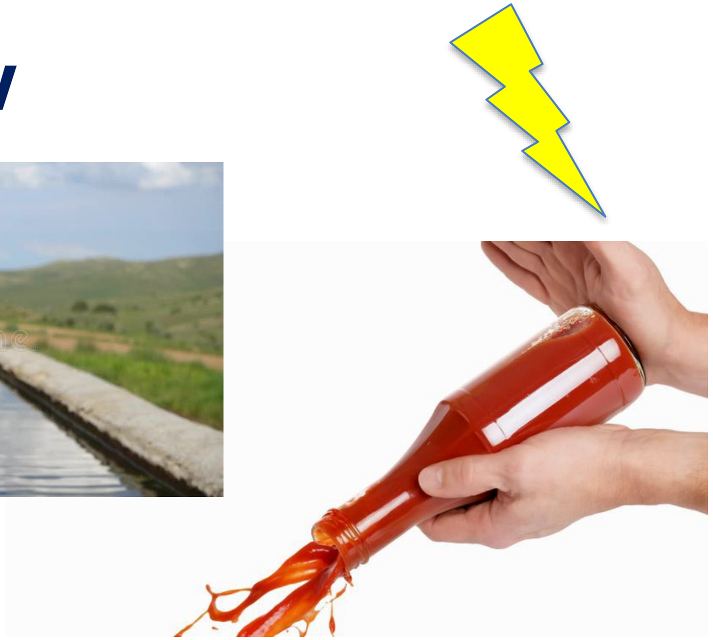
Viscosity

- Viscosity is a measure of internal friction (resistance) to flow

Substance	Viscosity (mPa·s)
Air	0.017
Acetone	0.3
Water	0.9
Mercury	1.5
Olive oil	80
Honey	2,000 - 10,000

Types of Fluids & Flow

Types of Fluids:



Newtonian: Viscosity is constant and independent of stress
Non-Newtonian: Viscosity changes with applied shear stress

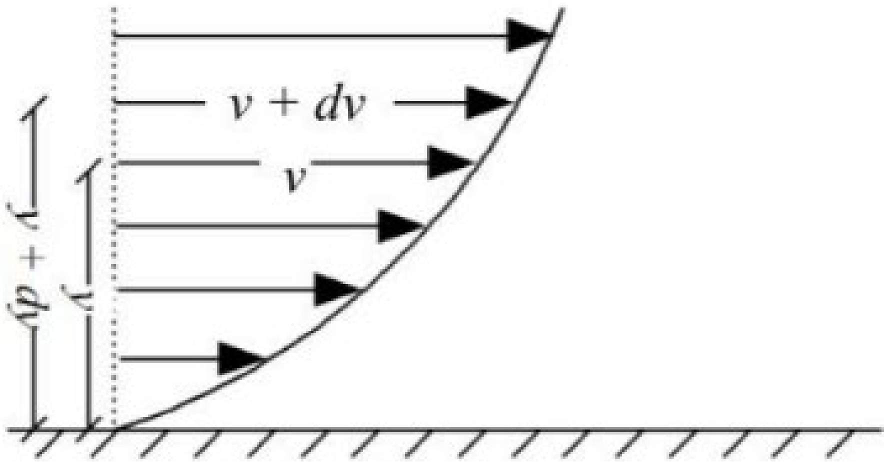
Types of Fluid Flow:

Laminar: Fluid particles move in smooth, parallel layers. Dominant in microfluidics.

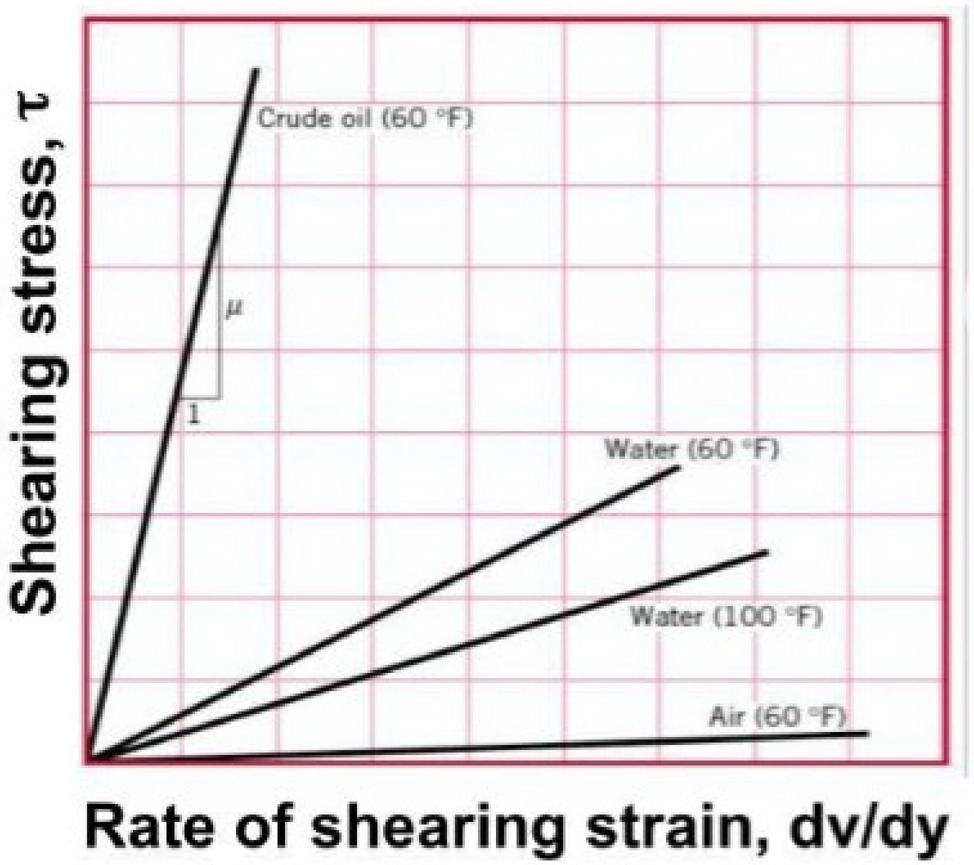
Turbulent: Fluid particles move in irregular, chaotic paths

Newtonian Fluids

- **Linear relationship between stress and strain**, i.e. viscosity is independent of stress and velocity

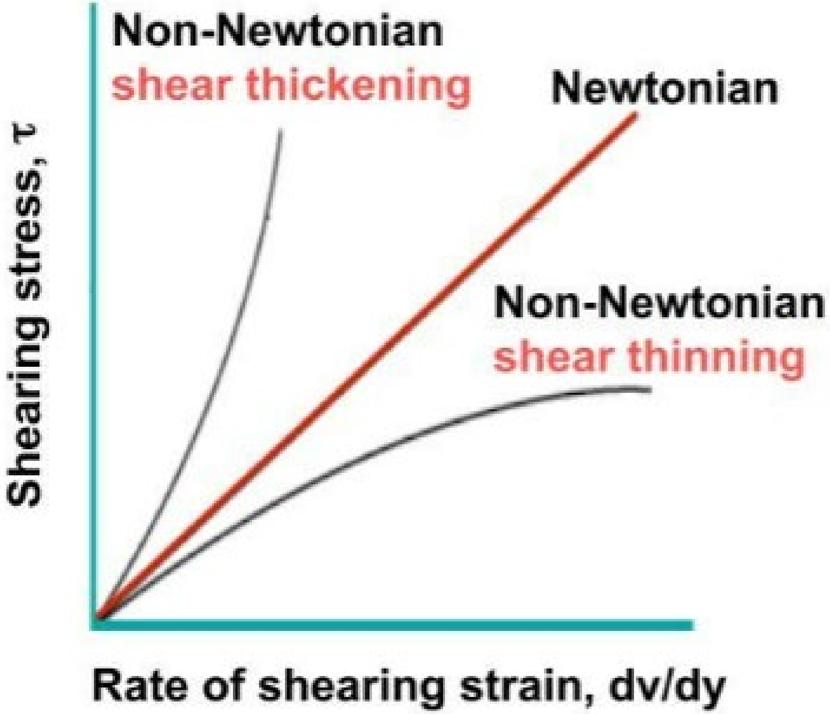


$$\tau = \mu \frac{dv}{dy}$$



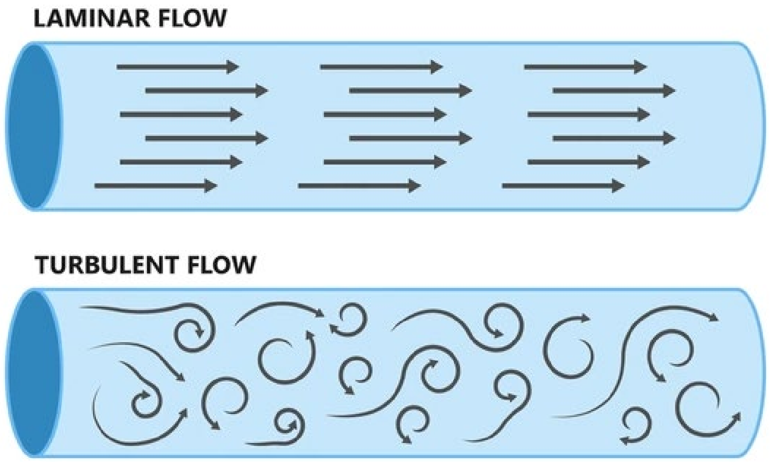
Non Newtonian Fluids

- **Non Linear relationship between stress and strain**, i.e. viscosity is dependent on stress and velocity



Laminar and Turbulent Flow

- **Laminar flow**:
  - Fluid particles move along smooth paths in layers
  - Most of energy losses are due to viscous effects
  - Viscous forces are the key players and inertial forces are negligible



- **Turbulent flow:**
  - An unsteady flow where fluid particles move along irregular paths
  - Inertial forces are the key players and viscous forces are negligible

Reynolds Number (Re)

- A dimensionless quantity that measures the ratio of inertial forces to viscous forces.

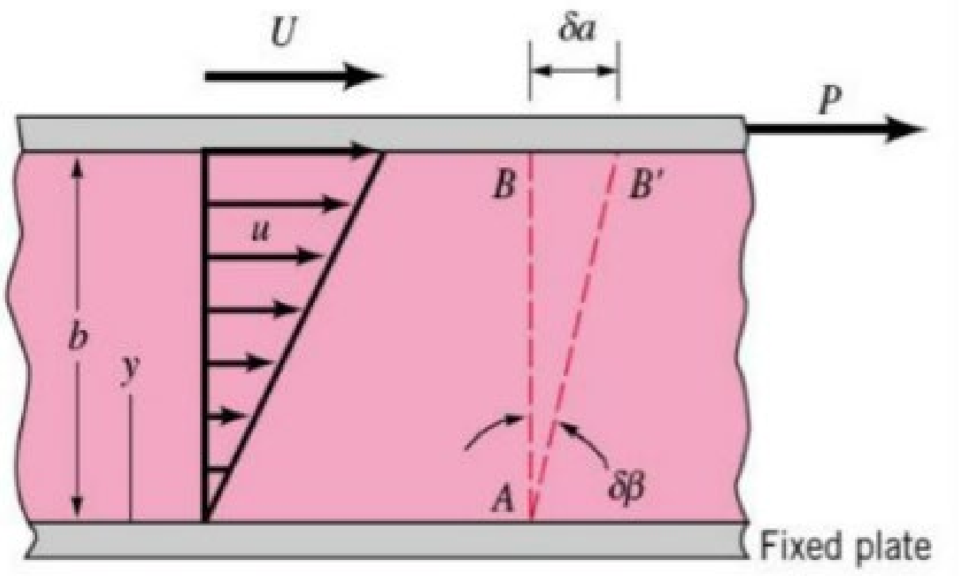
- Predicts flow patterns:
  - Re < 2000: Typically laminar flow.
  - Re > 2000: Typically turbulent flow.

- In microfluidic systems, due to the small channel dimensions (L), Re is typically < 1, meaning flow is always laminar.

$$Re = \frac{\rho v L}{\mu} \quad \text{where } L = \frac{4A}{P}$$

ρ	Density of the fluid
v	Mean fluid velocity
L	Characteristic length (hydraulic diameter)
μ	Dynamic viscosity
A	Cross-sectional area of the flow
P	Wetted perimeter

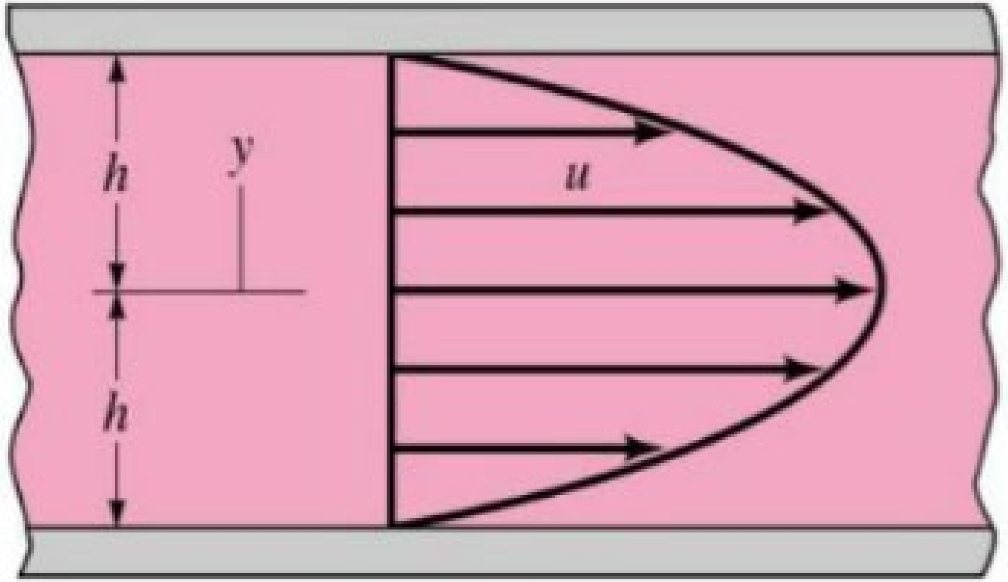
Couette Flow (laminar)



- One of the plates moves parallel to the other
- Steady flow between plates
- Obeys the no-slip condition at the channel walls.

Pressure-Driven Flow (Poiseuille Flow)

- Flow generated by a pressure difference between the inlet and outlet.
- Obeys the no-slip condition at the channel walls.
- Results in a characteristic parabolic velocity profile, with maximum velocity at the center of the channel and zero velocity at the walls.



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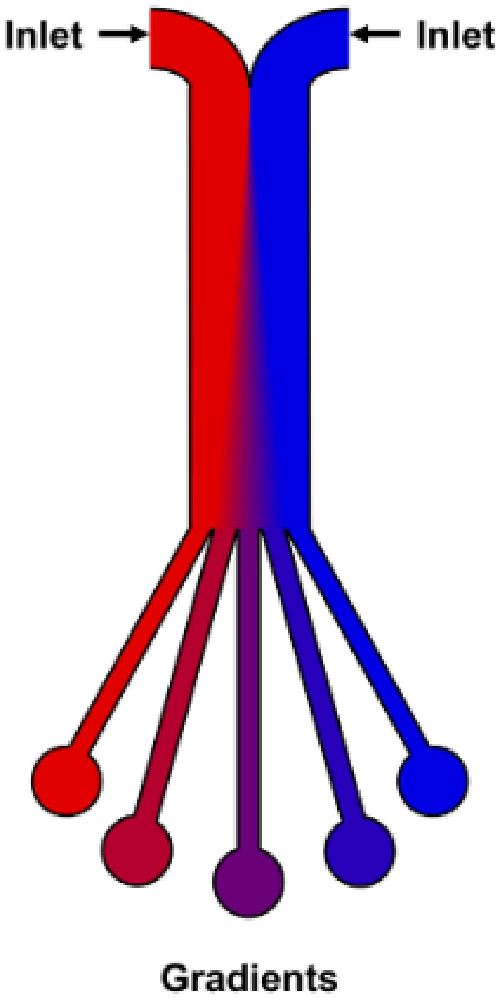
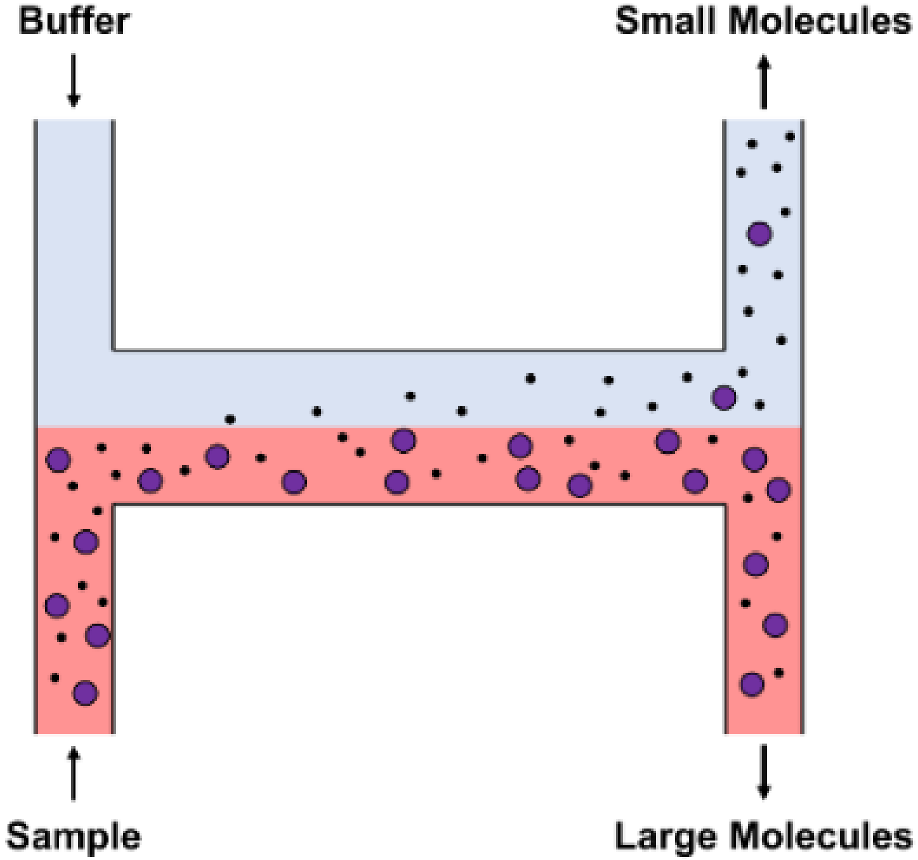
Special Phenomena: Laminar Flow

Gradient Generator



H-Channel Filter

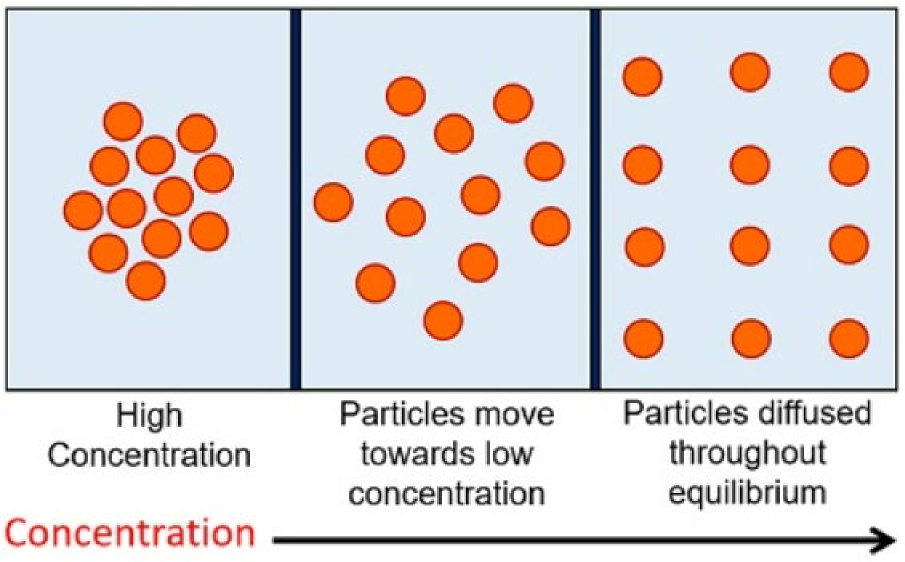


Special Phenomena: Diffusion and Mixing

- Diffusion is the transport of particles from a region of higher concentration to one of lower concentration by random motion.

$$X = \sqrt{2Dt}$$

- X: diffusion length
- D: diffusion constant
- t: time



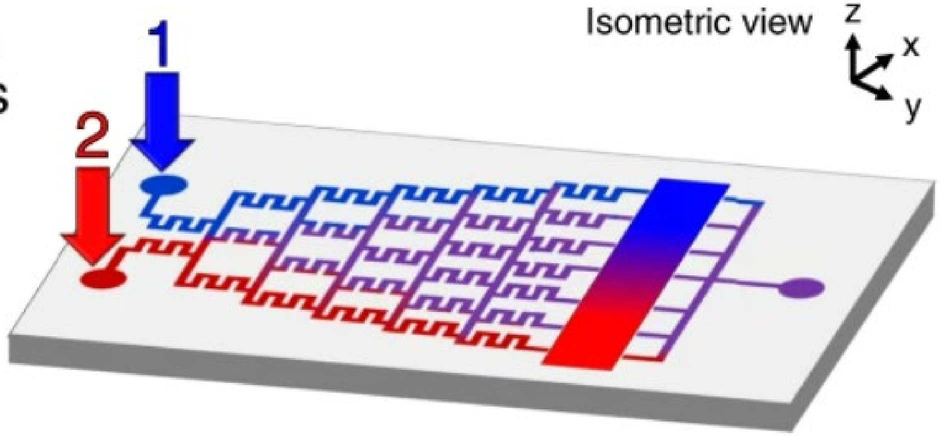
- For an antibody, $D \approx 40\ \mu m^2\ s^{-1}$
- For urea, $D \approx 1400\ \mu m^2\ s^{-1}$
- For $X = 100\ \mu m$, the time becomes: Antibody: 125 s; Urea: 3.6 s

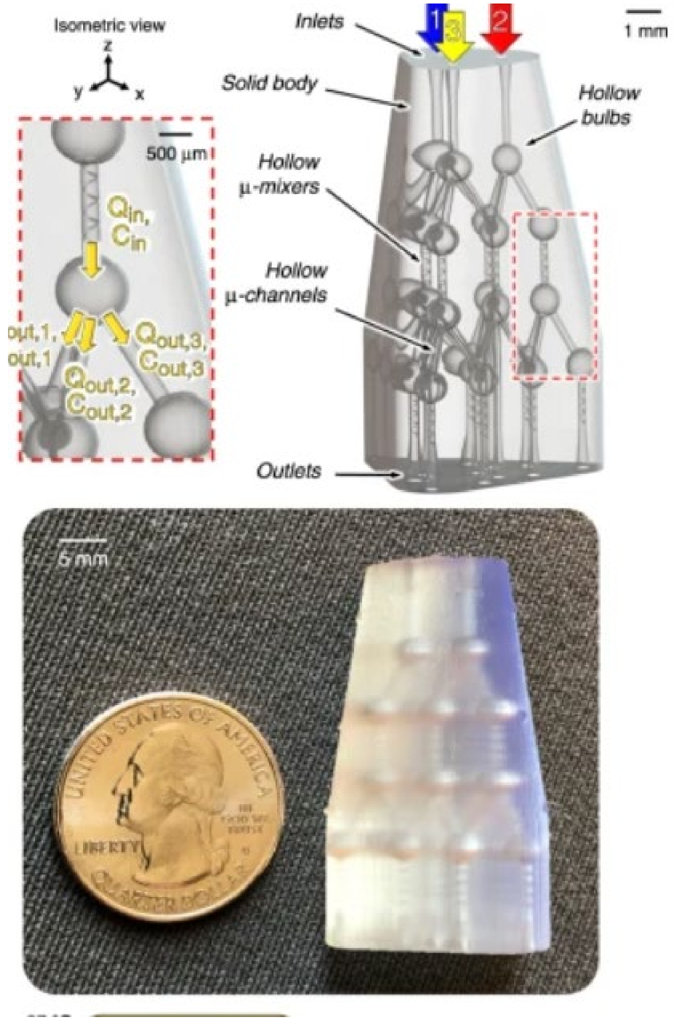
Application: Generating Biochemical Gradients

- Laminar flow and diffusion can be used to create stable, continuous concentration gradients.
- This is achieved by designing channel networks that repeatedly split, combine, and lengthen the path of different fluid streams.
- These gradients are valuable for cell culture experiments, such as studying cell migration or chemotaxis.

Generating chemical gradients

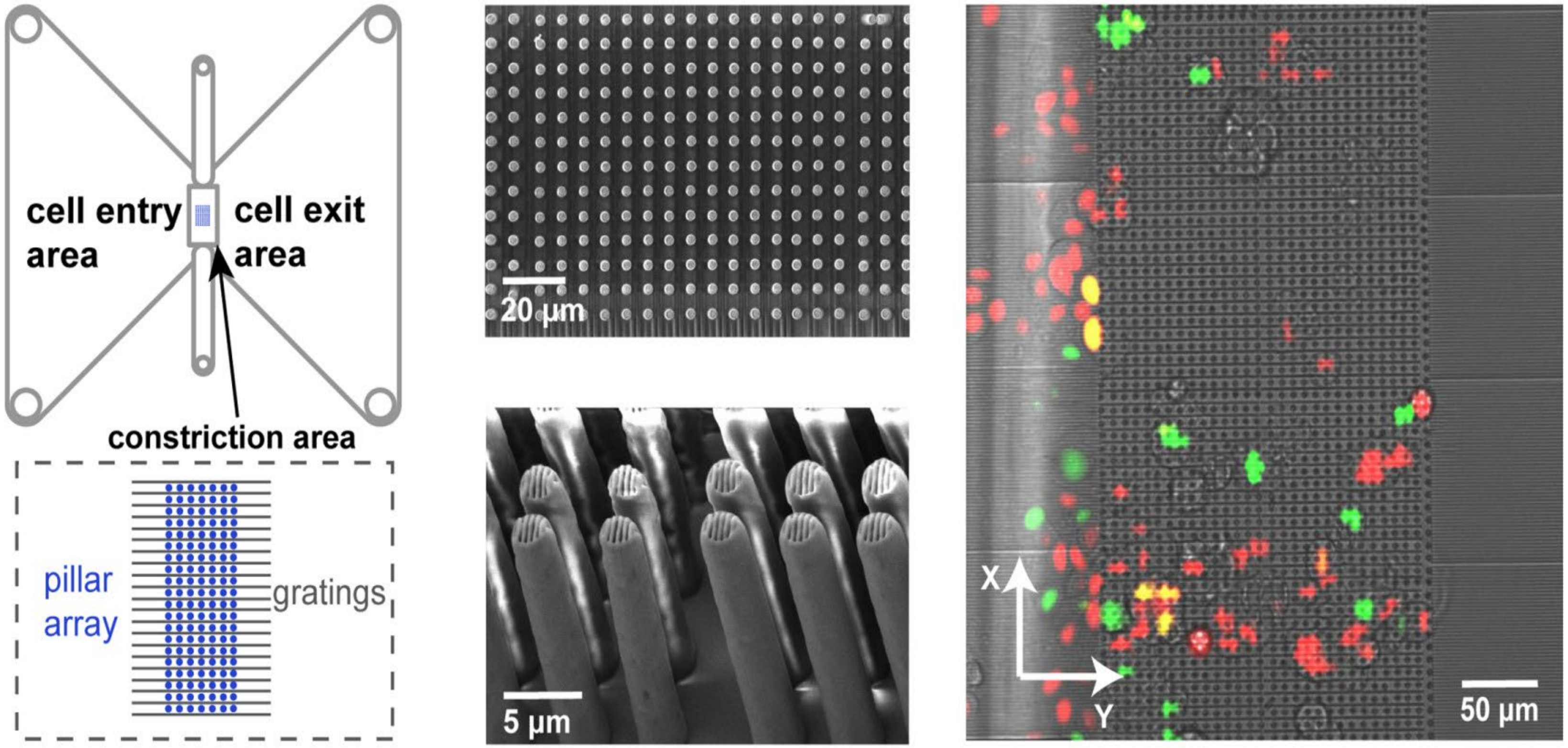
Two fluid input, planar µ-fluidics





Sweet et al. Microsystems & Nanoengineering (2020) 6:92

Studying chemotaxis



Panagiotakopoulou, M et al. *MBoC 2018*

Corallino,S, **[...]** Panagiotakopoulou, M et al. *Nat Commun 2018*

Special Phenomena: Capillary Action

- The movement of liquid within the spaces of a porous material or narrow tube due to the forces of adhesion, cohesion, and surface tension.

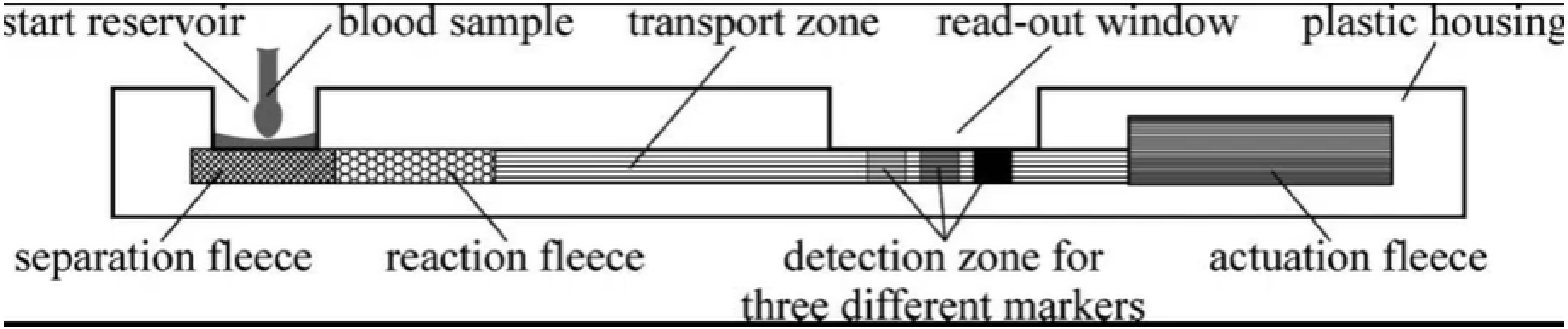
- This phenomenon allows for 'pumpless' flow in microfluidic devices.

The second billion dollar success of microfluidics

Test Strips or Lateral Flow Assays

Glucose strips: 2B dollar market

How do lateral flow assays work



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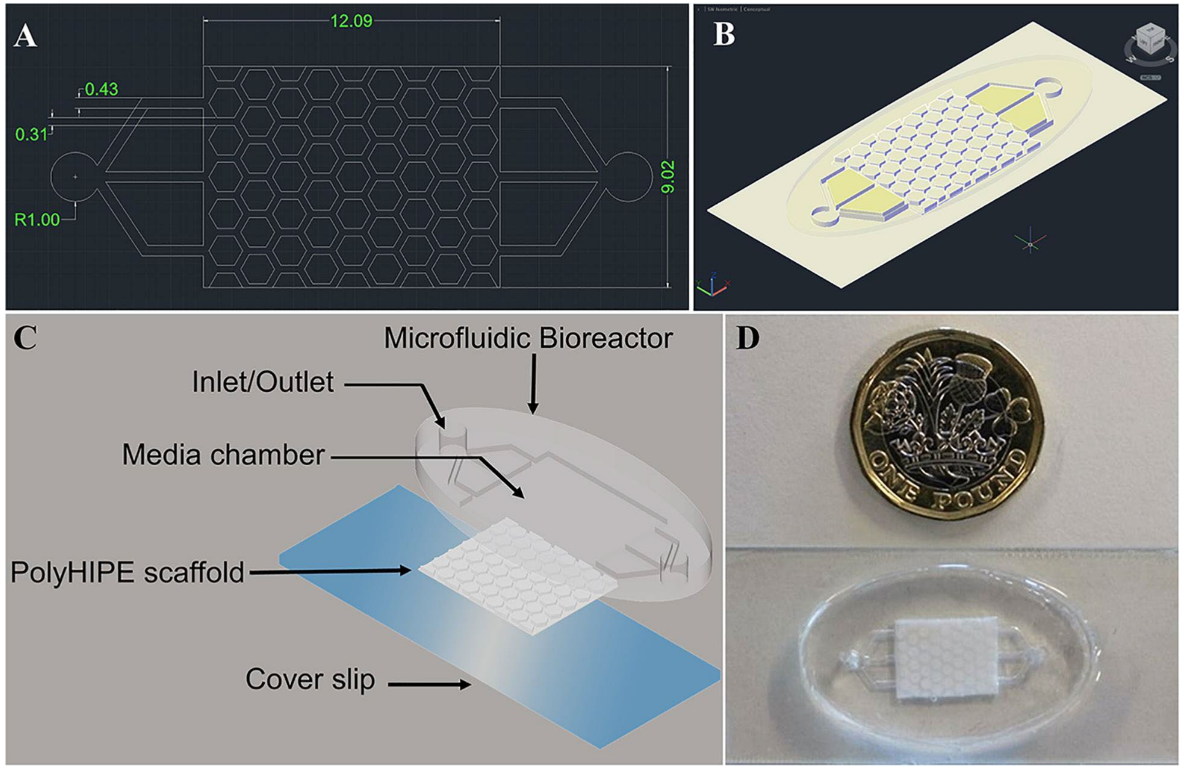
Lab on a Chip

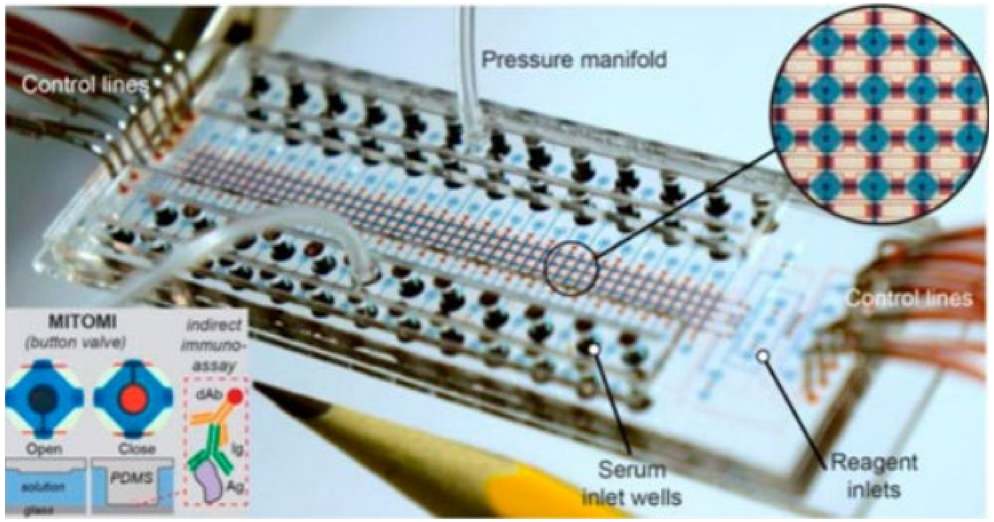
- Integrates multiple laboratory functions onto a single chip.
- Enables parallelization and high-throughput experimentation.



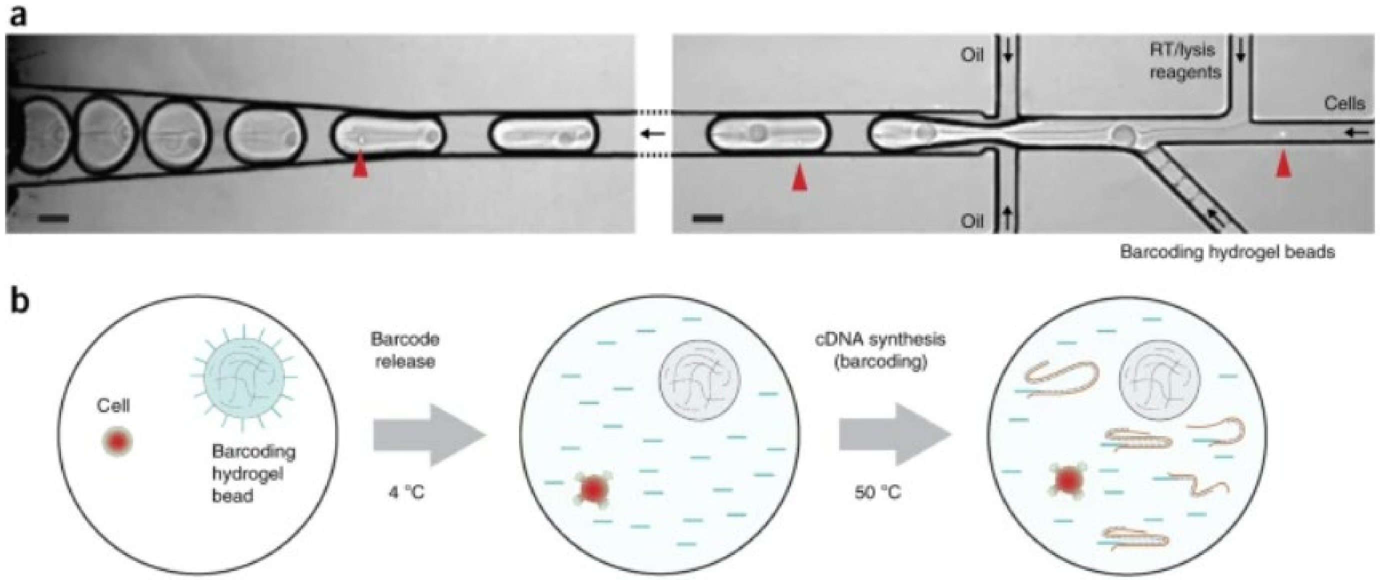
Applications Showcase

- **Immunoassays**: Micromosaic immunoassays (like ELISA) can be miniaturized for high-throughput, low-volume analysis of proteins.

- **Droplet-Based Microfluidics:** Generates thousands of individual picoliter-volume droplets that act as separate micro-reactors for single-cell analysis or high-throughput screening.



Rodriguez-Moncayo et al., 2021

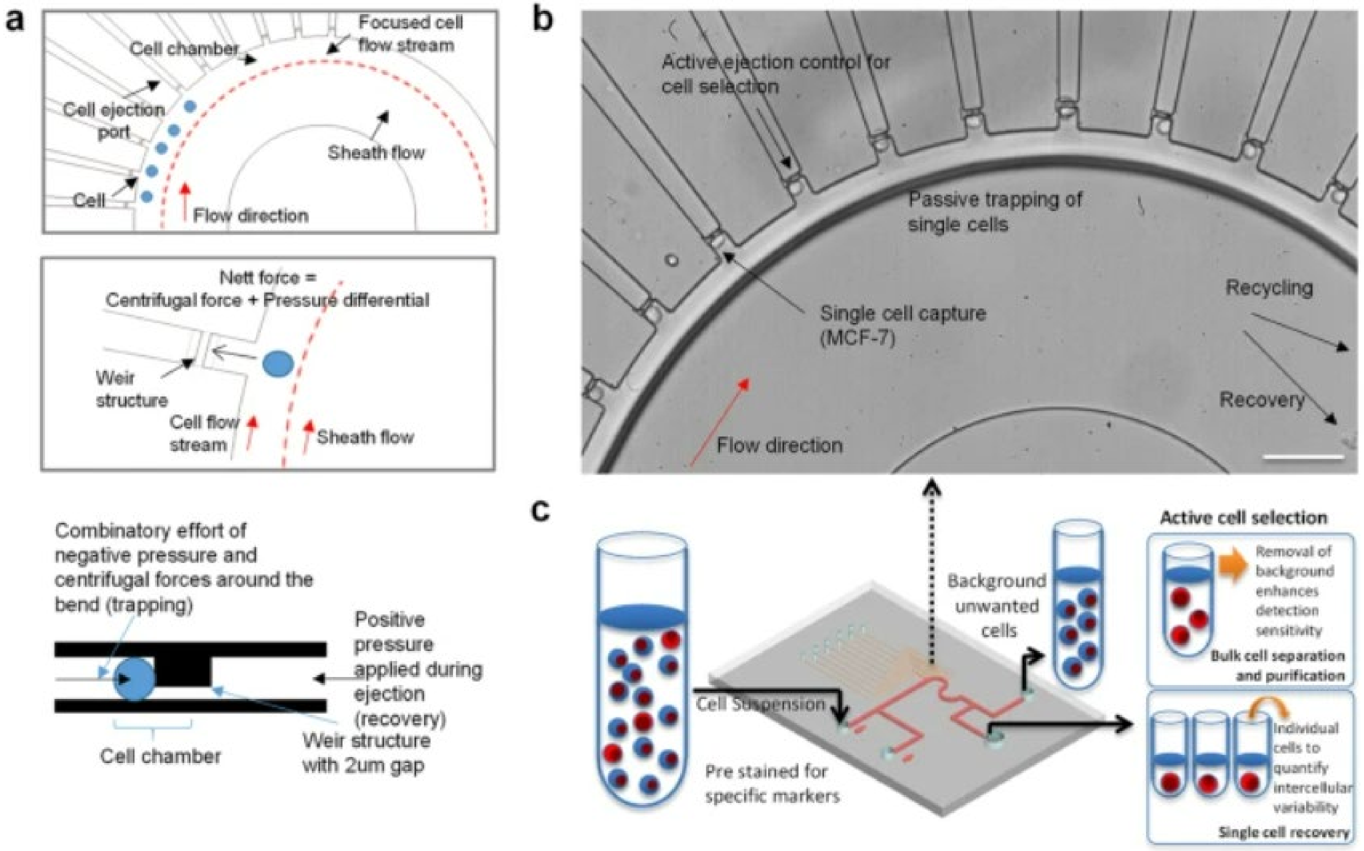


Zilionis et al., *Nature Protocols*, 2017

Applications Showcase

- **Rare Cell Isolation:** Devices can be functionalized to capture rare cells, such as circulating tumor cells (CTCs), from blood for diagnostics.

Figure 1: Demonstration of microfluidic single cell capture and recovery.



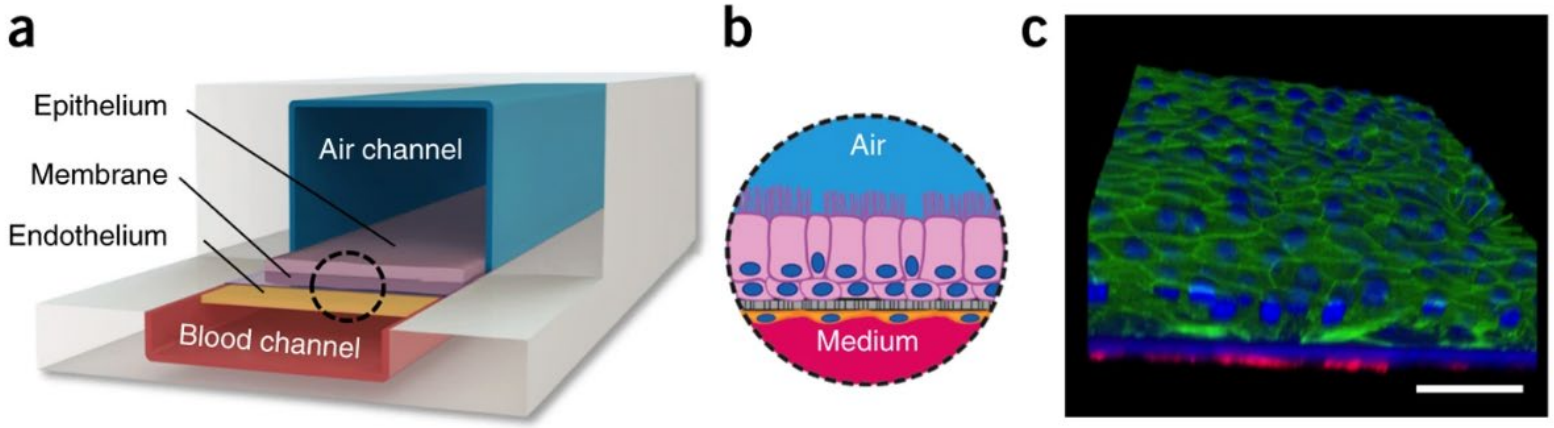
Yeo et al., *Scientific Reports*, 2016

Applications Showcase

- **Organs-on-Chips:** Recreate the physiological environment of human organs to study organ function and disease in vitro.

Figure 1: The human small airway-on-a-chip.

From: Small airway-on-a-chip enables analysis of human lung inflammation and drug responses *in vitro*



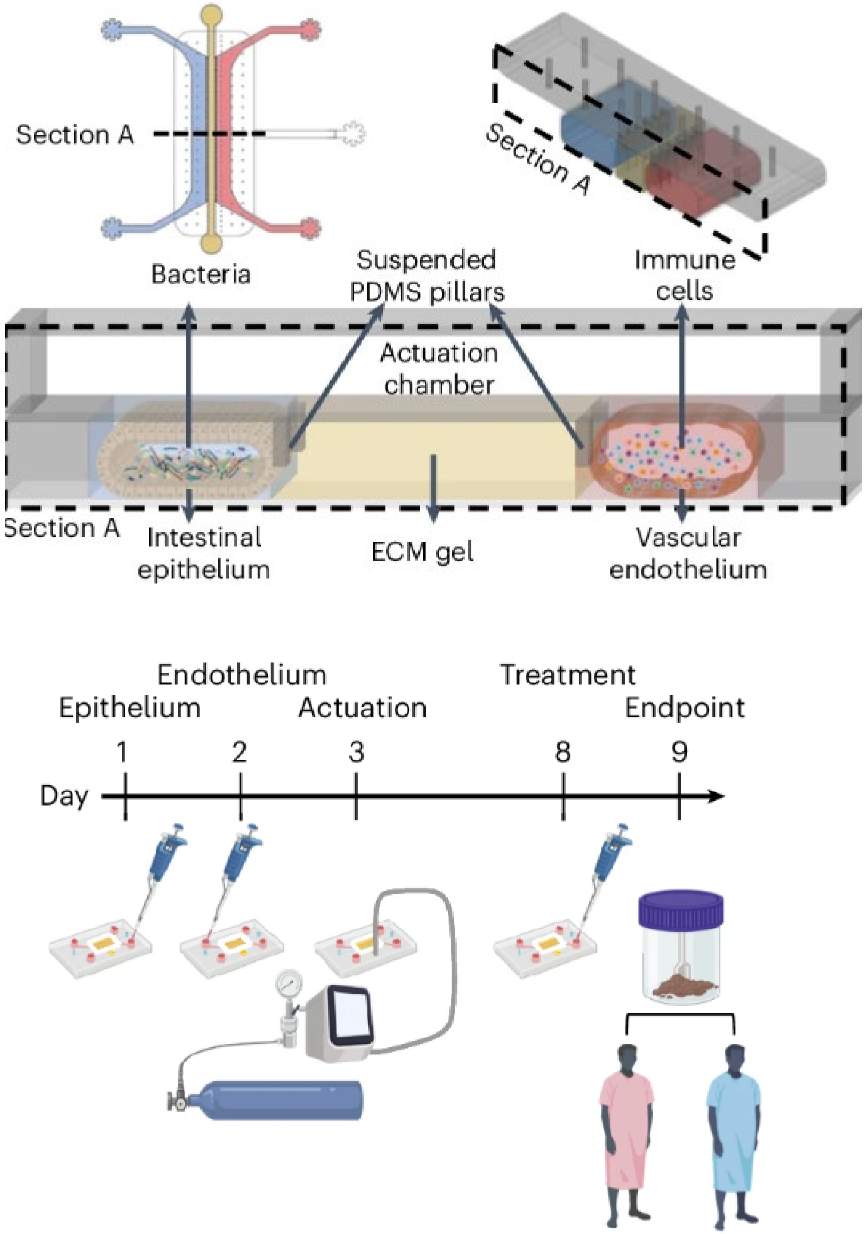
Benam et al., *Nature Methods*, 2016

Gut on a chip

Article | Open access | Published: 12 February 2025

A gut-on-a-chip incorporating human faecal samples and peristalsis predicts responses to immune checkpoint inhibitors for melanoma

- Gut microbiome shapes response to immune checkpoint inhibitors (ICIs).
- Mouse models lack human relevance.
- Gut-on-a-chip with human organoids and fecal microbiome mimics gut physiology.
- Gut-on-a-chip predicts patient-specific ICI responses.
- Gut-on-a-chip identifies microbial and epithelial biomarkers linked to outcomes.



Ballerini et al., *Nature Biomedical Engineering*, 2025

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Technical Challenges

1. Sample–Chip Interface:
    1. Sample variability
    2. Sample preparation bottleneck
    3. Volume control

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    2. Mixing limitations
    3. Clogging and fouling

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3. On-Chip Detection and Readout
    1. Miniaturizing detection modalities
    2. Signal amplification and noise reduction

Technical Challenges & Regulatory Challenges

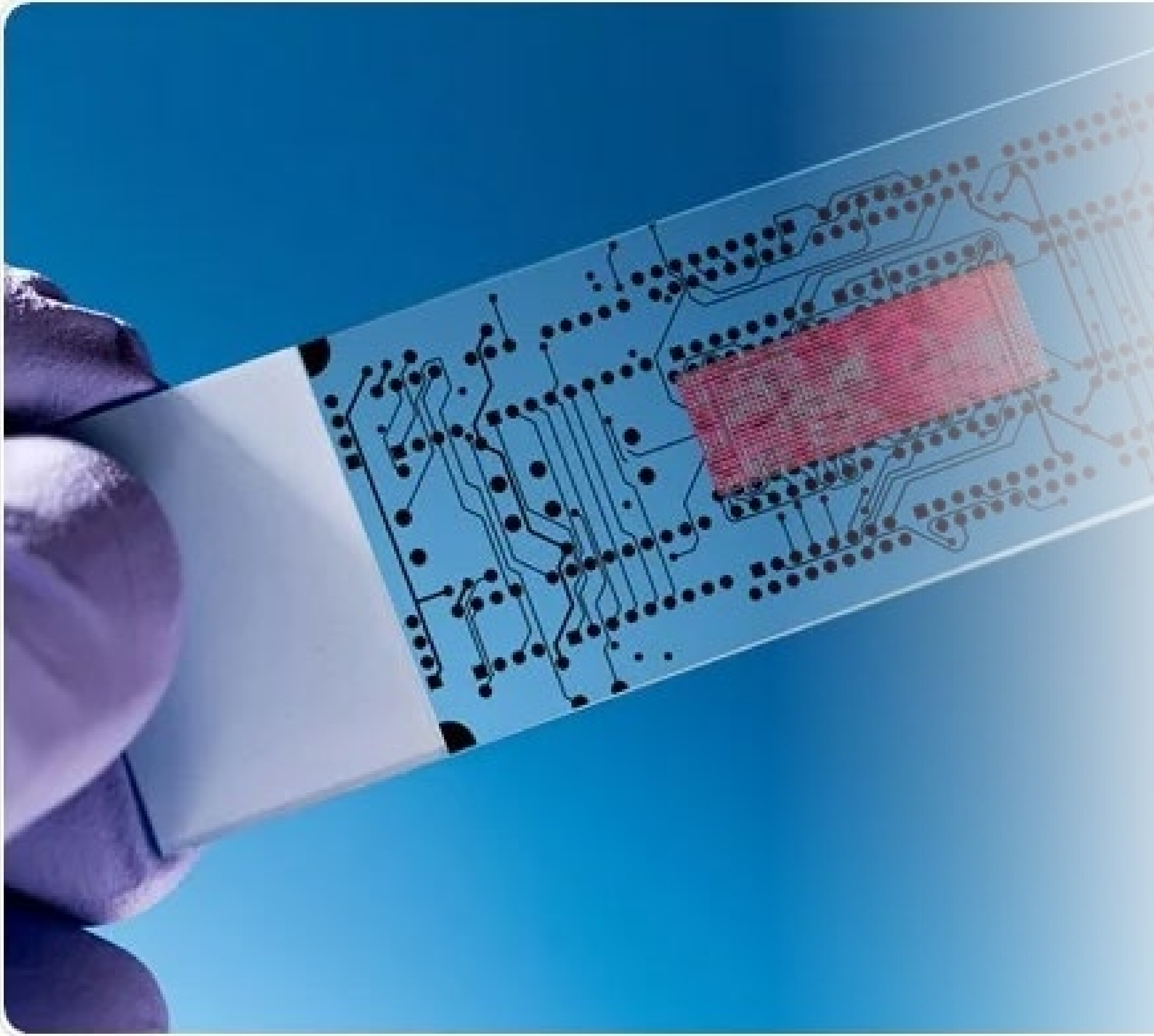
- Manufacturing Challenges
  - Material compatibility
  - Packaging and long-term stability

- Validation and Regulatory Hurdles
  - LoC systems must prove accuracy, reproducibility, and robustness under clinical or field conditions.

Other Commercialization Challenges

1. High Development Costs and Long Timelines
2. Market Fragmentation (a different chip disease)

3. **This** person



The end ☺

- Thank you for your attention!
- Questions and paper discussion

Surface Energy & Wettability

- Surface Tension: A result of cohesive forces between liquid molecules. Molecules at the surface experience a net inward pull, minimizing the surface area.
- Wettability: The ability of a liquid to maintain contact with a solid surface, resulting from the balance between adhesive (liquid-solid) and cohesive (liquid-liquid) forces.
- Contact Angle (θ): Measures wettability.
- Hydrophilic ($\theta<90°$): 'Water-loving.' Liquid spreads out.
- Hydrophobic ($\theta>90°$): 'Water-fearing.' Liquid beads up.