Biosensors

B. Tech.

Course No.: EEL 3050

L-T-P [C]: 3–0–2 [4]

Prof. AJAY AGARWAL

ELECTRICAL ENGINEERING

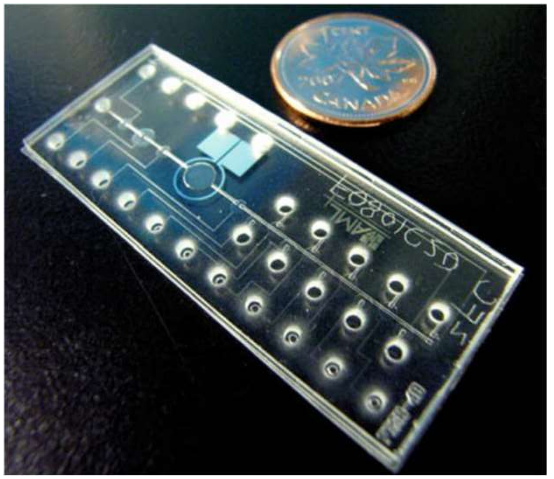
IIT JODHPUR

Lecture 26 dated 23rd Oct. 2024

Lab-on-a-Chip Biosensors:

- A lab-on-a-chip (LOC) is a device that integrates several laboratory functions onto a **small platform**, typically only millimeters or centimeters in size.
- It is mainly a **network** of channels & wells that are etched onto silicon or polymer substrates to build **miniature laboratories**

- LOCs normally handle
  - very small fluid volumes, i.e. in µL or nL &
  - Are of very small depth & width of **channels**, <1 mm, i.e., **in µm** scale.
- Pressure or electrokinetic **forces** move small volumes of liquid in a finely controlled manner through the channels.



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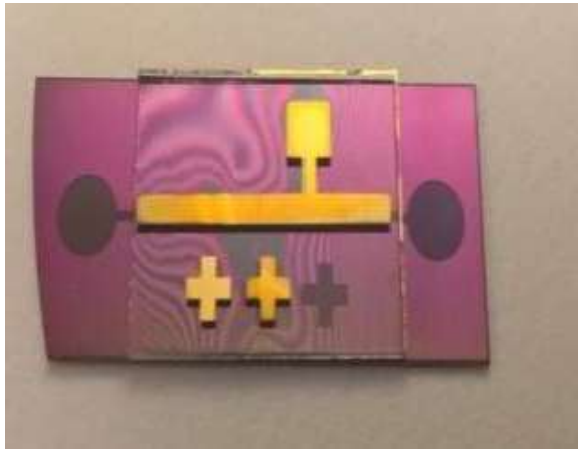
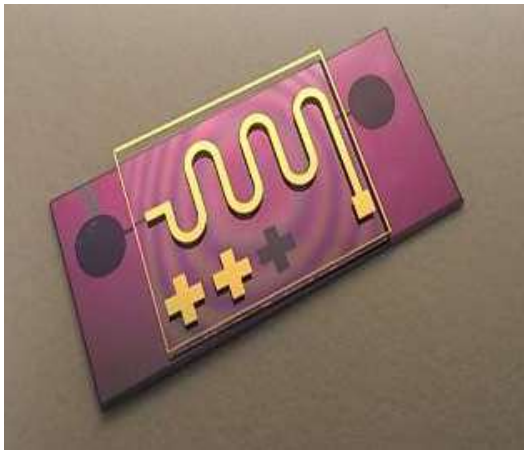
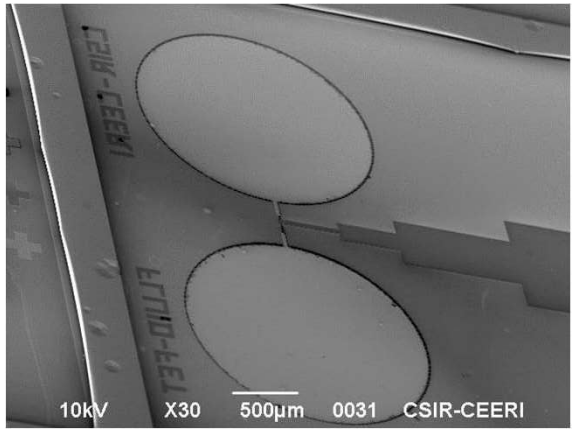
Microfluidics Platforms

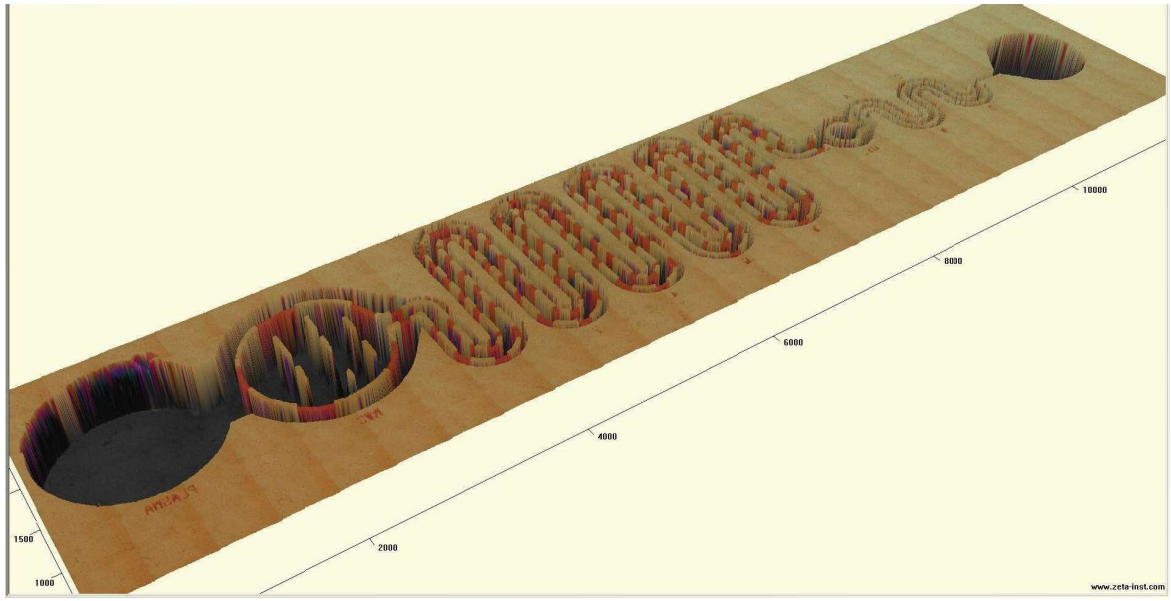




Micro-Viscometer



Fluid FET



Lab-on-a-Chip (LOC) for *Particles Separation & Counter*

Ajay Agarwal and Balyan Prerna, Indian Patent No. 2592/DEL/2013, May 06, 2016

Filtration of Blood cells

- Separation of WBCs and RBCs from blood.
- Most of the WBCs were retained in the WBC separation and collection region, however some cells tends to escape due to deformable nature of the cells.

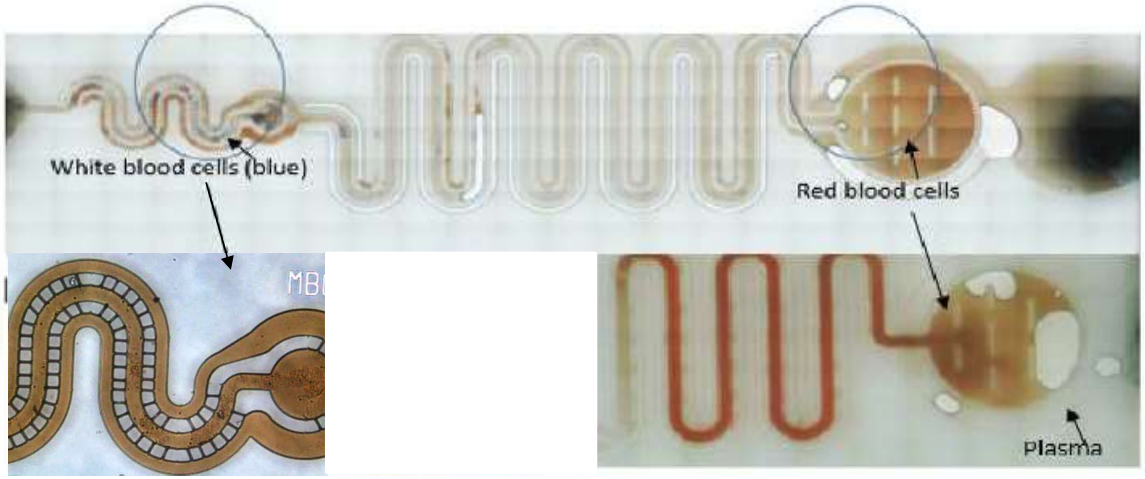
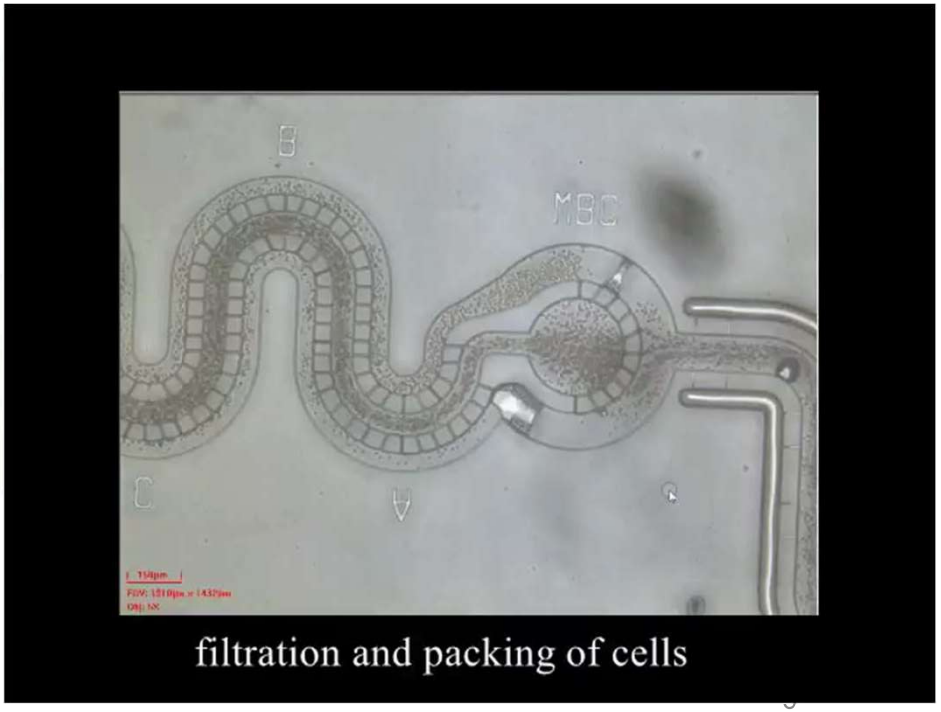
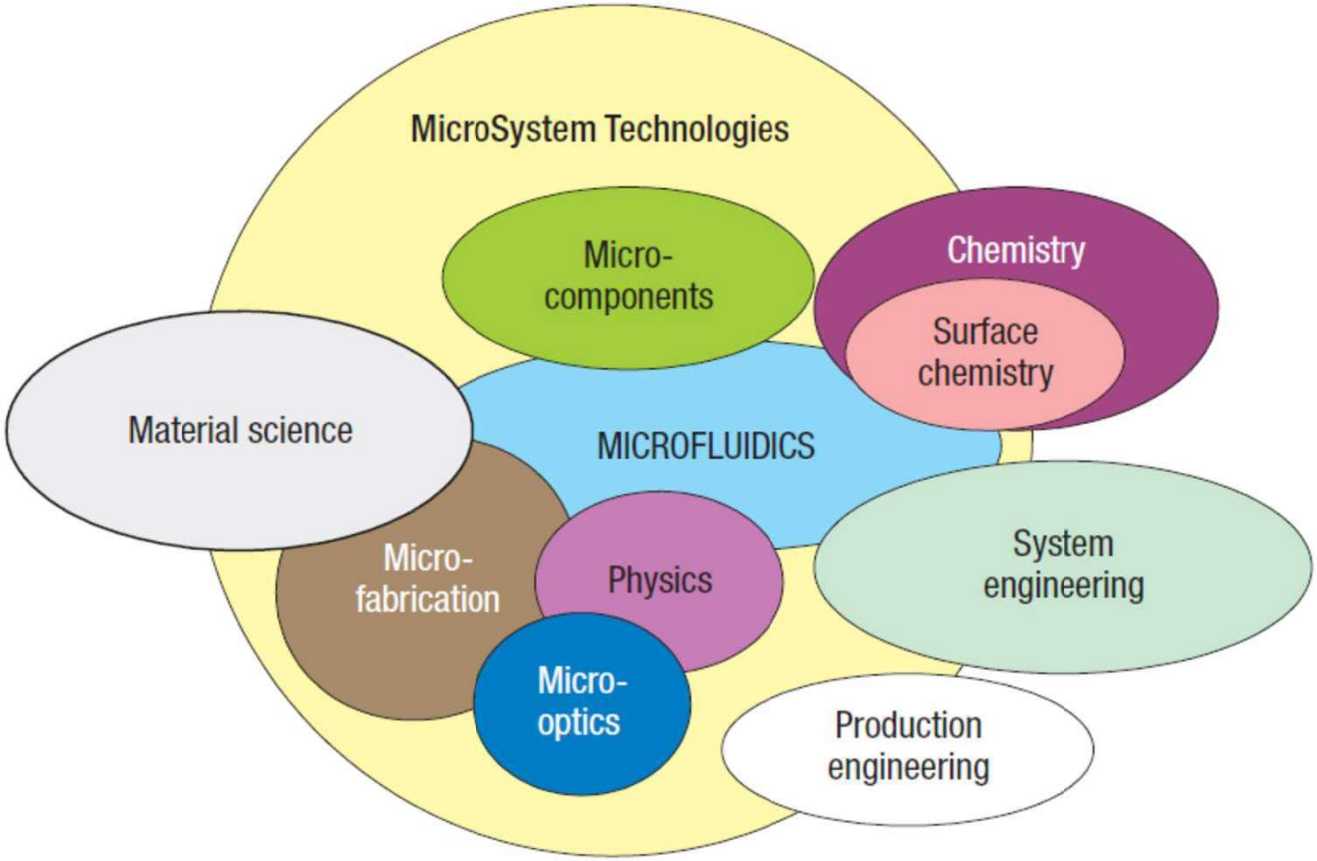


Figure: Separation of blood cells



Microfluidics is interdisciplinary

- related with various Science & Engineering areas



- Microfluidics deals with the manipulation/ control of fluids in μm scale.
- LOCs are also referred to as microfluidic devices or microfluidic chips.
- On a single integrated system, LOC enables sample
  - **handling**, mixing, **dilution**,
  - electrophoresis & chromatographic separation,
  - **staining**, & detection

- Electrophoresis separates components by their rate of migration in an electric field. It is often used to separate macromolecules like proteins, DNA, & RNA based on their charge, size, or binding affinity
- Chromatography separates components by how they distribute between a stationary phase & a mobile phase. The **mixture** is dissolved in a solvent & carried through a system with a fixed material. The components separate because they have **different** affinities for the stationary phase & are retained for different lengths of time.

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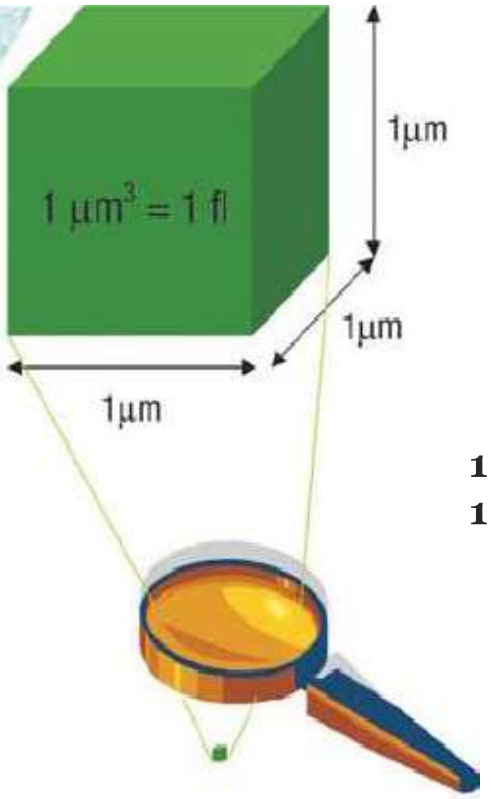
Lab-on-a-Chip Biosensors:

The main advantages of the LOC are:

- ease of use,
- speed of analysis,
- low sample & reagent consumption, and
- high reproducibility due to standardization & automation.

Downscaling of volumes

Litres	l	1
Decilitres	dl	10^{-1}
Centilitres	cl	10^{-2}
Millilitres	ml	10^{-3}
Microlitres	**µl**	**10^{-6}**
Nanolitres	**nl**	**10^{-9}**
Picolitres	**pl**	**10^{-12}**
Femtolitres	**fl**	**10^{-15}**
Attolitres	al	10^{-18}



1 m³ = 1000 L
1 cm³ = 1 mL

Micro to Nano Fluidics

- When fluids flow in nano-scale, the flow in non-continuous
- Nanofluids are dispersions of nanomaterials in base fluids
  - nanoparticles, nanofibers, nanotubes, nanowires, nanorods, nanosheet, or droplets.
- Nanofluids have some unique features that are quite different from dispersions of mm or μm sized particles.
- Compared to conventional cooling liquids such as water, kerosene, ethylene glycol and microfluids, nanofluids have been shown to exhibit higher thermal conductivities.
- Nanofluids do not block flow channels and induces only a very small pressure drop during flow - beneficial for heat transfer applications

Applications of nanofluids:

(a) heat transfer,

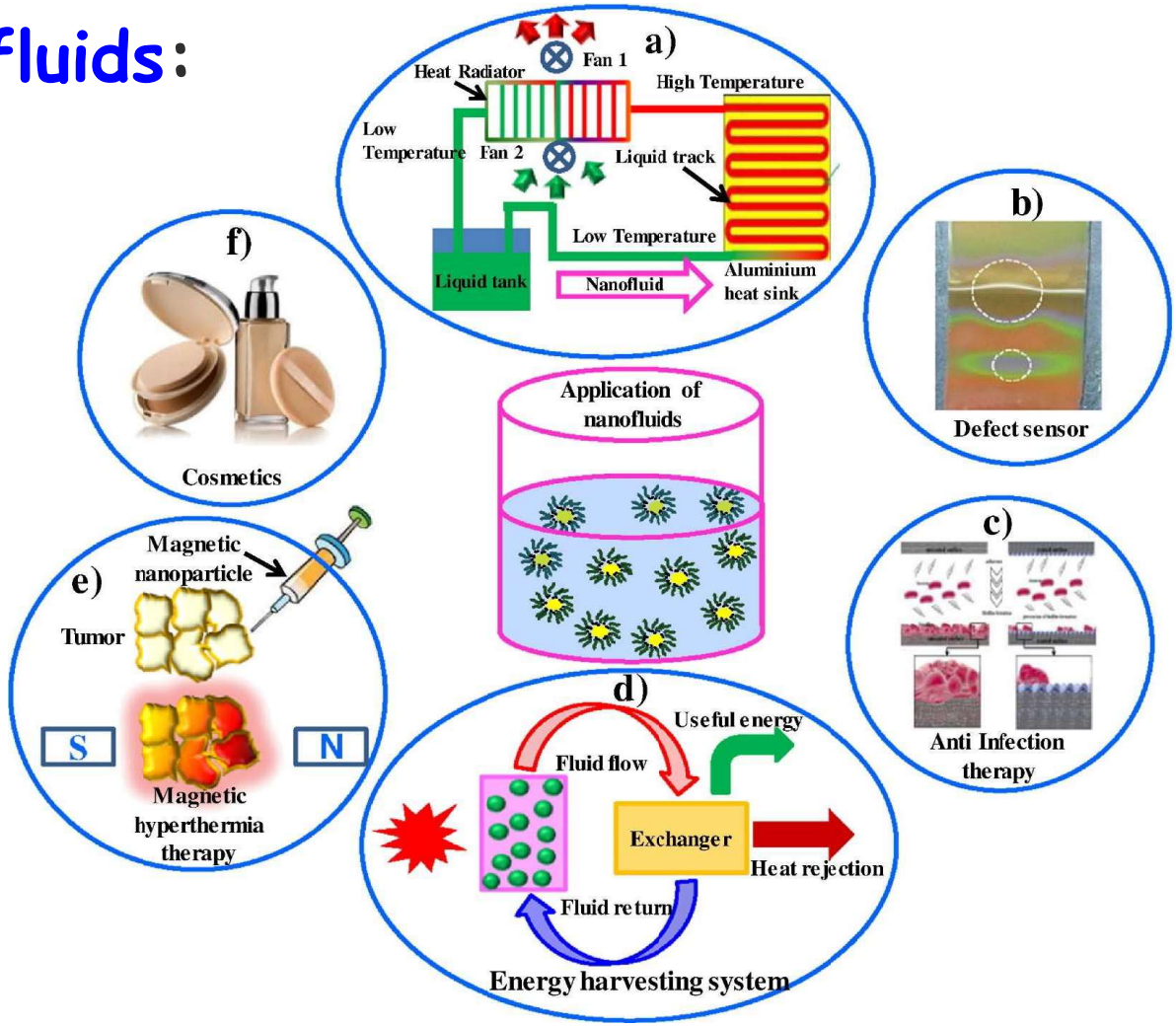
(b) defect sensors,

(c) anti infection therapy,

(d) energy harvesting system ,

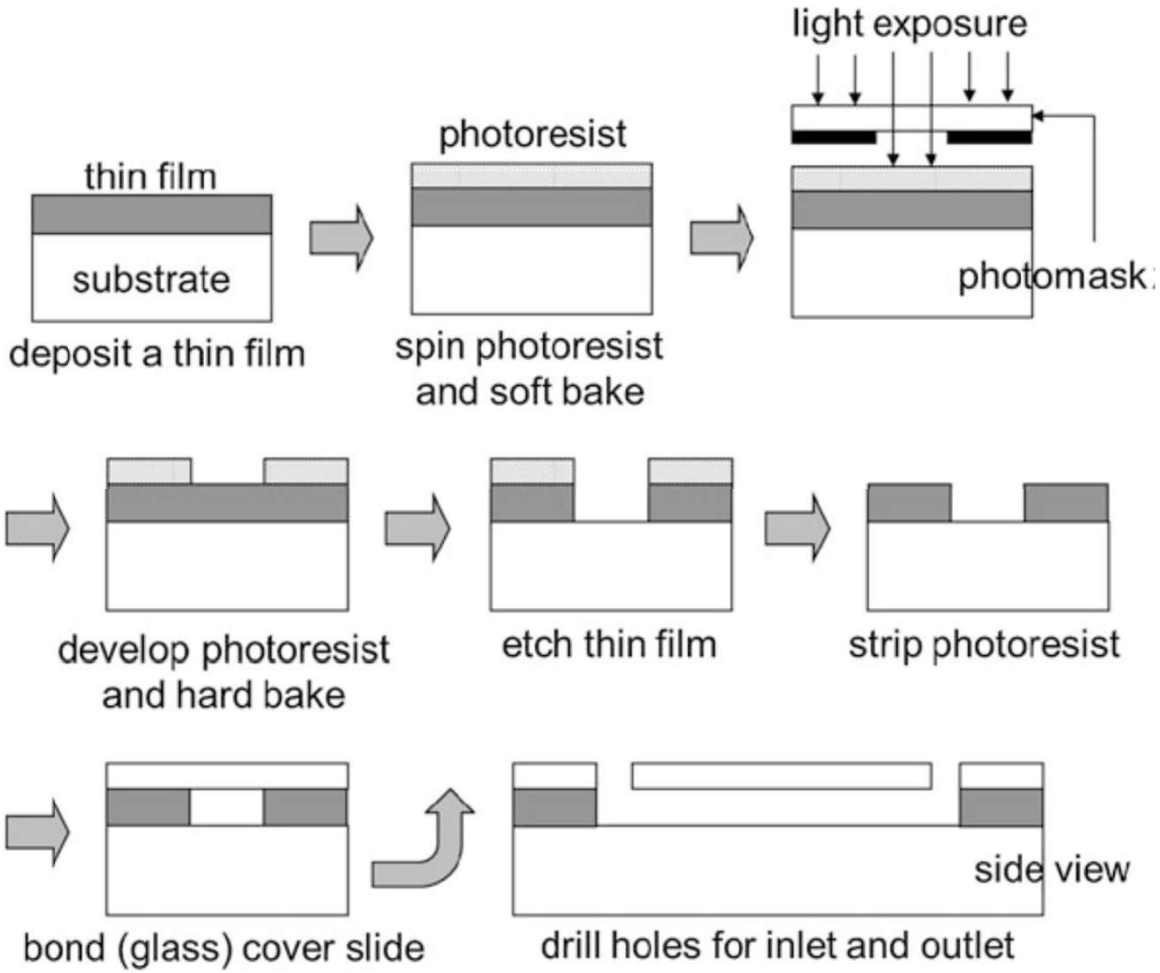
(e) hyperthermia and

(f) cosmetics



Microfluidic Devices fabrication

- MEMS technologies are used in realization of microfluidics' **key building blocks** such as flow channels, pumps and valves
- Typical microfluidic devices applications:
  - Chemical analysis, drug delivery, biological sensing, environmental monitoring, etc.
- Fluidic device design considers following effects:
  - type of flow (laminar or turbulent),
  - effect of bubbles,
  - capillary forces,
  - fluidic resistance &
  - capacitance



LOC fabrication with photolithography

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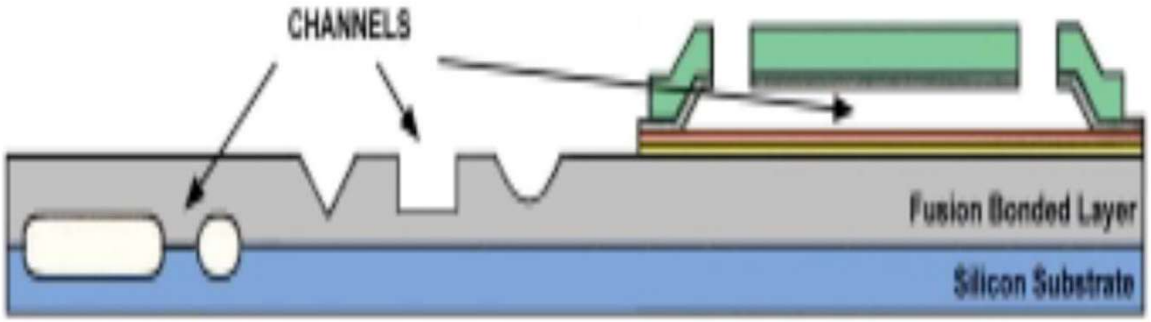
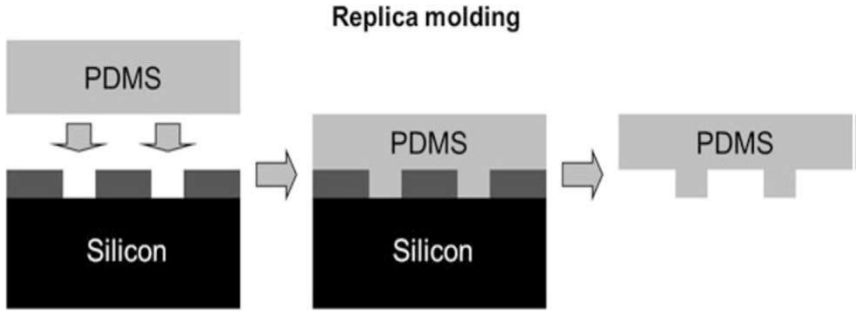
Lecture 28 dated 28th Oct. 2024

Microfluidic Devices

i. **Flow channels**: A wide variety of microfluidic channels have been fabricated using
   i. bulk micromachining (wet & dry etching),
   ii. surface micromachining &
   iii. moulding techniques



Various channels for microfluidic applications



Soft lithography: replica molding

ii. **Flow sensors**: MEMS flow sensors can be fluid-dependent flow or fluid-independent.

Fluid-dependent flow sensors measure the flow rate by heating a fluid 'upstream' & then recording its temperature 'downstream'.

- The flow rate is proportional to the temperature difference & transit time of the two actions.

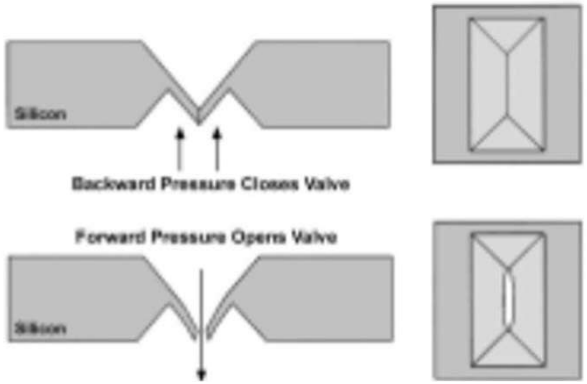
Fluid-independent flow sensors measure pressure or force exerted on an object by the fluid.

- Using a piezoresistive sensing mechanism, flow measurements are fairly linear; direction and magnitude can be sensed by this method.
- In addition, fluid independent flow sensors do not involve any form of heating & hence are more suited to biological fluid applications.

An example of a MEMS bulk drag-force flow sensor

iii. Valves

- Valves are classified as active or passive; depending on whether or not they have an external power or control source. One of the simplest MEMS valves is the **passive** check valve



Basic concept of passive silicon check valve

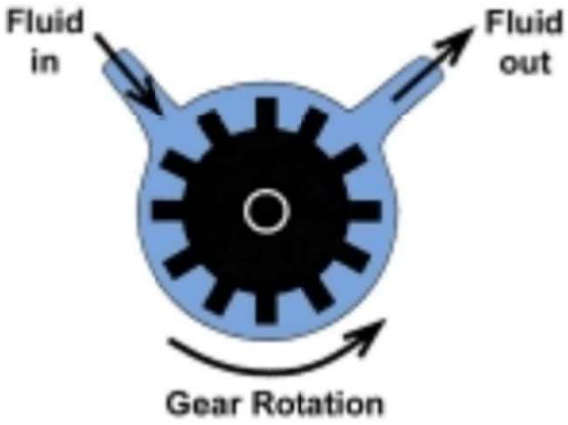
- Active MEMS valves can be actuated by many methods: thermal, piezoelectric, electrostatic & shape memory alloy means. **Thermal actuation** is commonly used.

iv. Pumps

- Pumps are an important part of microfluidic devices
- MEMS pumps are very sensitive to fine particles which often cause contamination & leakage of the device
- Membrane, rotary & ultrasonic pumps are common types of MEMS pumps

Rotary pumps

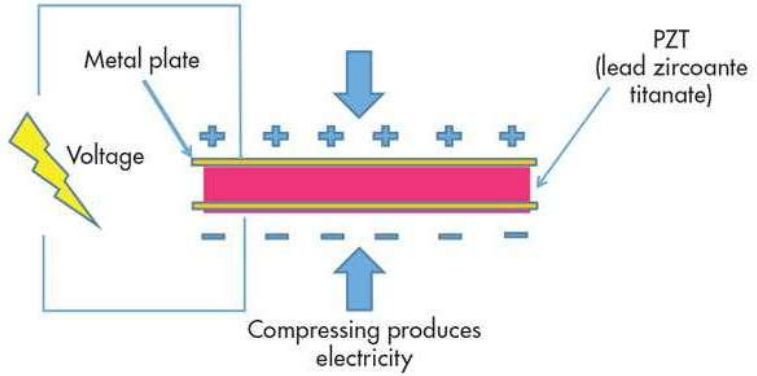
- LIGA is used to fabricate micromachined PMMA gears in MEMS microfluidic systems
- These gears can be driven using electroplated NiFe bars mounted on the gears
- Fluid is pumped by the action of the turning gears



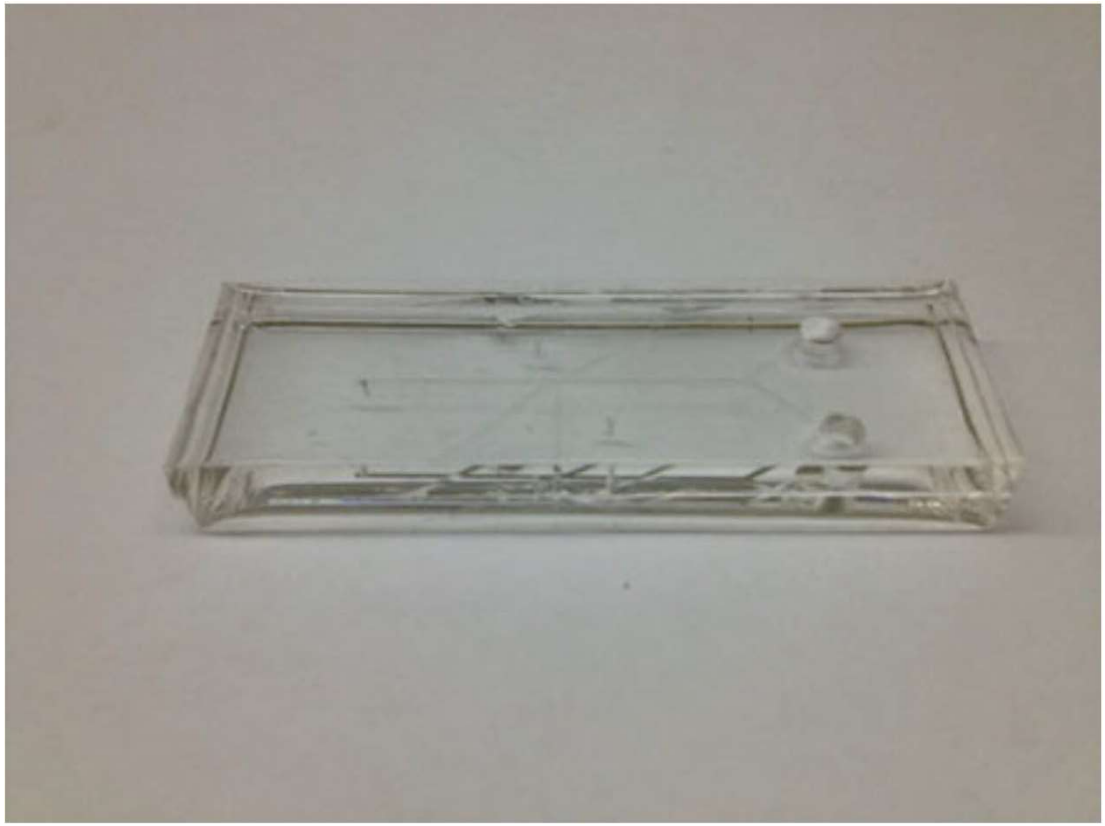
Basic concept of magnetic rotary micropump

vi. Droplet generators

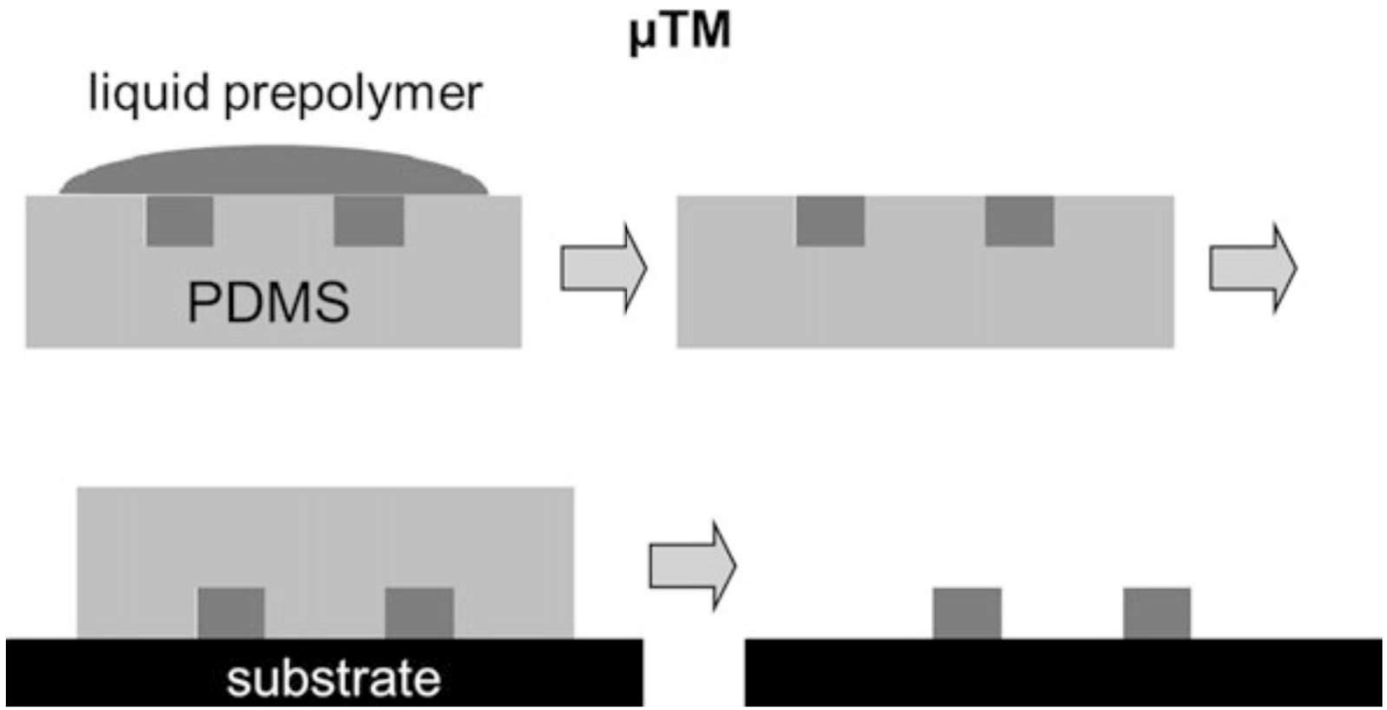
- The majority of droplet generators in commercial MEMS microfluidic devices are inkjet printer heads
- These rely on either thermal or piezoelectric actuation to eject ink droplets;
- Thermal actuation are common
- Piezoelectrically actuated valves offer the advantage of very high forces, but very small movement for very large voltages
- They find use in automotive fuel-injection valves & spray nozzles.



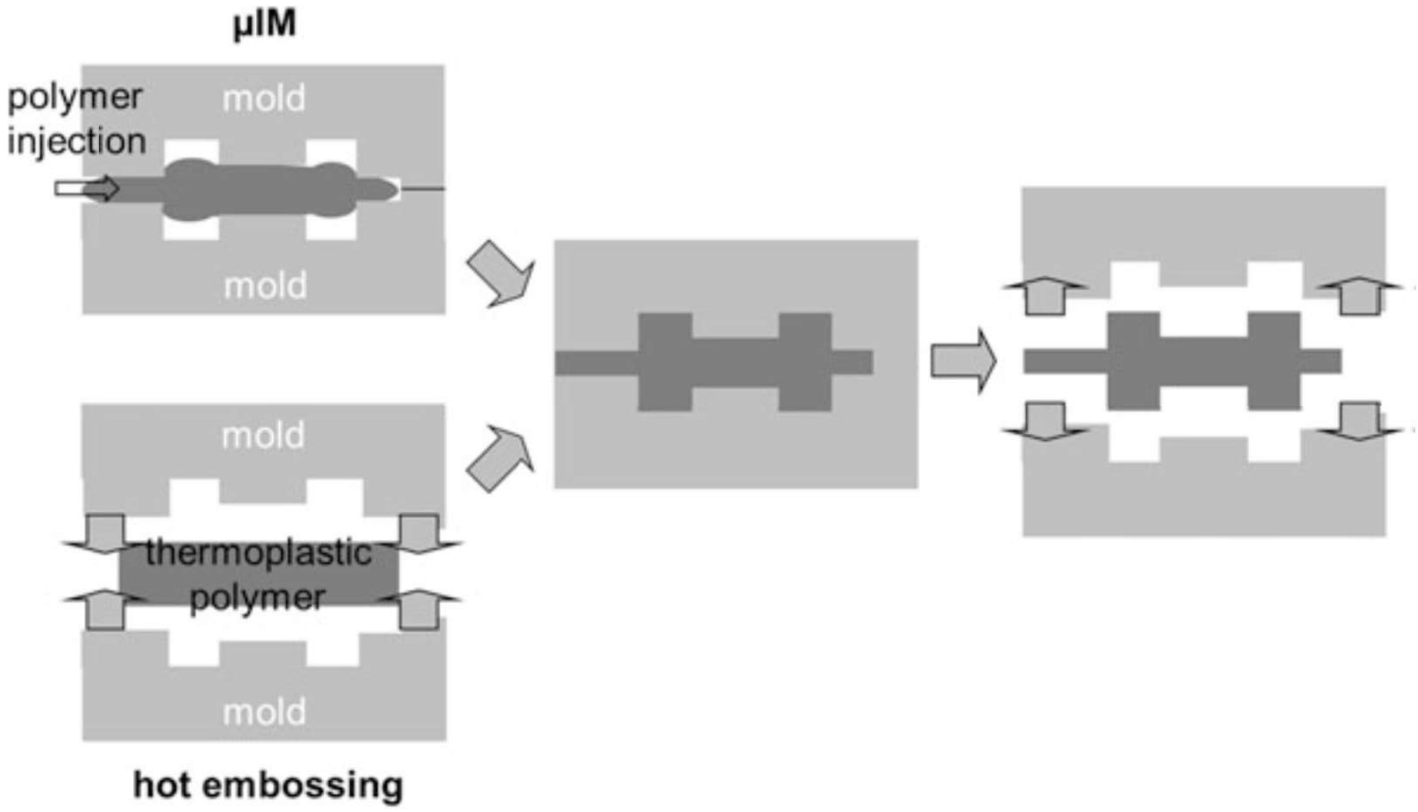
The piezoelectric effect



An LOC made out of PDMS replica molding



Micro-transfer molding (μTM)



Micro-injection molding (µIM) and hot embossing

Questions and Discussion?