

Building College-University Partnerships for Nanotechnology Workforce Development

Materials Modification in Nanotechnology

DNA and Protein Analysis using Nanotechnology

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Outline

- Micro array Technology
- Microfluidics Overview
- Basic Design and Material Processes

MicroBioLab

- This is a device that can dissect a very small amount DNA, protein, cells, or drug
- It can chemically analyze a liquid sample 10,000 times smaller than commercial analytical instruments
- This time-saving chip could be built for genetic diagnosis, DNA fingerprinting, and drug research
- Conserves test media, and reduces disposal issues

Micro Arrays

- How they work
 - Microarrays work by exploiting the ability of mRNA to bind to DNA templates.
- What they do
 - Analyzes gene expressions consisting of small membranes.
 - Can determine the expression levels of hundreds or even thousands of genes in cells by measuring the amount of mRNA in a single experiment



http://genechip.com/index.affx

Micro Arrays Uses

- Test structure that can be used with microfluidic technology to interrogate samples.
- Used to understand fundamental aspects of growth and development.
- Also used to identify and classify DNA sequence information and assign their function.



Micro Arrays

- Why they are important
 - You can survey large number of genes rather quickly.
 - Can compose and contrast cells and tissues from being healthy of diseased.
 - Show how and why certain genes can or can not work together.

Micro Arrays







www.als.lbl.gov/als/science/sci_archive/128dna.html

Advantages/Disadvantages

- Advantages
 - Very Small
 - Disposable
 - Sealed
 - Portable
 - Very Fast response time
- Disadvantages
 - Takes place of jobs

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Microfluidics Overview

Microfluidics is the science of designing, manufacturing, and formulating devices and processes that process and handle volumes of fluid on the order of Nano (10⁻⁹) or Pico (10⁻¹²) liters. Liquids in nanoliters

 $30 \text{ nL} = 1/1000^{\text{th}} \text{ of } 1 \text{ droplet}$



Growth of Microarrays

Microfluidic device market - Value and forecast

(Emerging Markets for Microfluidic Applications report, Yole Développement, 2011)



Micro Reaction Technology

The microfluidic device market will reach \$4 Billion in 2016

Analytical devices

Contributed by Frédéric Breussin, Business Unit Manager Microfluidics & Medical Technologies, Yole Développement

Growth of number of ISI publications found with microfluidic and nanofluidic over the past 20 years



Chemical Society Reviews From microfluidic applications to nanofluidic phenomena¹² Albert van den Berg ,Harold G. Craighead and Peidong Yang

Microfluidics Overview

- Microfluidic devices handle small amounts of fluid. Good when only small amounts are available, or good for conservation
- Generally use small amounts of energy
- Sealed system so contamination is well controlled
- Small size leads to mobility, no lab needed
- Reaction can be fast

Microfluidics Overview

Microfluidics is a multidisciplinary field intersecting engineering, physics, chemistry, biochemistry, nanotechnology, and biotechnology, with practical applications to the design of systems in which small volumes of fluids will be handled

> small volumes (µL, nL, pL, fL) small size

- low energy consumption
- effects of the micro domain

Typically fluids are moved, mixed, separated or otherwise processed. Numerous applications employ passive fluid control techniques like capillary forces

Physics of Microfluidics

- The small scale of microfluidics leads to unique conditions and considerations
- Factors like surface tension, unique flow characteristics, air traps, and many other factors contribute to the complexity of microfluidics.
- We will briefly examine selected factors
 - Flow
 - Mixing

Physics of Flow

- Electrokinetic effects, general term to describe the movement of ions in a fluid that is subjected to an electric potential.
- Two major types of flow types, electroosmosis, or electrophoesis
- Electroosmosis, sidewall driven
- Electrophroesis, particle flow

Electroosmosis

- If the walls of a channel have an electric charge (-) ions in the fluid with an opposite charge (+) will be attracted to the walls.
- A layer of immobile ions forms at the channel surface while a layer of mobile ions forms at the fluid side (electric double layer).
- When an electrical potential is applied to the channel the ions in the fluid will be attracted to the opposite pole
- These ions will drag along the remaining fluid.



Electro-Osmotic Flow (EOF)

- Relates greatly to electrokinetic effects
- Surface of fluid develops a charge, which influences fluid flow
- Creates different layers in the fluid which contain different charges, such as the stern and diffuse layers

Electro-Osmotic Flow



Advantages

- No moving parts.
- No wear.
- Low diffusion of the laminar flow.
- Simple design.

Disadvantages

- High voltages (100's – 1000'sV) makes it difficult to miniaturize.
- Chemical absorption to the channel walls.
- Sensitive to fluid and channel chemistry.
- Joule heating.

Electrophoresis

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- Movement of charged particles or molecules that are subjected to an electric field
- "Cations move toward the cathode and anions move toward the anode."





Applied Potential (electro-osmotic flow)



Mechanical Micropumps

- Fluidics using these pumps are delivered in a series of small volumes.
- This creates a pulsating flow, as would a heart pumping blood.
- Reciprocating pumps can have values to stop backflow of fluids.
- The advantage of not having valves is the simple construction.

Micropumps

• Piezoelectric Pump



Some Non-ideal Considerations

- Generally fluids at the micro scale do not want to mix
- Pressure wave affects mixing
- Curves in the design may cause mixing
- Materials may have intrinsic properties that cause mixing or non-mixing
- Because there are many variables, computer simulations are often used in the design of microfluidics

Laminar Flow

- When all of the fluid particles move in paths parallel to the overall flow direction.
- At the extremely small scale, fluids exhibit characteristics of laminar flow.
 - When multiple fluids are introduced, they want to flow in straight lines with little to no mixing occurring.



http://wetpong.net/wetpong

Laminar Flow



Laminar Flow



- Laminar flow is the norm, and it is often not desired in a device
- No turbulence
- Fluids mix by diffusion only
- Can be useful for fluid control, but makes solution formation difficult

Fluid Mixing

- Dealing with liquids in the amounts of nanoliters $-30 \text{ nL} = 1/1000^{\text{th}}$ of 1 droplet
- Reactions occur in milliseconds
- Macro mixing methods are difficult to miniaturize to this scale, smaller channels have laminar flow
- Generally bends, turns, and increasing channel dimensions increase mixing

- "Quick check number" used to determine if a fluid will have laminar or turbulent characteristics
- Represents a ratio of momentum forces to viscous forces in fluid (liquid or gas) flow
- Expresses the relationship of fluid density, velocity, channel dimensions, and viscosity coefficient. There are other variables that are not considered by this quick check equation.
- Named after Osborne Reynolds (1824-1912)

Quick approximation to determine whether the flow of a typical fluid is laminar or turbulent.

- D = Pipe Diameter
- V = Fluid Velocity
- p = Fluid Density
- μ = Fluid Viscosity

$$\frac{\mathbf{Re}}{\boldsymbol{\mu}} = \frac{\mathbf{D}.\mathbf{V}.\boldsymbol{\rho}}{\boldsymbol{\mu}}$$

- Liquids flow smoothly when they have a low Reynolds Number
- Microchannels with only 10's of microns in dimensions create small Reynolds Numbers creating linear, turbulent-free streams
- Mixing could be desirable to have a reaction, and low Reynolds numbers prevent mixing

- For Laminar Flow Re << 1
- For Turbulent Flow
 Re >> 1
- At the extremely small scale (70 micron diameter channels) fluids will flow in a laminar fashion.
- This is a problem

For example, for a DNA lab on a chip to work, materials must be mixed. Small channel will prevent this from happening Laminar flow depends upon boundary geometry

- Cylindrical pipe
- Parallel walls
- Wide open channel
- Around a sphere

Re < 2100 Re ≈ 1000 Re ≈ 500 Re ≈ 1

Water in a 50 ųm channel

$$\mathbf{Re} = \frac{\mathbf{D.V.}\boldsymbol{\rho}}{\boldsymbol{\mu}}$$

- D = 50 ųm
- V = 1 m/s
- p = 997.0 kg/m³

Re = .056 < 2100 = Laminar flow

Peclet Number

- Determines whether diffusion or convection is the dominant means of mass transportation.
- Diffusion > 1
- Convection < 1

Pe = vl/D

- v = velocity of the fluid
- I = characteristic
 length of the fluid
- D = diffusion coefficient

Peclet Number

- When fluids flow laminarly, the primary means of mass transportation is diffusion (extremely slow process).
- To allow for mixing to occur quickly, must change flow so that it is turbulent, (meaning convection is the primary means of mass transportation).
- In the next section, mixing will be accomplished with 90-degree bends to create fluid convection.

Mixers/Stirrers

- Microfluidic devices usually have laminar flow. The fluids entering must be mixed in the chip to get the desired end product.
- The most popular types of mixing is using channel angles.
- Mixing can also be done by using stirrers (electronic or magnetic). Could be costly.

Mixers



http://www.niherst.gov.tt/scipop/sci-bits/microfluidics.htm

FLUID MIXING IN PLANAR SPIRAL MICROCHANNELS



Illustration of Dean flow effects in a curved microchannel ('i' and 'o' denote the inner and outer channel walls respectively). The transverse flow field is characterized by the presence of two counter-rotating vortices located above and below the channel midplane. At higher k, the combined action of these vortices cause two fluid streams to almost completely switch positions within the channel.

Sundersan Argon P., and Victor M. Ugaz. "Fluid mixing in planar spiral microchannels." Lab on a Chip 6.1: 74-82

Dean Number

•The Dean number is typically denoted by the symbol D, and is defined as $-\frac{1}{2}$

 $D = \frac{\rho V d}{\mu} \left(\frac{d}{2R}\right)^{1/2}$

ho is the density of the fluid

 μ is the dynamic viscosity

V is the axial velocity scale

d is the diameter (other shapes are represented by an equivalent diameter,

R is the radius of curvature of the path of the channel.

Multivortex micromixing



Sundarsan, Arjun P., and Victor M. Ugaz. "Multivortex micromixing." Proceedings of the National Academy of Sciences 103.19 : 7228-7233



Mixing intensity as a function of Re at the end of each section for the four-arc (A), six-arc (B), eight-arc (C) and ten-arc (D) spiral channels.

Sundersan Argon P., and Victor M. Ugaz. "Fluid mixing in planar spiral microchannels." Lab on a Chip 6.1: 74-82

Multivortex Micromixing



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Valves

- The majority of vales in microfluidics are like diodes, with flow limited to one direction.
- This reduces backflow, block-ups, and contamination.
- Common terms for this type of device are gates, check, or flapper valves.

Valves

 Cantilever (microvalve) Application: switches, resonators, chemical and biological sensors, accelerometers





ip.sandia.gov

Integrating the Parts

- Pump are used to move the fluid through the channels.
- Valves are used to control where and which direction the fluid flows.
- Mixers/stirrer keep fluids together and stop laminar flow.
- Many devices are made from the simple components reviewed

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