
Building College-University Partnerships for Nanotechnology Workforce Development

# Materials Modification in Nanotechnology

## DNA and Protein Analysis using Nanotechnology

**Part 2**

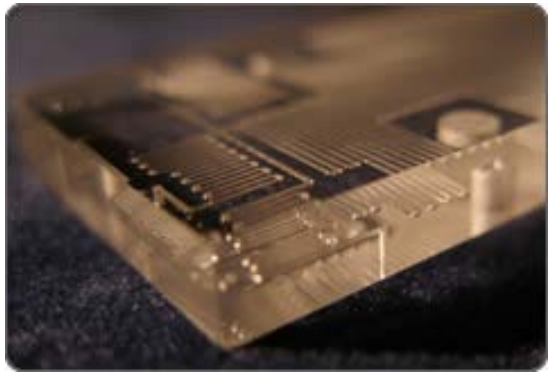
**Terence Kuzma**

# Outline

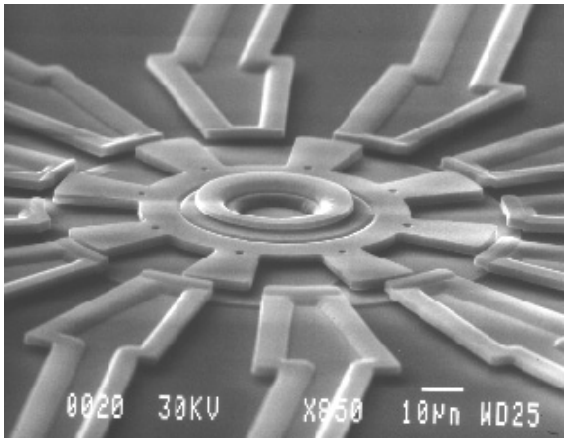
- Micro array Technology
- Microfluidics Overview
- Common Materials and Processes

# Common Materials

- $SiO_2$ – etching and stacking (most used in the recent past, but a bit expensive driving alternatives)
- Metals – Additive and Subtractive Processes



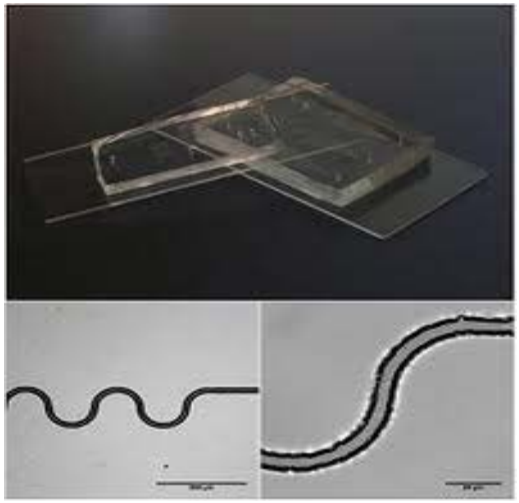
http://www.energi-tech.co.uk/microfluidics.htm




http://www.tmi.vu.lt/legacy/pfk/funkc_darinia i/nanostructures/nano_robots.htm

# Common Materials

- Polymers – physical deformation and shaping
- Paper – substrate used for flow and cheap



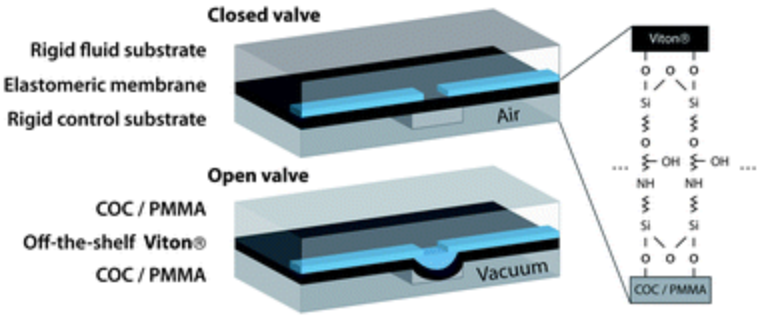
http://www.websters-online-dictionary.org/definitions/Microfluidics?cx=partner-pub-0939450753529744%3Av0qd01-tdlq&cof=FORID%3A9&ie=UTF-8&q=Microfluidics&sa=Search#922

# Common Materials

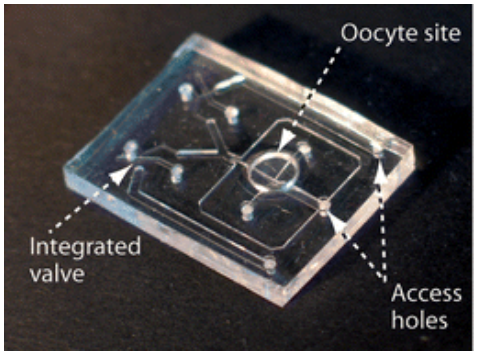
- $SiO_2$ – Plasma etching or chemical etching
  - Expensive, dangerous
- Metals – sacrificial layers
  - Expensive (materials wasted), much more complex
- Polymers – photopatterning, molding, embossing
  - Inexpensive, easy to mass produce
- Paper – Active or passive results
  - Inexpensive, ease of flow, generally slow

# Common Polymer Materials

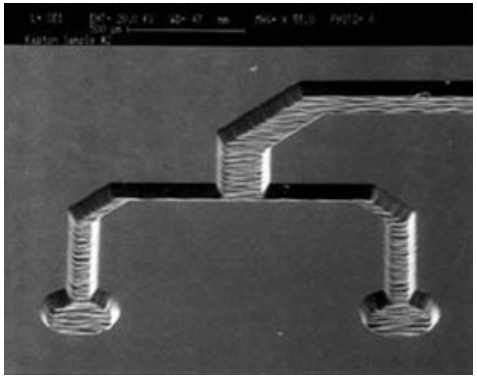
- Polymers
- PMMA, PDMS, Polyimides, SU-8



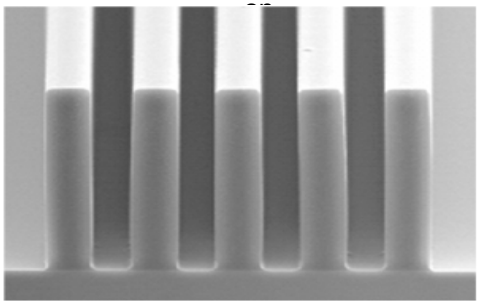

http://www.nanotechclearinghouse.com/module-NewsFeeds-view-option-viewfeed-fid-97-startnum-123.html




http://www.rsc.org/Publishing/Journals/lc/article.asp?Type=Issue&Journalcode=LC&Issue=11&SubYear=2008&Volume=8&Page=0&GA=



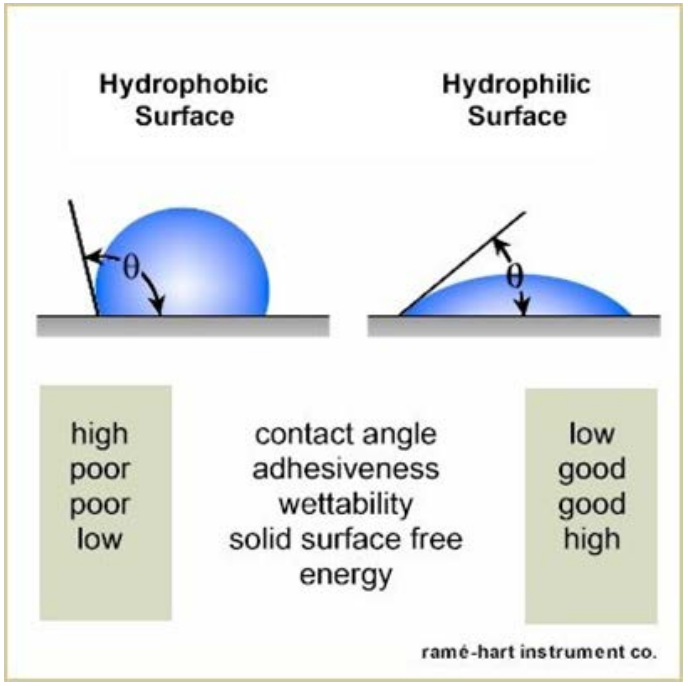
http://medicaldesign.com/engineering-prototyping/research-development/biomems-evolution-advancement-20091201/




http://www.nkc-mems.com/product_e/su8_3000.html

# Common Materials

- PDMS
- Non-toxic, optically transparent, surface is easily modified
  - Naturally hydrophobic, Oxygen plasma treatment renders it hydrophilic
  - Useful for fluid flow and surface bonding
  - Hyperelastic
  - Biocompatible




http://www.ramehart.com/contactangle.htm.

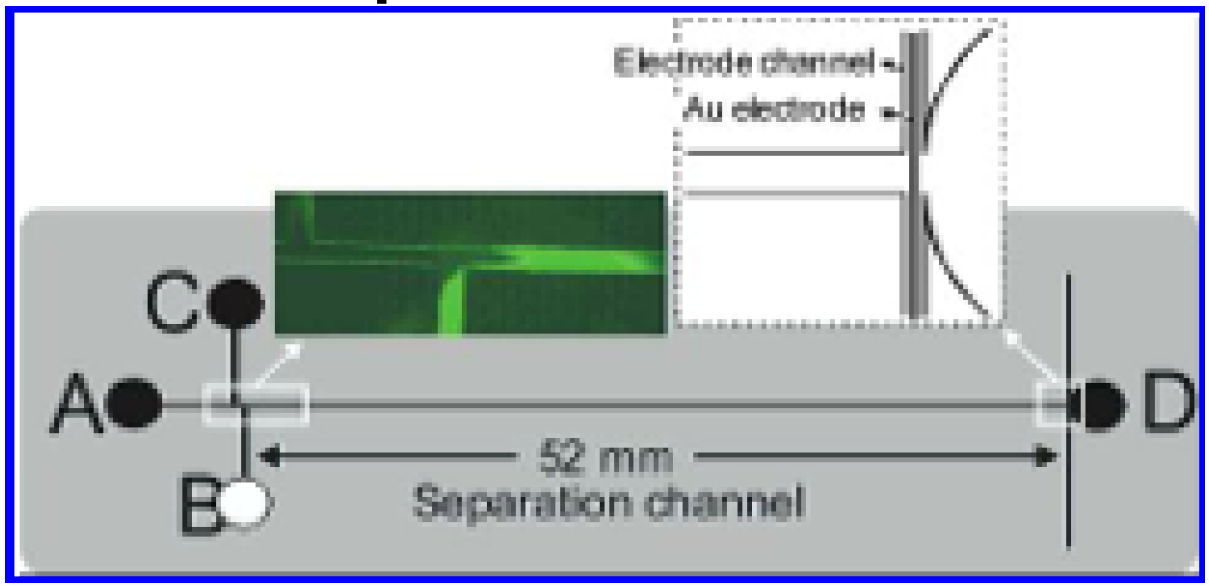
# Common Polymer Materials

- PMMA – thermoplastic, used for molding, opaque to UV light
- PDMS – thermoset, non-toxic, optically transparent, cured
- Polyimides – thermoset, used for MEMS, high strength, dielectric strength, heat resistance, photopatterned
- SU-8 – typically sacrificial layer, high mechanical strength, high aspect ratios, negative photoresist

# Common Polymer Materials

| Compared Fields | Polymers | | | |
|---|---|---|---|---|
| | Polyimides | PMMA | PDMS | SU-8 |
| **Primary Manufacturer** | HD-Microsystems | Plaskolite INC | Dow Corning | MicroChem Corp. |
| **Brand Name** | HD-4100 series | Optix Acrylite | Sylgard 184 | SU-8 |
| **Approximate Cost** | $2,185/kg | $2.70/kg | $16.40/kg | $500/kg |
| **Optical Transparency** | Yes | Yes (opaque to UV) | Yes | Yes (>340 nm) |

# Pulsed Amperometric Detection




Capillaryelectrophoresis chip with integrated pulsed amperometric detection. Channels: 50 μm width, 50 μm deep. Sample loop: 580 μm long. The diagram shows the electrode position at the end of the separation channel and the connections to the electrochemical analyzer.

. Henry, “Direct Determination of Carbohydrates, Amino Acids, and Antibiotics by Microchip Electrophoresis with Pulsed Amperometric Detection” Anal. Chem. 2003, 75, 4778-4783

# Pulsed Amperometric detectors

- ELECTROCHEMICAL DETECTORS
- Pulsed Amperometric Detection (PAD)
- This follows established electrochemical liquid detector technology
- This detector is based on the measurements of the current resulting from oxidation/reduction reaction of the analyte at a suitable electrode. Since the level of the current is directly proportional to the analyte concentration, this detector could be used for quantification.
- Can be used for the separation and detection of underivatized carbohydrates, amino acids, and sulfur-containing antibiotics in an electrophoretic microchip

http://hplc.chem.shu.edu/NEW/HPLC_Book/Detectors/det_elec.html

# Pulsed Amperometric detectors

•*Direct Determination of Carbohydrates, Amino Acids, and Antibiotics by Microchip Electrophoresis with Pulsed Amperometric Detection (2003)*

- Lab on a chip configuration for microchip electrophoresis with pulsed amperometric detection (PAD)
- The configuration consists of a layer of polydimethylsiloxane (PDMS) that contains the microfluidic channels, reservoirs, and a gold microwire, sealed to a second layer of polydimethylsiloxane.
- The separation and the direct detection of underivatized carbohydrates, amino acids, and two antibiotics were achieved by optimizing the electric field, the electrolyte composition, and the PAD parameters.
- The inclusion of a Au wire microelectrode was also demonstrated, showing very good stability and mass limits of detection in the femtomole range.

• . Henry, “Direct Determination of Carbohydrates, Amino Acids, and Antibiotics by Microchip Electrophoresis with Pulsed Amperometric Detection” Anal. Chem. 2003, 75, 4778-4783

# Pulsed Amperometric detectors

| **Pulsed Amperometric Detection Parameters for Detection of Carbohydrates, Amino Acids and Antibiotics** | | | |
|---|---|---|---|
| *Test Material* | *Clean* | *Reactivate* | *Detect* |
| carbohydrates | +1.4 V | -0.5 V | +0.7 V |
| amino acids | +1.8 V | -0.5 V | +0.7 V |
| antibiotics | +1.8 V | -0.5 V | +0.5 V |
| Cleaning, 0.05 s; reactivation, 0.025 s; and detection, 0.15 s. | | | |

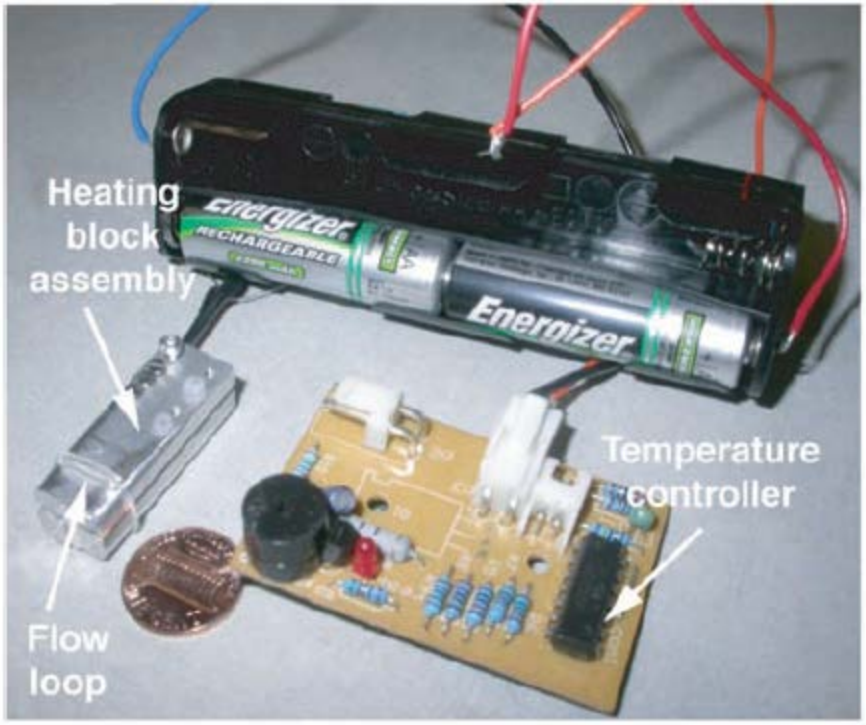
. Henry, “Direct Determination of Carbohydrates, Amino Acids, and Antibiotics by Microchip Electrophoresis with Pulsed Amperometric Detection” Anal. Chem. 2003, 75, 4778-4783

# A POCKET-SIZED CONVECTIVE PCR THERMOCYCLER

- Many diagnostic assays rely on the polymerase chain reaction (PCR), which requires thermocycling and conventional macro instruments that are relatively slow and consume considerable electrical power to perform repeated heating and cooling steps
- Microfluidic thermocycling system that harnesses natural convection phenomena to amplify DNA rapidly by the PCR in a greatly simplified format.
- A key element of this design is an architecture that allows the entire thermocycling process to be actuated pseudo-isothermally by simply maintaining a single heater at a constant temperature, thereby enabling a pocket-sized battery-powered device to be constructed at a cost of about US$10.

Agrawal, Nitin, Yassin A. Hassan, and Victor M. Ugaz. "A Pocket-Sized Convective PCR Thermocycler." *Angewandte Chemie International Edition* 46.23: 4316-4319

# A Pocket-Sized Convective PCR Thermocycler

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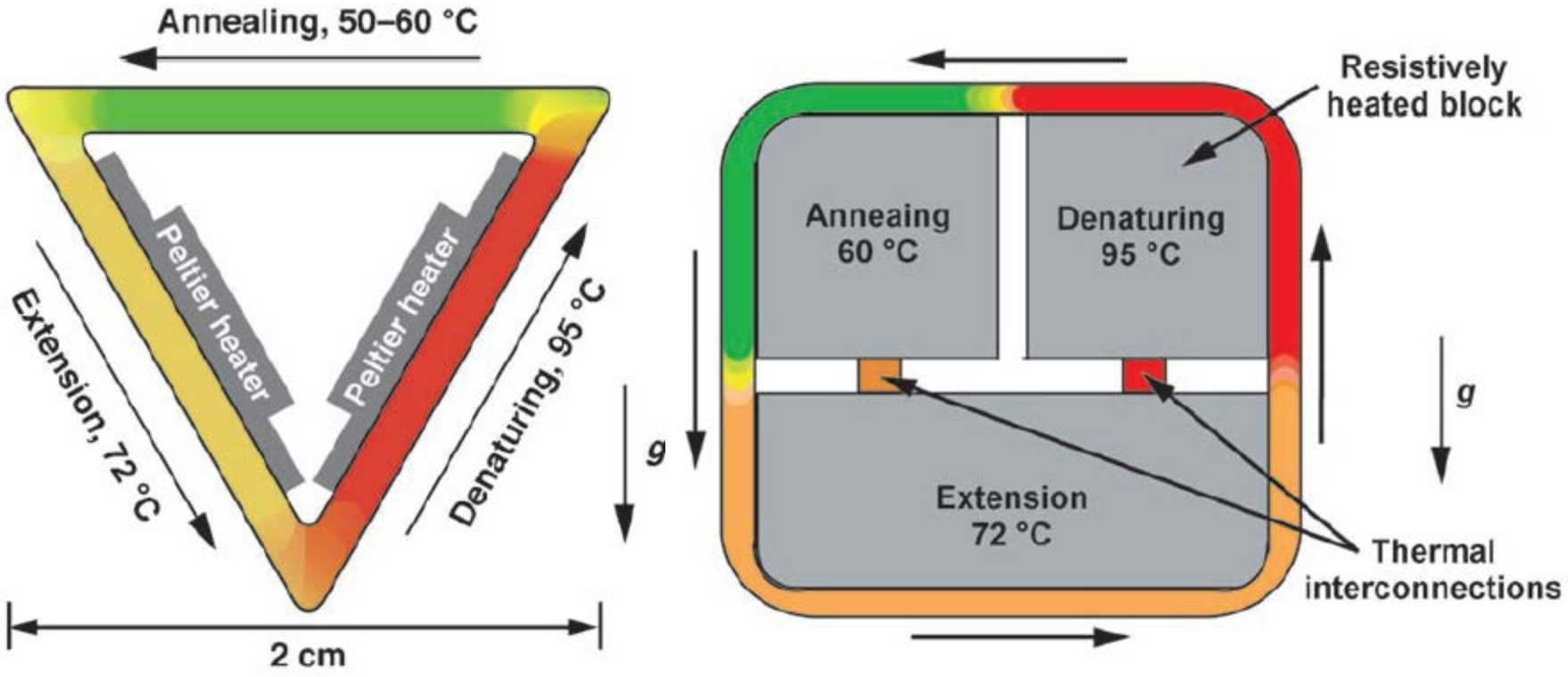


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- **Paper – Active or passive results**
  - **Inexpensive, ease of flow, generally slow**

# Paper based systems

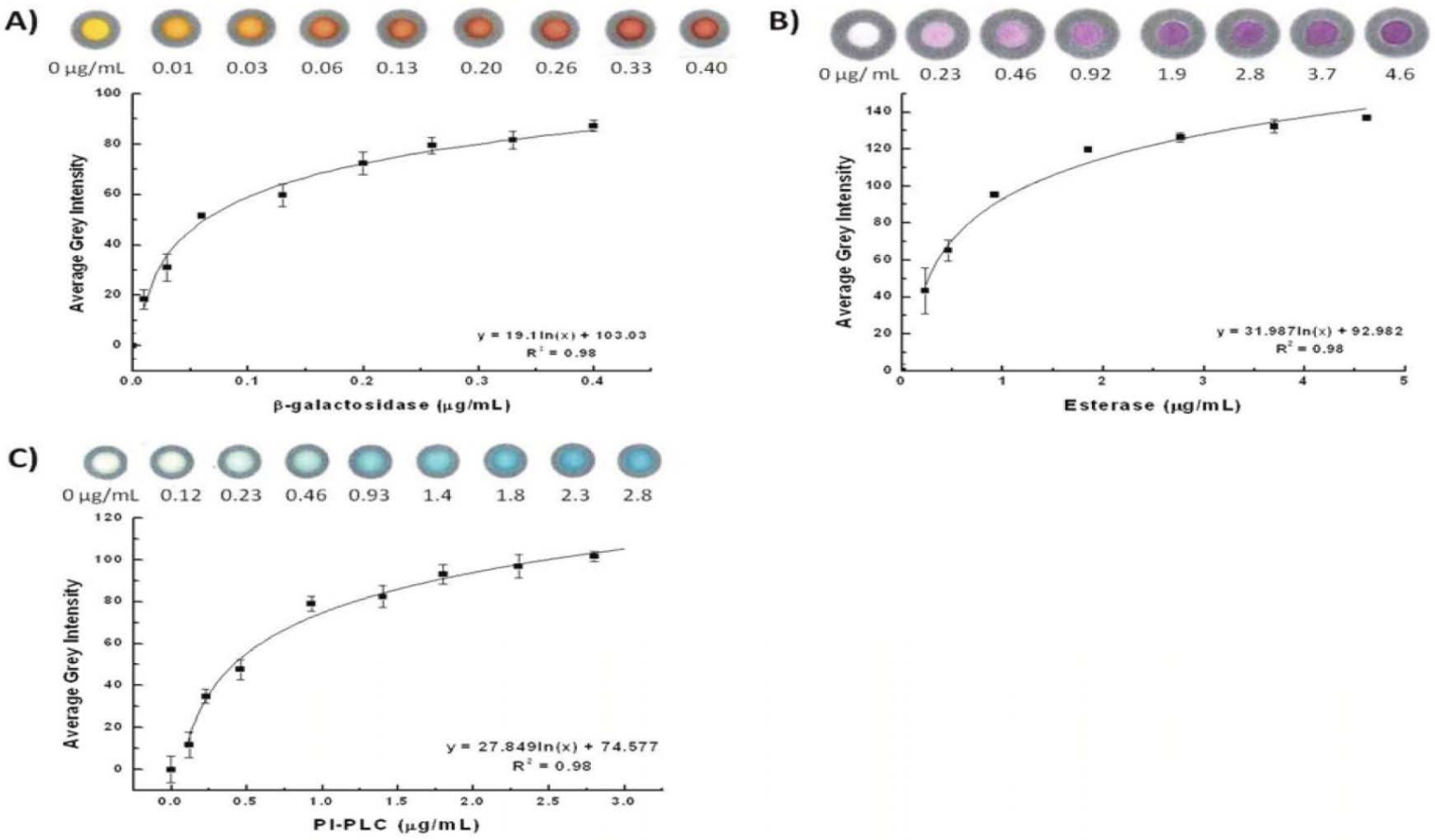
- 1988 The first commercial immunoassay, Unipath launches home pregnancy test kits
- 1995 US Patent 5,409,664 describes a laminated assay device for detection of cholesterol with walls made by hydrophobic printing or cutting
- 2003 US Patent 6,573,108 presents the first example of a tangential flow device, incorporation of multiple channels, timers to show when the assay is over, and a filtration step for sample pretreatment. Walls could be made by screen printing, dipping in polymer with a template held against paper, or by a computer-controlled deposition system. Researchers proposed polymers such as heteropolysaccharides, acrylic polymers and copolymers, and silanes
- 2007 The first scientific journal publication by the Whitesides group describing a multichannel system with photoresist walls
- 2008 The first international conference on bioactive paper in Finland

# Paper based systems

- Colorimetric assays are conducted in the paper "wells," utilizing the interaction between species-specific enzymes and chromogenic substrates
- The presence of pathogenic bacteria is indicated by a color change, a result that may be easily interpreted by the user without the need for complex instrumentation
- Semiquantitative analysis is performed by creating a digital image of the devices with an office scanner
- Created by use of wax printing on filter paper, wax defines flow regions
- Recent technology emulates conventional PDMS/Si systems

Jana C. Jokerst, Jaclyn A. Adkins, Bledar Bisha, Mallory M. Mentele, Lawrence D. Goodridge, and Charles S. Henry, "Development of a Paper-Based Analytical Device for Colorimetric Detection of Select Foodborne Pathogens', Anal. Chem. 2012, 84, 2900−2907

# Paper based systems




Determination of lowest detectable amount of (A) β-galactosidase, (B) esterase, and (C) PI-PLC enzymes via optimal substrate concentrations. Average grey intensities are plotted vs the amount of enzyme in each spot

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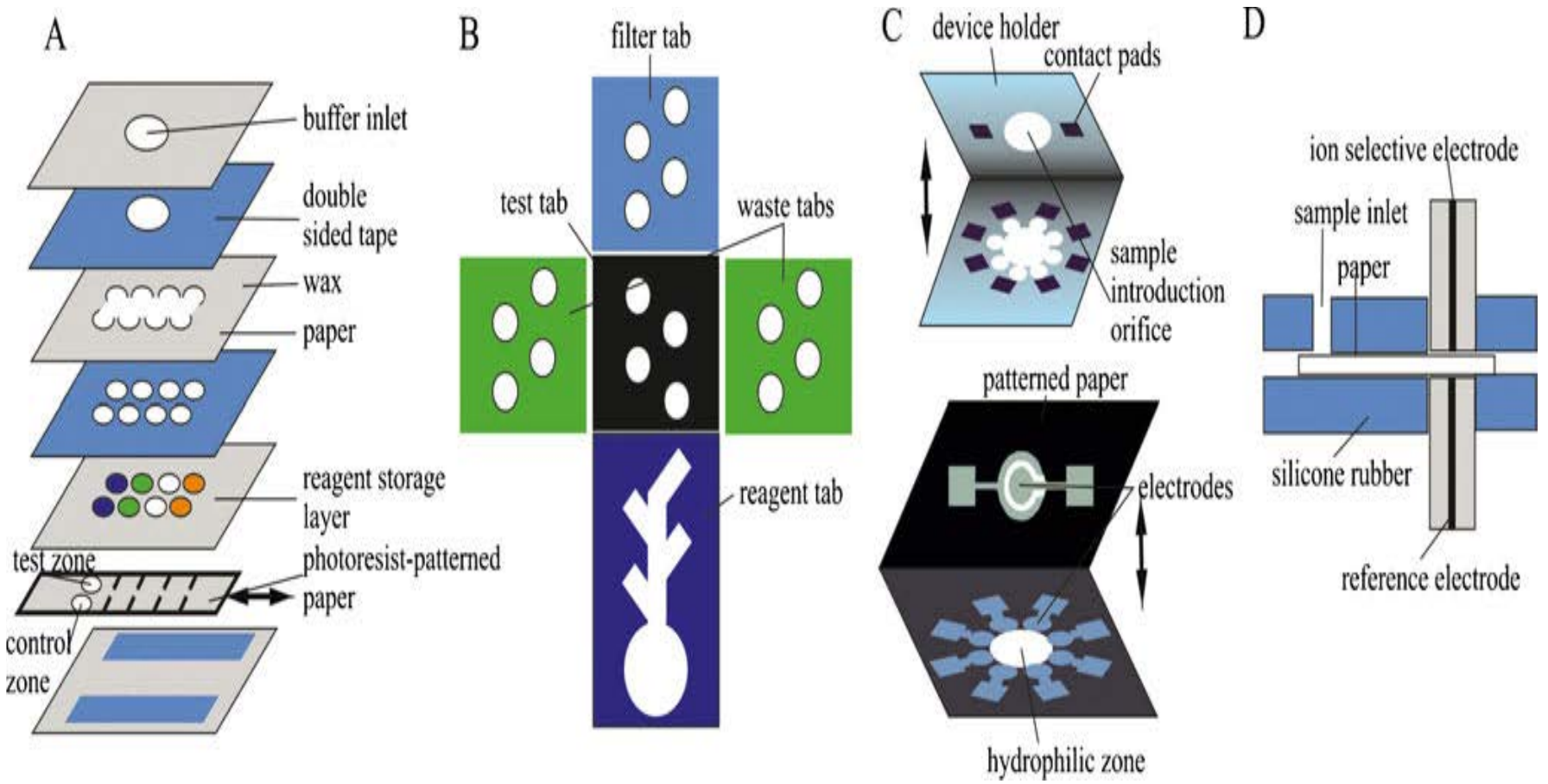


Immunoassays:
a Whitesides group assay with a movable strip, b. origami-based device for detection of tumor markers, c. electrochemiluminescence detection of tumor markers, d potentiometric immunoassay

# Paper based systems

- Used for the separation and detection of underivatized carbohy- drates, amino acids, and sulfur-containing antibiotics
- This paper device determined glucose, lactate, and uric acid in biological samples using oxidase enzyme reactions (similar to previous research on a silicon/pdms system)
- These include glucose oxidase, lactate oxidase, and uricase
- These techniques are previously expressed in other technical publications by Dr. Henry in conventional devices

Wijitar Dungchai, Orawon Chailapakul, and Charles S. Henry ,Electrochemical Detection for Paper-Based Microfluidics *Anal. Chem.* 2009, *81,* 5821–5826

# Advantages/Disadvantages

- Advantages
  - Very Small
  - Disposable
  - Sealed
  - Portable
  - Very Fast response time as compared to conventional lab work
- Disadvantages
  - Takes place of jobs

# Summary

- Microfluidics is an important emerging technology, that can analyze DNA, proteins and other materials of interest. Key points to this technology are fluid flow, components, and scaling
- Many applications using microfluidic techniques may provide employment