Microfluidic Sensors

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Outline:-

- Introduction
- Microfluidics technology
- Micro-fabrication techniques
- Liquid flow
- N-S equation from Euler equation
- Non dimensional N-S equation
- Reynolds number
- Stokes equation or diffusion equation
- Bio-sensors (GO_x and GDH based)
- Magnetic bead method cell detection
- Applications And motivations
- References

What is Microfluidic Sensors

Besically we divide the definitions

- **Micro**-So we should have at least one of the following features
  (i)Small Volume
  (ii)Small Size
  (iii)Low energy Consumption
- **Fluidics**-Controlling and handling of liquids and/or gases.
- **Sensor**-It converts a non electrical quantity into an electrical. or we can say that "Sensors are used to detect the physical and chemical properties of a system by controlling and displaying the various parameters.

Microfluidic Technology

- Possible to operate on micro-scale liquids for **controlling** and **sensing** purposes.
- On the scaling goes down,the risk on the design and development of sensors is also high by considering the sensitivity,selectivity and stability of the sensors.
- Micro-fabrication techniques comes from the **MEMS (Micro Electro Mechenical System)** technology.
- **MEMS**-The integration of mechanical elements,sensors,actuators and electronics on a common **silicon** substrate through micro-fabrication technology.
- **Why MEMS**-(i)Integrated multiple functions (ii)Improved performance (iii)Reducing manufacturing cost and time.

Materials we used for MEMS

We have divided these materials-

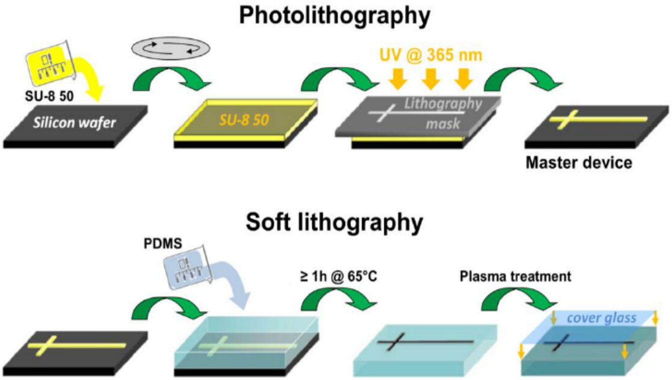
Materials for MEMS		
Substrates	Thin Films	Packaging
Plastic Glass Ceramic S/C-(Si,Ge,GaAs) MgO,Alumina and Sapphire	S/C Dielectric(SiO2,Si3N4) Metal(Al,Au,Pt) Polysilicon Special materi- als(PZ,STO,BST)	Ceramics Metals Plastics

Micro-fabrication Techniques

We have lot of micro-fabrication techniques to make devices-

Different Patterning for techniques		
Lithographic Patterning	Precision machining	Beam Machining
Surface μ*machining*	Precision milling and turning	Laser processing
Bulk μ*machining*	Micro EDM	E-beam
SU-8 and Electroforming	Embosing	Ion Beam machining
X-ray lithography	Precision Bonding	
Liga process		

Photolithography process

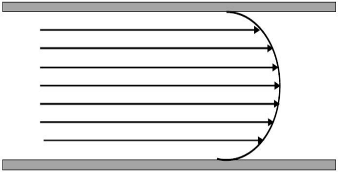


How microfluidics liquid flow?

Reynolds Number-

Dimensionless quantity that helps to predicts flow patterns

- So here range from 10nm to 10microns at these length scale Reynolds number is low and the flow is laminar
- **Laminar Flow**-Particles goes in uniform manner, means that particles can not go from one layer to another layer.



Laminar Flow

- So the velocity vector will be constant

Navier-Stokes Equation

Conservation of momentum or force equation or balance equation

- It is based on 'Newton's second law'
- It tells us about the motion of the fluid
- with the help of 'Euler equation' we can derive the N-S equation.
- **Euler Equation**-In this equation we take inviscid fluids(i.e, no viscosity).
- the eaquation is that

$$\boxed{\frac{\partial v}{\partial t} + v.\nabla v = \frac{-1}{\rho} * \nabla p}$$

Derivation of N-S equation

- When we include shear stress, so extra term will be shown in euler equation, thus

$$\mu\left(\frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2} + \frac{\partial^2}{\partial z^2}\right)v - \nabla p = \rho\frac{\partial v}{\partial t} + \rho v.\nabla v$$

After rearranging terms

$$\boxed{\frac{\partial v}{\partial t} + v.\nabla v = -\frac{1}{\rho}\nabla p + \frac{\mu}{\rho}(\nabla^2)v} \tag{1}$$

- final N-S equation we generally write
- this is non-linear PDE's so that difficult to solve.
- consider ∇p and $v.\nabla v$ are zero,then we get a diffusion equation.

$$\boxed{\frac{\partial v}{\partial t} = \nu(\nabla^2)v}$$

where ν = kinematic viscosity

Non-dimensional N-S equation

- we consider the dimensionless variables and substitute to make it dimensionless
- $\mathrm{t}^* = ft, \vec{x}^* = \frac{\vec{x}}{L}, \vec{v}^* = \frac{\vec{v}}{v}, \vec{\nabla} = \frac{\nabla^*}{L} and, p^* = \frac{LP}{v\mu}$

- after substituting we get

$$\boxed{vf\frac{\partial v^*}{\partial t^*} + \frac{v^2}{L}\vec{v}^*(\vec{\nabla}^*.\vec{v}^*) = -\frac{\mu v}{\rho L^2}\vec{\nabla}^* p^* + \frac{\mu v}{\rho L^2}(\nabla^*)^2 v^*}$$

- multiply by $\frac{L}{v^2}$ because each term has dimensions $[\mathrm{LT}^{-1}]$, the final non dimensional NS equation we get

$$\boxed{(\frac{fL}{v})\frac{\partial v^*}{\partial t^*} + \vec{v}^*(\vec{\nabla}^*.\vec{v}^*) = -(\frac{\mu}{\rho vL})\vec{\nabla}^* p^* + (\frac{\mu}{\rho vL})\nabla^{*2} v^*}$$

where $(\frac{fL}{v}) \rightarrow$ strouhal number and $\frac{\mu}{\rho vL} \rightarrow$inverse of Re

Definition

Reynolds Number-

It is the ratio of inertial forces to viscous forces within fluids

- thus

$$Re = \frac{\text{Inertial forces}}{\text{Viscous Forces}} = \frac{\text{mass x acceleration}}{\text{(dynamic viscosity) x(velocity/distance) x (area)}}$$

after solving we finally get the value of reynold number

$$Re = \frac{\text{v x L}}{\nu}$$

- let if particles flowing in constant speed and kinematic viscosity also fixed,so "Re" depends only on length L.
- if L is small-**Laminar flow**-dominated by viscous forces
- L is large -**Turbulant flow**-dominated by inertial forces

Stokes equation

- flow with large viscosity equation obtained

$$\boxed{Re(\frac{\partial v^*}{\partial t^*} + \vec{v}^*(\vec{\nabla}^*.\vec{v}^*)) = -\nabla p^* + \nabla^2 \vec{v}^*}$$

- Flow where inertia term is smaller than viscous term i.e.,Re$\rightarrow$ 0, thus inertial term can be neglected

$$\boxed{Re\frac{D\vec{v}^*}{Dt^*} = -\nabla p^* + \nabla^2 \vec{v}^*}$$

- At low Re the same equation obtained as a diffusion equation,called **Stokes equation**$\rightarrow$ $\boxed{-\nabla p + \nabla^2 \vec{v^*} = 0}$

Sensor for diabetes:Glucose bio-sensor

Measures the level of glucose in the blood

- **Basic principle**-determines the concentration of glucose in the solution
- Three main parts-(i)Biological recognition (ii)Transducers (iii)Signal processing system
- The majority of current glucose bio-sensors are of electro-chemical type.
- In electro-chemical sensors we mostly use amperometric glucose biosensors,most commonly devices available.
- Glucose measurements are based on interactions with the enzymes.
- Co-factor-Helper molecules,which helps to start the activity to happen.
- Three enzymes families-(i)Glucose oxidase(ii)GDH(iii)Hexokinase

Glucose Oxidase based biosensors

- FAD(flavin Adenine Dinucleotide) works as co-factor
- $\boxed{Glucose + GO_x + FAD \rightarrow Glucolectone + GO_x + FADH_2}$
- FAD regenerated by reacting with oxygen and form H_2O_2
- H_2O_2 is oxidized at catalytic at Pt anode.

$$\boxed{H_2O_2 \rightarrow 2H^+ + O_2 + 2e}$$

- The electrode easily recognizes the number of e^- transfer and this e^- flow is proportional to the number of glucose molecules present in the blood.

GDH based biosensors

GDH based amperometric bio-sensors have been increasing recently

- GDH familiy includes- (i)Pyrro-Quinoline-Quinone(PQQ),(ii)Nicotinamide-Adenine Dinucleotide(NAD)
- PQQ is efficient enzyme system but it is relatively expansive
- So use NAD as cofactor

$$\boxed{GDH + NAD \rightarrow NADH}$$

- NAD is major e^{-} acceptor in the oxidation of glucose

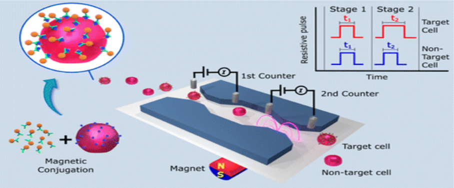
$$\boxed{Glucose + NAD^{+} \rightarrow Gluconolectone + NADH}$$

$$\boxed{NADH \rightarrow NAD^{+} + H^{+} + 2e^{-}}$$

Cell detection by microfluidic magnetic bead

Novel cell detection device and microfluidic coulter counting technology

- Measure cells size distribution,concentration and detect target cells
- Consists of two identical micro Coulter counters separated by a fluid chamber



- By magnetic interaction of magnetic beads and magnetic field, target cells were retarded by the magnetic field
- Transit time of a target cell by the second counter was longer than the first counter
- From transit time delay we can detect target cells and concentration

Microfluidics Applications

- Microfluidics sorter chip for C.Elegans live imaging
- PH control-Solid state sensor
- Drug administering
- Gradient generations-Concentrations
- Cell analysis- cellular biosensor
- DNA bio sensor- detect the DNA sequences
- Cancer cell detection
- Microfluidic temperature sensors
- Microfluidic gas sensors- detect concentration of a particular gas
- Point of care-Pregnancy testing,HIV diagnosis and glucose testing

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