Introduction to Microfluidics: Basics and Applications

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Hands-on Workshop in Micro and Nanobiotechnology

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wikisites.mcgill.ca/djgroup
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
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Microfluidics

- **Fluidics**: handling of liquids and/or gases
- **Micro**: has at least one of the following features:
  - Small volumes
  - Small size
  - Low energy consumption
  - Use of special phenomena (we’ll talk more about this later)

A microfluidic channel is about the same width as a human hair, 70 µm
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Advantages of Microfluidics

- Low sample and reagent consumption; fluid volumes (µl; nl; pl; fl)
- Small physical and economic footprint
- Parallelization and high throughput experimentation
- Unique physical phenomena: use of effects in the micro-domain:
  - Laminar flow
  - Capillary forces
  - Diffusion

Advantages of Microfluidics

- Low sample and reagent consumption; fluid volumes (µl; nl; pl; fl)
- Small physical and economic footprint

Advantages of Microfluidics: Lab on a Chip

- Parallelization and high throughput experimentation

- Sample preparation
- Extraction of molecules
- Amplification
- Purification
- Control of chemical reactions
- Surface functionalization
- Detection
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Fluid Mechanics

- Law: Conservation of mass
- Law: Conservation of momentum
- Assumption: Incompressibility
- Assumption: No-slip boundary condition, i.e. velocity of the fluid flow at a surface is zero
No-slip Boundary Condition
Basic Properties

- Types of fluids:
  - Newtonian fluids
  - Non-Newtonian fluids

- Types of fluid flow:
  - Laminar
  - Turbulent
Newtonian Fluids

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

\[ \tau = \mu \frac{dv}{dy} \]

Shearing stress, \( \tau \)

Rate of shearing strain, \( \frac{dv}{dy} \)
Viscosity

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

<table>
<thead>
<tr>
<th>Substance</th>
<th>Viscosity (mPa·s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air</td>
<td>0.017</td>
</tr>
<tr>
<td>Acetone</td>
<td>0.3</td>
</tr>
<tr>
<td>Water</td>
<td>0.9</td>
</tr>
<tr>
<td>Mercury</td>
<td>1.5</td>
</tr>
<tr>
<td>Olive oil</td>
<td>80</td>
</tr>
<tr>
<td>Honey</td>
<td>2,000 – 10,000</td>
</tr>
</tbody>
</table>
Non-Newtonian Fluids

- Non-linear relationship between shear stress and shear strain
- Examples: paint, blood, ketchup, cornstarch solution

Rate of shearing strain, $\frac{dv}{dy}$

Shearing stress, $\tau$

- Non-Newtonian shear thickening
- Newtonian
- Non-Newtonian shear thinning
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:
  - Measure of flow turbulence
  - Re < 2000 for laminar
  - Due to small dimensions
  - Re < 1 in microfluidic systems

\[ Re = \frac{\rho v L}{\mu} \]
where
\[ L = \frac{4A}{P} \]
Laminar and Turbulent Flow

- Laminar Flow
- Turbulent Flow
Couette Flow (Laminar)

- **Couette flow:**
  - One of the plates moves parallel to the other
  - Steady flow between plates
  - No-slip condition applies
Poiseuille Flow (Laminar)

- Poiseuille flow:
  - Pressure-driven flow
  - No-slip condition applies
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Laminar Flow

Diffusion

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, \( D \approx 40 \, \mu\text{m}^2 \text{s}^{-1} \)
For urea, \( D \approx 1400 \, \mu\text{m}^2 \text{s}^{-1} \)

For \( X = 100 \, \mu\text{m} \), the time becomes:

Antibody: 125 s; Urea: 3.6 s
Diffusion and Mixing

Direction of Flow

University of Hertfordshire, STRI, http://www.herts.ac.uk/research/stri.html
Generating Biochemical Gradients

Generating Biochemical Gradients

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Capillary Phenomenon and Liquid Transport
Capillary Phenomenon and Liquid Transport
Capillary Phenomenon

Pressure of the liquid column:  \( \Delta P = \rho gh \)

Capillary pressure:  \( \Delta P = -\frac{2\gamma}{r} \)

\( \gamma \): Surface tension

Height of liquid column:  \( h = \frac{2\gamma \cos \theta}{\rho gr} \)

\( \theta \): Contact angle
Surface Tension

- Surface tension is a property of cohesion (the attraction of molecules to like molecules)

- When an interface is created, the distribution of cohesive forces is asymmetric

- Molecules at the surface may be pulled on more strongly by bulk molecules
Wettability

- Adhesion vs. cohesion
- Contact angles are a way to measure liquid-surface interactions

![Diagram of contact angles showing \( \gamma_{SL} \), \( \gamma_{LG} \), and \( \gamma_{SG} \) with \( \theta_C \).]

Hydrophobic

Hydrophilic
Capillary Systems
Capillary Systems

Experiment in this course
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Microfluidic and Lab-on-a-Chip Devices

- **Microfluidic Devices**
  - **Closed chips**
    - Continuous flow
  - **Droplet-based**
  - **Digital microfluidics**
    - Electrowetting-on-dielectric
    - Surface acoustic waves
    - Optoelectrowetting
  - **Microfluidic probes (MFP)**
  - **Open Chips**
  - **Micro-arrays**
    - Ink-jet printing
    - Pin-printing technology
    - Microcontact printing

- **External pressure**
- **Capillary effect**
- **Electrokinetic mechanisms**
Immunoassay

- A biochemical test that measures the concentration of a substance in a biological liquid
  - *Enzyme-Linked ImmunoSorbent Assay* (ELISA)
  - Sandwich assays

![Diagram of the Immunoassay process](image-url)
Micromosaic Immunoassay

- Immobilization
- Capture 1
- Capture 2
- Recognition
- Sample Loading
- Detection
- Fluorescently-labelled Detection Antibodies

Micromosaic Immunoassay

Micromosaic Immunoassay

Capture 1
Capture 2

Fluorescently-labelled Detection Antibodies

Immobilization
Recognition
Reading Signal

Droplet-Based Microfluidics

Isolation/Detection of Rare Cells

Recapitulating Organ Function on a Chip

Microfluidic Probe for Perfusion of Brain Slices


Technology developed in our laboratory
Thank You!

QUESTIONS?
Microfluidics advantages

- Parallelization and high throughout experimentation

*Source: The National Institute of Standards and Technology (NIST)*
Incompressible vs compressible:

Gas particles are very spread out, so can be compressed

Liquid particles are not spread out, so hard to be compressed

Source: The Nucleus Learning website
Surface energy of various liquids

<table>
<thead>
<tr>
<th>Liquid</th>
<th>$\gamma$</th>
<th>$\gamma^{LW}$</th>
<th>$\gamma^{AB}$</th>
<th>$\gamma^{+}$</th>
<th>$\gamma^{-}$</th>
<th>$\eta$</th>
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</thead>
<tbody>
<tr>
<td>Hexane</td>
<td>18.4</td>
<td>18.4</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.00326</td>
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<tr>
<td>Heptane</td>
<td>20.3</td>
<td>20.3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.00409</td>
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<tr>
<td>Octane</td>
<td>21.6</td>
<td>21.6</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.00542</td>
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<tr>
<td>Decane</td>
<td>23.8</td>
<td>23.8</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.00907</td>
</tr>
<tr>
<td>Dodecane</td>
<td>25.35</td>
<td>25.35</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.01493</td>
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<tr>
<td>Methanol</td>
<td>22.5</td>
<td>18.2</td>
<td>4.3</td>
<td>$=0.06$</td>
<td>$=77$</td>
<td>0.00544</td>
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<tr>
<td>Ethanol</td>
<td>22.4</td>
<td>18.8</td>
<td>2.6</td>
<td>$=0.019$</td>
<td>$=68$</td>
<td>0.01074</td>
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<tr>
<td>Chloroform</td>
<td>27.15</td>
<td>27.15</td>
<td>0</td>
<td>3.8</td>
<td>0</td>
<td>0.00473</td>
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<tr>
<td>cis-Decalin</td>
<td>32.2</td>
<td>32.2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.0338</td>
</tr>
<tr>
<td>1-Bromonaphthalene</td>
<td>44.4</td>
<td>44.4</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.0489</td>
</tr>
<tr>
<td>Methylene iodide</td>
<td>50.8</td>
<td>50.8</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.028</td>
</tr>
<tr>
<td>Ethylene glycol</td>
<td>48.0</td>
<td>29.0</td>
<td>19.0</td>
<td>1.92</td>
<td>47.0</td>
<td>0.199</td>
</tr>
<tr>
<td>Formamide</td>
<td>58.0</td>
<td>39.0</td>
<td>19.0</td>
<td>2.28</td>
<td>39.6</td>
<td>0.0455</td>
</tr>
<tr>
<td>Glycerol</td>
<td>64.0</td>
<td>34.0</td>
<td>30.0</td>
<td>3.92</td>
<td>57.4</td>
<td>14.90</td>
</tr>
<tr>
<td>Water</td>
<td>72.8</td>
<td>21.8</td>
<td>51.0</td>
<td>25.5</td>
<td>25.5</td>
<td>0.010</td>
</tr>
</tbody>
</table>
### Surface energy of various solids

<table>
<thead>
<tr>
<th>Polymer</th>
<th>$\gamma$</th>
<th>$\gamma^{L,W}$</th>
<th>$\gamma^{AB}$</th>
<th>$\gamma^\oplus$</th>
<th>$\gamma^\ominus$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teflon FEP</td>
<td>17.9</td>
<td>17.9$^a$</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Polyethylene</td>
<td>33.0</td>
<td>33.0$^d$</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Nylon 6,6</td>
<td>37.7</td>
<td>36.4$^c$</td>
<td>1.3</td>
<td>0.02$^c$</td>
<td>21.6$^c$</td>
</tr>
<tr>
<td>Polymethyl-methacrylate (PMMA)</td>
<td>40.0</td>
<td>40.0$^e$</td>
<td>0</td>
<td>0$^e$</td>
<td>14.6$^e$</td>
</tr>
<tr>
<td>PMMA</td>
<td>40.6</td>
<td>40.6$^b$</td>
<td>0</td>
<td>0$^b$</td>
<td>12$^b$</td>
</tr>
<tr>
<td>PMMA</td>
<td>41.4</td>
<td>41.4$^c$</td>
<td>0</td>
<td>0$^c$</td>
<td>12.2$^c$</td>
</tr>
<tr>
<td>Polystyrene</td>
<td>42</td>
<td>42$^f$</td>
<td>0</td>
<td>0$^f$</td>
<td>1.1$^f$</td>
</tr>
<tr>
<td>“Cell culture” polystyreneg</td>
<td>46.8</td>
<td>43.7</td>
<td>3.1</td>
<td>0.12$^e$</td>
<td>20.0</td>
</tr>
<tr>
<td>Polyvinylalcohol</td>
<td>42</td>
<td>42$^e$</td>
<td>0</td>
<td>0$^e$</td>
<td>17–57$^{e,h}$</td>
</tr>
<tr>
<td>Polyethyleneoxide (PEG – 6,000)</td>
<td>43.0</td>
<td>43.0$^e$</td>
<td>0</td>
<td>0$^e$</td>
<td>64$^e$</td>
</tr>
<tr>
<td>Polyethyleneoxide (PEG – 6,000)</td>
<td>45.9</td>
<td>45.9$^e$</td>
<td>0</td>
<td>0$^e$</td>
<td>58.5$^e$</td>
</tr>
<tr>
<td>Polyoxytetramethylene glycol$^i$ (MW ≈ 2,000)</td>
<td>44.0</td>
<td>41.4$^k$</td>
<td>2.6</td>
<td>0.06$^i$</td>
<td>27.6$^i$</td>
</tr>
<tr>
<td>Co-poly(ethylene glycol, propylene glycol)$^i$ (MW ≈ 2,000)</td>
<td>47.5</td>
<td>42.0$^m$</td>
<td>5.5</td>
<td>0.13$^n$</td>
<td>58.8$^n$</td>
</tr>
</tbody>
</table>
Autonomous control with hydrogels

• **Superhydrophobic Surfaces:**
  Hydrophobic surface having nano-scale roughness.

• **Hydrophilic Surfaces:**
  “Water-loving surface” Water tries to maximize contact with surface.

• **Hydrophobic Surfaces:**
  “Water-fearing surface” Water tries to minimize contact with surface.

CONTACT ANGLE

<table>
<thead>
<tr>
<th>0°</th>
<th>5°</th>
<th>35°</th>
<th>40°</th>
<th>100°</th>
<th>115°</th>
<th>160°</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma Cleaned Glass</td>
<td>Polyethylene Glycol SAM</td>
<td>Polystyrene PTFE (Teflon)</td>
<td>Superhydrophobic Isotactic Polypropylene</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>