Key Topics

• Biochips/Biosensors and Device Fabrication
• Cells, DNA, Proteins
• Micro-fluidics
• Biochip Sensors & Detection Methods
• Micro-arrays
• Lab-on-a-chip Devices
Continuous Fluid Flows

Navier Stokes Equation (dimensional form)

\[ \rho \frac{DV}{Dt} = \rho \frac{\partial \vec{V}}{\partial t} + \rho (\vec{V} \cdot \nabla) \vec{V} = \rho \vec{g} - \nabla p + \mu \nabla^2 \vec{V} \]

Scale equation:

\[ V = u V' ; \quad \dot{x} = L x' ; \quad p = \frac{\mu u}{L} p' ; \quad t = \frac{L}{u} t' \]

\[ \text{Re} \left( \frac{DV}{Dt} \right) = \text{Re} \left( \frac{\partial V}{\partial t} + (V \cdot \nabla) \vec{V} \right) = \text{Re} \cdot Fr^{-2} \frac{\vec{g}}{|\vec{g}|} - \nabla p + \nabla^2 V \]

where \( \text{Re} = \frac{\rho u L}{\mu} \), \( Fr^{-2} = \frac{gL}{u^2} \)
Dimensionless Parameters

- Assume water flow:
  \( \mu = 10^{-3} \text{ kg/(s-m)} \), \( \rho = 10^3 \text{ kg/m}^3 \)
- Length \( \sim 10 \mu \text{m} = 10^{-5} \text{ m} \)
- Velocity \( \sim 1 \text{ mm/s} = 10^{-3} \text{ m/s} \)
- Then: \( \text{Re} = 10^{-2}, \text{Fr}^2 = 100, \)
- N-S equation becomes Poisson Eqn

\[
0 = -\nabla p + \nabla^2 V
\]
Re in BioChips and Laminar Flow

• Reynolds number, \( \text{Re} = \frac{L V_{\text{avg}} \rho}{\mu} \)
  • \( \text{Re} \) = inertial forces/viscous forces implies inertia relatively important
    – \( L \) is the most relevant length scale,
    – \( \mu \) is the viscosity, \( \rho \) is the fluid density,
    – \( V_{\text{avg}} \) is the average velocity of the flow.

• Reduced \( \text{Re} \)
  – Higher \( \mu \) (molasses)
  – Reduce flow rate (traffic in Rome!)
  – Reduce \( L \) (i.e. micro devices)

• \( \text{Re} \) is usually much less than 100, often less than 1.0 in micro devices

• Flow is completely laminar and no turbulence occurs.
Microfluidic Mixing

- Mixing only by diffusion (or novel structures using hydrodynamics)

Regnier, et al. Purdue
Particle Separation

- Particle separation/filter in micro-fluidic devices - without a membrane
- Smaller particles will diffuse farther and will get separated from the flow
- Diffusion distance: $x^2 = 2Dt$
  \[ D = \frac{k_b T}{6\pi \eta a} \]
  - biotin ($D \sim 350 \ \mu m^2/s$)
  - albumin ($D \sim 65 \ \mu m^2/s$)
Microfluidic Flow

- **Pressure driven flow**
  - Parabolic profile
  - No-slip boundary condition
    (Velocity at interface is zero)

- **Electrokinetic flow**
  1. Electroosmosis (EOF)
  2. Electrophoresis (EP)
  3. Dielectrophoresis (DEP)

Electroosmotic Flow

- $Q_{EOF} = \varepsilon \ E \ \zeta \ A/\eta$
- $\zeta =$ zeta potential, $\eta =$ viscosity
- Charges at interface
- Counter ion accumulation at interface
- Results in plug flow
- Electrophoresis also takes place

Deprotonation of silanol groups occurs when the pH value of aqueous solution above PZC.

Pressure driven flow
Electroosmotic Flow in Nano-channels

Surface was assumed positively charged. Concentration of Cl ions in bulk is 0.01 M. Concentrations near surface and at middle of channel are 3.21 M and 0.2 M, respectively. ————simulation with uniformly charged wall atoms;  -----simulation with discrete wall atom charges. From Freund 2002.
Electrophoresis: charged species drift when placed under an electric field

\[ \nu = -\mu \frac{dV}{dx} \]
- \( \nu \) - electrophoretic velocity
- \( \mu \) - electrophoretic mobility
- \( \frac{dV}{dx} \) = applied electric field
DNA Gel Electrophoresis

- DNA has phosphate backbone which is negatively charged - hence DNA drifts in an E-field.
- The charge/mass (e/m) ratio is constant hence electrophoretic mobility is independent of size in liquid medium.
- Thus, another sieving medium is needed where separation can take place due to difference in length.
- The separation region is filled with a gel - sieving matrix with pores through which the DNA molecules can traverse.
- The field stretches the molecules and they move in a snake-like fashion through the pores of the gel.

\[ \mu \propto \frac{1}{\log_{10} \text{fragment size}} \] (sieving effect)

- Polyacrylamide gel is used to separate DNA molecules of 10-500 bases - pores are small.
- Agarose gel is used to separate larger molecules (300-10,000 base pairs).
DNA Electrophoresis

- Separation $\Delta L = \Delta \mu E t$
- Resolution of separation is measured by planes $N$,
  - $N = (\# \text{ of distinguishable bands within the length of the gel})^2$
  - $N = \mu V/2D$
    - $D$ is the diffusion coefficient

- Higher voltages increase resolution but Joule heating is an issue and needs to be considered
- Separation can also be done in capillaries since higher fields can be used (higher velocities and shorter times)
DNA Electrophoresis

Diagram showing the process of DNA electrophoresis:
- Mixture of DNA fragments of different sizes.
- Power source connected to anode and cathode.
- Gel with glass plates.
- Longer fragments.
- Shorter fragments.
- Completed gel.

Image of a person working on a gel electrophoresis experiment.

Graph showing nucleotide pairs and chromosome numbers.
DNA Electrophoresis in a Chip

- Small sample size
- Higher fields, higher velocities
- Faster results

Mastrangelo, Burns, Univ. of Michigan

Fig. 22. Injection and separation of DNA fragments on integrated device. The channel is 500 ×50 μm² (50 bp ladder, 0.13 μg/μL, SYBR Green, 8 V/cm, 10% T: 2.6% polyacrylamide) [136].
Dielectrophoresis

Simplest approximation:

\[
F = 2\pi\varepsilon_0\varepsilon_m r^3 \text{Re}\left[f_{CM}\nabla|E_{RMS}|^2\right]
\]

\[
f_{CM}(\varepsilon_p, \varepsilon_m) = \frac{\varepsilon_p - \varepsilon_m}{\varepsilon_p + 2\varepsilon_m}
\]

\[
\varepsilon_p = \varepsilon(\omega)
\]
Dielectrophoresis on Interdigitated Electrodes

Polystyrene beads: $\varepsilon_p < \varepsilon_m \rightarrow$ negative DEP

Cells: $\varepsilon_p < \varepsilon_m \rightarrow$ Negative DEP
Cells: $\varepsilon_p > \varepsilon_m \rightarrow$ Positive DEP

Interdigitated electrodes on a chip

A Dielectrophoretic Filter

Schematic of the device cross-section
X-component of DEP force at different heights

- Bead diameter: 0.7 µm
- Bead conductivity: 2e-4 S/m
- Relative permittivity of bead: 2.6
- Bead density: 1.05 g/cm³
- Medium (DI water) conductivity: 2.5 S/m
- Relative permittivity of medium: 80
- Medium density: 1.0 g/cm³
- Voltage: 1Vrms
- Frequency: 580KHz
Y-component of DEP force at different heights

![Graph showing Y-component of DEP force at different heights. The x-axis represents the horizontal position of the bead in micrometers, and the y-axis represents the vertical DEP force in Newtons.]
Forces on a particle in a micro-fluidic flow

- 1. DEP Force
- 2. Sedimentation Force

\[ F_{\text{sedi}} = \frac{4}{3} \pi R^3 (\rho_p - \rho_m) g \]

- 3. Hydrodynamic Drag Force:

\[ F_{\text{HD-drag}} \approx 6\pi k R \eta (\nu_m - \nu_p) \]

- Assume a parabolic laminar flow profile:

\[ \nu = 6\langle \nu \rangle \frac{x}{h} \left(1 - \frac{x}{h}\right) \]

\[ \langle \nu \rangle = \frac{U}{wh} \]

- 4. Hydrodynamic lifting force

\[ F_{\text{HD-lift}} \approx 0.153 R^2 \eta \left. \frac{1}{(x - R)} \frac{d\nu_m}{dx} \right|_{x=0} \]

- Two orders of magnitude smaller than typical DEP lifting force
- Neglected here
Trapping of beads (- DEP) and microorganisms (+ DEP)

Holding voltage of the negative DEP traps on interdigitated electrodes versus flow rate for polystyrene beads with different diameters in DI water (conductivity ~1.5 μS/cm) at 1MHz.

- Simulation
- Experiments

- 2.38 μm bead
- 5.44 μm bead

Flow rate (μl/min): 0, 0.02, 0.04, 0.06, 0.08, 0.1, 0.12

Voltage^2 (V^2p-p): 0, 50, 100, 150, 200, 250, 300, 350

- Vaccinia virus
- B. Cereus spores
- Listeria innocua bacteria

H. Li, Y. Zheng, D. Akin, R. Bashir, submitted to IEEE/ASME JMEMS
Dielectrophoretic Trapping of *Vaccinia* virus (positive DEP)

- Fluorescent imaging of nano-scale virus particles (Vaccinia virus and Human Corona Virus)
- Trapping of viruses in DEP filters
- Dual labeling of viruses with fluorescent dyes

Virus Size ~ 250x350nm
Picture taken at: 10Vpp, 1MHz, DI water ~1.5μS/cm, flow rate ~0.1μl/min

Release voltage vs. diameter for particle collecting the electrode edge, considering the Brownian motion.

Equivalent external force due to Brownian motion is estimated to be $20kT/\Delta d \approx 8.2 \times 10^{-15} \text{ N},$

$k$ is Boltzmann constant, $T$ is the absolute temperature in Kelvin, and $\Delta d$ is the trap width, assumed to be $10 \mu \text{m}$

Polarization factor $= 0.5,$ flow rate $0.1 \mu \text{m/min},$ in the channel with cross-section $350 \times 11.6 \mu \text{m}^2,$ interdigitated electrodes with $23 \mu \text{m}$ width and $17 \mu \text{m}$ spacing

$$V^2 2\pi r^3 \text{Re} [f_{CM}] \nabla E^2 = 36\pi \eta kr \left( \frac{r}{h} - \frac{r^2}{h^2} \right) \approx 36\pi \eta k \frac{r^2}{h}$$

$$V = \sqrt{\frac{18\eta k}{r\nabla E^2 \text{Re} [f_{CM}] h}}$$
Micro-fluidic Characterization

- Micro-Particle Imaging Velocimetry (µPIV)

Wereley, et al. Purdue

Gomez, et al. 2001
Key Topics

- Biochips/Biosensors and Device Fabrication
- Cells, DNA, Proteins
- Micro-fluidics
- **Biochip Sensors & Detection Methods**
- Micro-arrays
- Lab-on-a-chip Devices
Biochip Sensors

- Detect cells (mammalian, plant, etc.), microorganisms (bacteria, etc.), viruses, proteins, DNA, small molecules
- Use optical, electrical, mechanical approaches at the micro and nanoscale in biochip sensors
Sensing Methods in BioChips

Mechanical Detection
Surface Stress Change Detection

\[ \Delta z = 4 \left( \frac{l}{t} \right)^2 \left( 1 - \frac{v}{E} \right) (\Delta \sigma_1 - \Delta \sigma_2) \]

- \( \Delta z \) = deflection of the free end of the cantilever
- \( L \) = cantilever length
- \( t \) = cantilever thickness
- \( E \) = Young’s modulus
- \( v \) = poisson’s ratio
- \( \Delta \sigma_1 \) = change in surface stress on top surface
- \( \Delta \sigma_2 \) = change in surface stress on bottom surface

Mass Change Detection

\[ f = \frac{1}{2\pi} \sqrt{\frac{k}{m}} \]

\[ \Delta m = \frac{k}{4\pi^2} \left( \frac{1}{f_1^2} - \frac{1}{f_1^2} \right) \]

- \( k \) = spring constant
- \( m \) = mass of cantilever
- \( f_0 \) = unloaded resonant frequency
- \( f_1 \) = loaded resonant frequency

Electrical Detection

Conductometric Detection

Amperometer Detection

Potentiometric Detection

Optical Detection

DNA detection on chip surfaces

Protein detection on chip surfaces

Cell detection on chip surfaces
1. Microcantilever Stress Sensors

**Mechanical Detection**

Surface Stress Change Detection

\[ \Delta z = 4 \left( \frac{l}{t} \right)^2 \frac{(1 - \nu)}{E} (\Delta \sigma_1 - \Delta \sigma_2) \]

- \( \Delta z \) = deflection of the free end of the cantilever
- \( L \) = cantilever length
- \( t \) = cantilever thickness
- \( E \) = Young’s modulus
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- \( \Delta \sigma_1 \) = change in surface stress on top surface
- \( \Delta \sigma_2 \) = change in surface stress on bottom surface

0.2µm thick, 100µm long, silicon cantilevers
Microcantilever Stress Sensors

IBM Zurich Research: DNA Detection

Microcantilever Stress Sensors

Detection of PSA, Prostate Specific Antigen (cancer marker protein in blood)

- PSA ~ 30kDa ~ 30 x 1e3 x 1.66e-24gm
- In 1ng/ml ~ 2e10 molecules/ml
- Area of 20um x 60um, each protein 10nm x 10nm → ~1e8 proteins

Wu et al, Nature Biotechnology, 19, September 2001

Deflections have been measured with a resolution of \(0.4 \times 10^{-12}\) m.*
Polymer/Silicon Cantilever Sensors

- Environmentally sensitive micro-patterned polymer structures on cantilevers
- Hydrogel patterned on cantilever and then exposed to varying pH

- $\Delta \text{pH} = 1 - 10\text{e}-5$
- pH = 6.5 $\rightarrow$ ~ 1.9e5 H$^+$ in 1000$\mu$m$^3$
- $\Delta \text{pH} = 5\text{e}-4$ $\rightarrow$ change of ~ 150 H$^+$

2. Microcantilever Mass Sensors

Unloaded Resonant Frequency:

\[ f_0 = \frac{1}{2\pi} \sqrt{\frac{k}{m}} \]

Spring constant for a rectangular shaped cantilever beam:

\[ k = \frac{Et^3w}{4l^3} \]

Loaded Resonant frequency:

\[ f_1 = \frac{1}{2\pi} \sqrt{\frac{k}{m + \delta m}} \]

\[ \Delta m = \frac{k}{4\pi^2} \left( \frac{1}{f_1^2} - \frac{1}{f_0^2} \right) \]

- \( k \) = spring constant
- \( m \) = mass of cantilever
- \( f_0 \) = unloaded resonant frequency
- \( f_1 \) = loaded resonant frequency

Mass Change Detection

PSD comparing measurements done using thermal and piezo driven

![Diagram](image-url)
Detection of Bacterial Mass

\[ \omega_o^2 = \frac{k}{m} \]

Detection of Listeria Cell Mass

Non-specific binding of *Listeria innocua* bacterial cells to a cantilever beam

\[ m^* = \left( \frac{x}{L} \right) m \]

Minimum Detectable Mass

\[ \delta m = 0.24 \cdot l \cdot w \cdot t \cdot \rho \cdot \left( \frac{1}{1 - \frac{2\pi\delta f (0.98)l^2}{t} \sqrt{\frac{\rho}{E}}} \right)^2 - 1 \]

- E. Coli ~ 1-10 \times 10^{-14} g
- Virus Mass Range
- 100kDa Protein
- DNA bp ~ 10^{-21} g

Width, \( w = 1 \mu m \)
\( \Delta f = 1 \text{kHz} \)
Thickness = 10 nm
Thickness = 500 nm

Minimum detectable mass (in g) vs. resonant frequency (in Hz)
Minimum Detectable Mass

- The frequency measurement is limited by thermo-mechanical noise on the cantilever beam.
- Minimum Detectable Frequency, \( \Delta f, \text{min} = \)
  \[
  \frac{1}{A} \sqrt{\frac{f_0 k_B T B}{2 \pi kQ}}
  \]
- Minimum Detectable Mass, \( \Delta m, \text{min} = \)
  \[
  \frac{1}{A} \sqrt{\frac{4 k_B T B}{Q} m_{\text{eff}}^{5/4}}
  \]
  \[
  \frac{k^3}{k^{3/4}}
  \]
- \( k_B \) = Boltzmann constant
- \( T \) = Temperature in Kelvin
- \( B \) = Bandwidth measurement, (~ 1 kHz)
- \( Q \) can increase by 100X by driving the cantilevers

![Graph showing Minimum Detectable Mass for Silicon Cantilever Beams](graph)

- Width of cantilever beam = 1 \( \mu m \)
- Thickness of cantilever beam = 10 nm

Length of cantilever beam (\( \mu m \))

Minimum Detectable Mass (g)
Fabrication Process Flow

Materials Legend

- Silicon
- Silicon dioxide
- PECVD Silicon dioxide

Cross-sectional view

Top view

(a)

(b)

(c)

(d)

(e)

Etch Window

Bottom of channel
SEM Pictures of Cantilevers

Frequency Shift vs. No. of Particles

- 1 kHz frequency shift for 160 ag
- Sensitivity ~ 6.3 Hz/ag

Average mass of Vaccinia Virus ~ 9.5fg
Work on going to integrated concentration elements
Integrated Abs on cantilevers

To probe the amount of thiolate binding to the Au contacts, we have measured the frequency spectra before and after the thiolate self-assembly. Figure 14 shows the measured shift in the resonant frequency for DNP-PEG4-C11thiol binding on 50- and 400-nm-diam Au contacts. The measured frequency shifts were 125 Hz and 1.10 kHz, corresponding to calculated masses of 6.3 and 213.1 ag, respectively.

FIG. 14. Experimentally measured frequency spectra before (solid line) and after (dashed line) the adsorption of the thiolate on (a) 50- and (b) 400-nm-diam Au contact. Rectangular beam dimensions were \( l = 10 \mu m \), \( w = 1 \mu m \), and \( t = 250 \) nm.

Electrical/Electrochemical Detection

1. amperometric biochips, which involves the electric current associated with the electrons involved in redox processes,

2. potentiometric biochips, which measure a change in potential at electrodes due to ions or chemical reactions at an electrode (such as an ion Sensitive FET), and

3. conductometric biochips, which measure conductance changes associated with changes in the overall ionic medium between the two electrodes.
1. Amperometric Detection

\[
\beta\text{-D-Glucose} + \text{O}_2 + \text{H}_2\text{O} \rightarrow \text{D-gluconic acid} + \text{H}_2\text{O}_2
\]

hydrogen peroxide is reduced at -600mV at Ag/AgCl anode reference electrode.

- Detection of Glucose, Lactate, Urea, etc.
- Enzyme entrapped in a gel
- Surface regeneration and sensor reusability

Perdomo, et al., 2000
Detection of DNA Hybridization

- Capture probes are attached to electrodes.
- Target DNA binds to complementary probes.
- DNA sequences, called signaling probes, with electronic labels attach to them (ferrocene-modified DNA oligonucleotides, E1/2 of 0.120 V vs. Ag/AgCl, act as signaling probes).
- Binding of the target sequence to both the capture probe and the signaling probe connects the electronic labels to the surface.
- The labels transfer electrons to the electrode surface, producing a characteristic signal.

Drummond, Hill, Barton, Nature Biotech, v21, n10, Oct 2003, p1192
http://www.motorola.com/lifesciences/esensor/tech_bioelectronics.html
2. Potentiometric Sensors

- ISFETs, ChemFETs, etc.
- Potential difference between the gate and the reference electrode in the solution
- Change in potential converted to a change in current by a FET or to a change in capacitance in low doped silicon
- Gate material is sensitive to specific targets
- pH, Ions, Charges
Nanoscale pH Sensors

- Label Free !!
- Detection of pH change
- Detection of protein binding

Integrated Silicon Nanowire Sensors

Objectives:
- Bio-sensors with electronic output
- Capability of dense arrays integrated with ULSI silicon
- Direct Label Free Detection of DNA and Proteins

Electrical response of the device upon exposure to oxygen (red dotted lines) and nitrogen (blue solid lines)

Field Effect Sensing of DNA

3. Conductometric Biochips

- Conductometric sensors measure the changes in the electrical impedance between two electrodes, where the changes can be at an interface or in the bulk region and can be used to indicate biomolecular reaction between DNA, Proteins, and antigen/antibody reaction, or excretion of cellular metabolic products.
Nanoparticle Mediated DNA Detection

- Au nanoparticles assemble between two electrodes if DNA is hybridized
- Silver staining of the Au nanoparticles
- Conductance changes between micro-scale electrodes indicate DNA hybridization
- Sensitivity of $5 \times 10^{-13}$ M shown

Micro-fluidic Devices for Conductance Detection of Bacterial Metabolism

- Detection of Cell Growth by measuring their metabolic activity in micro-fluidic devices

![Image of micro-fluidic device]

**Electrode-Electrolyte Interface Model:**

\[ Z_w = \frac{1}{(j\omega)^n B} \]

- Commercially available Dynal magnetic beads with Listeria Antibodies
- *Listeria Monocytogenes* concentration of about $5 \times 10^6$ cfu/ml
- Beads concentration of about $3 \times 10^7$ beads/ml
- Capture done for 30 min
- About 80 beads captured inside the measurement chamber in the chip
- Total admittance ($1/\text{impedance}$) at 1kHz vs. time

4. Cell-Based Sensors/Biochips

- The transductions of the cell sensor signals maybe achieved by:
  - the measurement of transmembrane and cellular potentials,
  - impedance changes,
  - metabolic activity,
  - analyte inducible emission of genetically engineered reporter signals, and
  - optically by means of fluorescence or luminescence.

5. Micro/Nano-scale Coulter Counter

Trans chamber

Cis chamber
Micro-pore for cellular studies

- Micro-devices for single cell characterization – utilize the charge properties
- Micro-fabricate a pore where single entity can pass

Optical Picture of a Pore in a micro-fabricated filter

Cross section of micro-fabricated pore
Microscale Coulter Counter

I-T Diagram for Live Listeria, 1e8/ml, V = 40 V, 05112010

Velocity (cm/s) vs. Electrical Field (V/cm)

Live *Listeria innocua* with pore

Mobility = \(-5e-7 \text{ cm}^2/\text{V-s}\)

\[ v = -5e-7 \times E - 0.007; R^2=0.814 \]

Nanoscale DNA Coulter Counter

- α-hemolysin channel, a biological protein based-pore, was utilized.
- Pore size is 2.6 nm.
- Both RNA and DNA molecules were observed traversing the nanochannel.

Fabrication Techniques

- Solid-state based nanopore. Made in silicon nitride membrane.
- Pore size: 3 nm and 10 nm.
- The relation among DNA lengths and translocation times and applied biases were determined.


TEM of Li’s nanopore. b. DNA measurement setup in Li’s work. From Li et. al. Nature Materials, 2003
DNA Translocation

Current fluctuations when DNA was passing through the pore

Histograms of relation among DNA lengths, translocation times and applied biases.

Li et. al. 2003
Start with a (100) 4 inch SOI wafer. Thickness: 525 um. SOI: 250 nm, Buried oxide layer: 400 nm.

1. Grow thermal oxide on wafer surface and open etch window to etch through the handle layer. Etch stops on buried oxide layer.

2. Ox 1000 A
   Si 1400 A
   Ox 4000 A
   Grow thermal oxide on wafer surface and open etch window to etch through the handle layer. Etch stops on buried oxide layer.

3. Ox 1000 A
   Si 1400 A
   Ox 4000 A
   On SOI layer, open another etch window to etch through the SOI layer. Etch stops on buried oxide layer.

4. Remove buried oxide layer and regrow 100 nm thermal oxide.

5. Shrink the pore to 3–5 nm by TEM.
Pore shrinking and shape changing (After Thermal Oxidation, Oxide Thickness = 50 nm)

Slopes in the plot are the shrinkage rates. Different initial pore size had different shrinkage rates.


Explanation – Minimization of Surface Energy

**Surface free energy:**

\[ \Delta F = \gamma \ \Delta A = 2 \pi \ \gamma \ \left( rh - r^2 \right) \]

where \( \gamma \) is the surface tension of the fluid, \( \Delta A \) is the change in surface area.

\( r \) is the radius of the pore right after the final oxidation,

\( h \) is oxide thickness.

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From Storm et. al. 2003

The shrinkage/expanding of pores with different radii and oxide thicknesses.

<table>
<thead>
<tr>
<th>Sample name</th>
<th>Average radius of the pore ( r ) (nm)</th>
<th>Grown oxide thickness ( d ) (nm)</th>
<th>The ratio of ( r/d )</th>
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<tr>
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<td></td>
<td></td>
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<td>103003.4 S</td>
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Integrated Optical Detection