Lecture 3: Microfluidics and bioMEMS

- Electrokinetics and (di)electrophoresis
- Electrowetting
- Polymer microfluidics: valves and pumps
- Applications: lab-on-chip, PCR, diagnostics
Microfluidics

- Microfluidic systems consist of components for fluid handling at the micro-scale, such as channels, pipes, valves, membranes, reservoirs.

- Fluid flow can be continuous (channels) or discrete (droplets).

\[
\begin{align*}
1 \text{ l} & = (10 \text{ cm})^3 \\
1 \text{ ml} & = 1 \text{ cm}^3 \\
1 \text{ µl} & = 1 \text{ mm}^3 \\
1 \text{ nl} & = (100 \text{ µm})^3 \\
1 \text{ pl} & = (10 \text{ µm})^3 \\
1 \text{ fl} & = 1 \text{ µm}^3
\end{align*}
\]
Overview

• Introduction: Lab on a Chip

• Moving Fluids on Chips
  – Electro-osmosis
  – Electrophoresis
  – Dielectrophoresis
  – Electrowetting

• Applications
  – Fluidic VLSI
  – PCR on a chip
  – Rapid diagnostics systems
“Lab on a Chip”

Integrate a biochemical laboratory into a small disposable package:

• Reduced volume of chemicals
• Reduced power consumption
• Reduced risk
• Increased speed
• Parallelism
• Portable, cheap
• ...

Caliper Technologies
2D Droplet Manipulation Demo

How Does It Work?

There are two major techniques using electrostatic fields that are commonly used to control small objects suspended in a liquid:

• **Electrophoresis and Dielectrophoresis:** Motion of a charged or polarized particle caused by a non-uniform electrostatic field

• **Electrowetting:** Spreading of a droplet over a larger surface area due to change in surface energy caused by an electrostatic field

• Both phenomena are related and essentially shift the energy equilibrium of liquid interfaces in an electrostatic field

• Other techniques: optical trapping, thermocapillary effect...
Electrokinetic Flow (1)

Electrokinetic flow allows transport of neutral fluids in narrow channels

Principle:
• A double layer of charged ions forms along the walls of a microfluidic channel
• An applied electric field along the channel moves the mobile ions in this double layer
• The fluid layer in close proximity is drawn along with moving ions.
Electrokinetic Flow (2)

Figure: Kovacs’98, p. 851
Electrophoresis (1)

Electrophoresis allows transport of charged particles in neutral fluids

**Principle:**
- The velocity of an ion of charge $z_i$, in a homogeneous medium, is proportional to the applied electric field.
- Therefore, ions will move at characteristic velocities determined by their charges, radii, and mobilities.
- This is the basis for electrophoretic sample separation into constituent species for analysis.
Electrophoresis (2)

Spatial resolution of the separated ions cannot exceed that of the initially injected “plug”.

Figure: Kovacs’98, p. 850
Dielectrophoresis (DEP)

• A neutral object is first polarized by an electrostatic field, and then experiences a force because of field gradient

• Direction of force is independent of field polarity (works with AC)
• If medium is more polarizable than object: positive DEP, otherwise negative DEP

• Electrostatic analogy to induced magnetism
• Example: charged clothes that attract lint
Dielectrophoresis (DEP)

Positive Dielectrophoresis

Field gradient is stronger where lines converge

Polarization charges are equal and opposite

Polarizable particle in an inhomogeneous electrical field

www.dielectrophoresis.org
Electrophoresis and Dielectrophoresis

\[ \vec{F} = q\vec{E} + (\vec{p} \cdot \nabla)\vec{E} \]

- \( q\vec{E} \): electrophoretic force
- \( q \): charge of particle
- \( (\vec{p} \cdot \nabla)\vec{E} \): dielectrophoretic force
- \( \vec{p} \): polarization of particle
Massively Parallel DEP (1)

Electrode array controlled by CMOS circuitry and opposing ground plate creates “potential cages” for particles, droplets, or cells

[Medics project, LETI, France]
Massively Parallel DEP (2)

Silicon chip with zoom on the electrode matrix (320x320 20μm electrodes)
Massively Parallel DEP (3)

Figure 4: Sequence of K562 cell manipulation. (a) shows a predefined grid of cages which have trapped cells in 280mM mannitol. Two cells have been chosen and commands are entered to move them 8 steps to the left (b to e) and out of view.
Capillary Gel Electrophoresis

- size-based separation of biological macromolecules such as oligonucleotides, DNA restriction fragments and proteins;
- gel materials: cross-linked polyacrylamide, agarose or even solutions of linear polymer
Step 1: Injection of Buffer Solution
Step 2: Injection of Sample Solutions
Step 3: Start of Electrophoresis
Step 4: EP Separation
• Under equilibrium, the electric force and the friction force balance.

\[ F_{elec} = z_i e E = \text{net charge} \times \text{electric field} \]

\[ F_{fric} = f_i v_i \]

\( f_i \): friction coefficient of species \( i \) is a function of gel pore sizes and size of particles.

This yields \( v_i = \frac{z_i e}{f_i} E = \mu_i E \)
Microfluidic Components

• Channels, valves, pumps have been built in many variations in MEMS.
• 2½D geometry is well-suited for channels and reservoirs.
• For an overview of microfluidic components see Kovacs’ book
• Note that the large number of valve and pump designs suggests:
  – None of them is ideal
  – Most of them are too complicated and will not make the jump to commercial applications
  – In the future: stamping and molding of mass-produced, cheap plastic devices rather than silicon-based systems
Pneumatic Valves and Pumps (1)
Pneumatic Valves and Pumps (2)
Pneumatic Valves and Pumps (3)
Fluid “VLSI”

S. Quake et al.
Fluidigm
Bio MEMS Applications

- Minimally invasive microsurgery instruments
- In vitro and in vivo experiments at cellular scale
- Implantable sensors and computers for health monitoring, prostheses, and human augmentation
  - cochlear implants
  - retinal implants
  - neuronal implants
- DNA amplification (PCR)
- Gene Probe Arrays
- Biometrics