Key Topics

- Biochips/Biosensors and Device Fabrication
- Cells, DNA, Proteins
- Micro-fluidics
- Biochip Sensors & Detection Methods
- Micro-arrays
- Lab-on-a-chip Devices
1. Fluorescence: Markers that emit light at specific wavelengths and enhancement, or reduction (as in Fluorescence Resonance Energy Transfer) in optical signal can indicate a binding reaction.

2. Chemiluminescence: Generation of light by the release of energy as a result of a chemical reaction.
   - Light emission from a living organism is termed bioluminescence (sometimes called biological fluorescence),
   - light emission which take place by passage of electrical current is designated electrochemiluminescence.
DNA Hybridization in Microarrays

- Basis for detection of unknown nucleotides
- Example: Bio-chips for identification of DNA
  - Hybridization of an unknown, fluorescently tagged strand with a many known strands - reaction will determine the sequence of the unknown (or vice versa)
  - Strands can be lithographically (Affymetrix) or electronically (nanogen) defined at a specific location
Electronic Placement of DNA Probes

(a) Metal Contact
Capture probes
Attachment layer

(b) Metal Contact
Capture probes
Attachment layer

(c) Metal Contact
Attachment layer
Target probe (w. fluo. Label)
Capture probes

(d) Metal Contact
Attachment layer
Capture probes

(e) Metal Contact
Attachment layer
Capture probes

(f)
DNA Biochips (Nanogen)

Technology Features:

• Biochips for DNA detection, antigen-antibody, enzyme-substrate, cell-receptor and cell separation techniques.
• Takes advantage of charges on biological molecules.
• Small sequences of DNA capture probes to be electronically placed at, or "addressed" to, specific sites on the microchip.
Hybridization.

- A test sample can be analyzed for the presence of target DNA molecules by determining which of the DNA capture probes on the array bind, or hybridize, with complementary DNA in the test sample.

- Fluorescence output

www.nanogen.com
Light Directed DNA Synthesis on a chip (Affymetrix)

Light Directed DNA Synthesis on a chip (Affymetrix)

Table 1. Combinatorial synthesis of polynucleotide probe arrays

<table>
<thead>
<tr>
<th>Probe Length</th>
<th>Chemical Steps</th>
<th>Number of Possible Probes</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>16</td>
<td>256</td>
</tr>
<tr>
<td>8</td>
<td>32</td>
<td>65536</td>
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<tr>
<td>16</td>
<td>64</td>
<td>~4.3×10^9</td>
</tr>
<tr>
<td>20</td>
<td>80</td>
<td>~1.1×10^{12}</td>
</tr>
</tbody>
</table>
Light Directed DNA Synthesis on a chip (Affymetrix)

- Fluorescence detection
- Ultimately will limit size of pixel in array

Applications:
- Polynucleotide array
- HIV resequencing
- mRNA expression monitoring
Protein Arrays

- Protein-Protein Interactions
- Protein small molecule interactions
- Derivatized substrates – glass, plastics
- High Throughput screening of chemical compounds

Note: Sensor Arrays

• Any of the individual sensors described earlier can be used in an array format to make micro/nano sensor arrays.
• The sensors in the array need addressing
• Each sensor can be functionalized with different bio-receptor molecule to detect different entities
• Examples, cantilever array, electrochemical detection in electrode arrays, cellular arrays for chemical detection, etc.
Lab-on-a-Chip/Integrated Devices

- Single chip device for DNA electrophoresis
- Sample loading and metering
- PCR on a chip (faster temperature cycling due to reduced thermal mass)
- Gel electrophoresis on chip

CD Format Biochips

- Micro-fluidic devices on a CD type platform using centrifugal and capillary forces for liquid transport
- Cheap plastic CDs
- Optical detection systems

Cellular Analysis on Chip

- Plastic biochips using hydrodynamic transport of cells
- Electric field mediated lysing
- Fluorescence detection (off-chip detectors)
- Analysis time of about 10 cells/minute
Polymer μSensor and Actuator

Process flow for the preparation of a hydrogel valve.

Hydrogel valve designs (2D and 3D)

A biomimetic valve based on bistrip hydrogel.

Design of the 96-channel CAE microplate and radial scanner. Mask pattern used to form the 96 straight channel radial microplate on a 150-mm diameter wafer.
Integrated Systems for Study of Microorganisms and Cells

“Lab on a Chip” for Enabled by BioMEMS and Bionanotechnology
Micro-fluidic Polymer Devices for Culture Bacteria and Spores

- Growth of bacteria inside a micro-fluidic polymer chip
- Rapid detection and reduced time to result

Woo-Jin Chang, Demir Akin, Miroslav Sedlek, Michael Ladisch, Rashid Bashir, "Hybrid Poly(dimethylsiloxane) (PDMS)/Silicon Biochips For Bacterial Culture Applications", Biomedical Microdevices 5:4, 281-290, 2003,
Future Directions

• Integrated device for analysis of single cells – applications and fundamental science

• Building cell by cell/tissue engineering using micro and nano fabrication techniques

• Integrated diagnostics and therapeutics (drug delivery)

• Tools for genetic manipulation of microorganisms and viruses – synthetic biology
Acknowledgements

Research Scientists/Post-docs:
• Dr. Demir Akin
• Dr. Dallas Morisette
• Dr. Rafael Gomez

Graduate Students:
• Sangwoo Lee
• Haibo Li
• Amit Gupta
• Hung Chang
• Yi-Shao Liu
• Samir Iqbal
• Oguz Elibol
• Angelica Davilia
• Kidong Park

Industries:
• BioVitesse, Inc. Co-Founder

Funding Agencies
• US Department of Agriculture (Food Safety Engineering Center)
• NASA Institute on Nano-electronics and Computing
• NSF, NSF Career Award
• National Institute of Health
• DARPA Nanotechnology Research
• Discovery Park at Purdue University

Faculty Collaborators
– Prof. D. Bergstrom (Med Chem)
– Prof. A. Bhunia (Food Science)
– Prof. M. Ladisch (Ag& Bio Engr)

Special Thanks
– Prof. S. Broyles (BioChem)
– Profs. D. Datta, D. Janes (ECE, NASA INAC), J. Cooper (BNC)