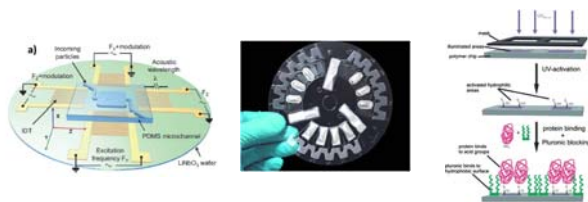


## Lab-on-a-Chip Part 1 – Cell & Molecule Manipulation

Prof. Steven S. Sallierman, <http://sallierman.umn.edu/>



---

---

---

---

---

---

---

---

## Cell & Molecule Manipulation

### • Methods to manipulate micro or nano scale objects:

- Optical
- Acoustic
- Electrical
- Centrifugal force
- Hydrodynamic
- Magnetic
- Surface modification

### • Examples

- Mechanical – barriers, porous membranes.
- Impedance
- Surface Acoustic Waves.
- Dielectrophoresis.
- Optical Tweezers and Scissors.
- Electrowetting & Digital
- Lab on a Disk – DNA, ELISA.
- Surface Modification – plasma, CVD, laser, UV radiation, biofunctionalization, selective protein adsorption, and PEG/gold.

Steven S. Sallierman

---

---

---

---

---

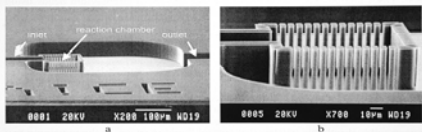
---

---

---

## Mechanical

- A filter chamber fabricated by DRIE in a silicon substrate - 3  $\mu\text{m}$  wide and 50  $\mu\text{m}$  high pillars, and 2  $\mu\text{m}$  spacing.
- This device was used for a *pyrosequencing reaction* whereby light emitted from the reaction chamber is collected by a CCD camera.
- Also useful for *bead-based DNA analysis, chromatography and immunoassays.*



Steven S. Sallierman

van der Wijngaert, W. and et al. Handling of beads in microfluidic devices for biotech applications. Lab-on-a-chip: Miniaturized Systems for Biochemical Analysis and Synthesis. Edited by R.E. Oostbroek and A. Van den Berg. Elsevier, The Netherlands (2003).

---

---

---

---

---

---

---

---

## Semipermeable Membranes...

- **Permselective membranes for cell immunoisolation:**
  - High density uniform pores allow sufficient permeability to nutrients and hormones while preventing the passage of immunoglobulins.
  - For example islet-cell transplantation.
- **Uniform pores can be micromachining in silicon.**
- **Polyethylene terephthalate (PET) membranes may be machined with an excimer laser to produce pores as sieves.**

Steven S. Satterman

---

---

---

---

---

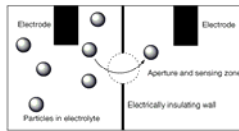
---

---

---

## Impedance Cell Sizing (Coulter principle)

- Cells passing through an aperture displace electrolyte and give rise to a change in impedance over the insulating wall.
- By giving the sensors a constant current, changes can be recorded by changes in voltage across the electrodes.
- Each cell crossing gives a pulse shaped response, the magnitude being related to the volume.
- *Thousands of cells can be analyzed in a second!*



Steven S. Satterman

---

---

---

---

---

---

---

---

## Acoustic Forces

- **Applications**
  - Single cell isolation.
  - Cell focusing and sorting.
  - Cell washing and patterning.
  - Cell-cell fusion and communication.
  - Tissue engineering.
- **Examples**
  - Forces acting on cells and molecules in fluid suspension.
  - Cell manipulation in 2D based on resonance, frequency change and nodes.
  - Acoustic cell separator.

Steven S. Satterman

Barani A, Pakirani H, Jannaleki M, et al. Microfluidic integrated acoustic waving for manipulation of cells and molecules. *Biosensors & Bioelectronics*. 2016;85:714-725.

---

---

---

---

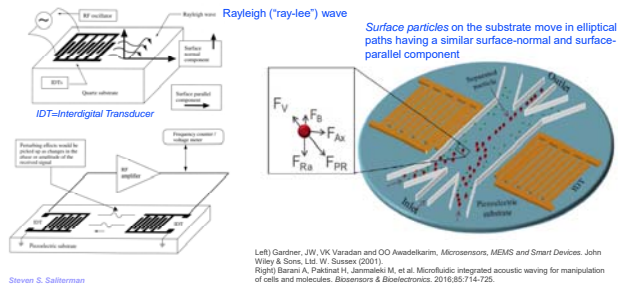
---

---

---

---

## Surface Acoustic Waves – Gardner et. al...



Steven S. Sallterman

---

---

---

---

---

---

---

---

---

---

## SAW Devices...



Steven S. Sallterman

<https://youtu.be/H0MJsbNDQM>

---

---

---

---

---

---

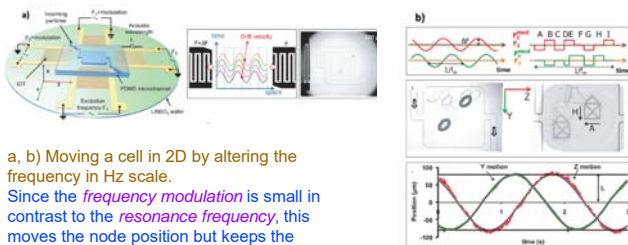
---

---

---

---

## Cell Manipulation in 2D & Resonance Frequency...



Steven S. Sallterman

Tran, S.B.Q, Marmottant, P., Thibault, P., 2012, *Appl. Phys. Lett.*, 101.

---

---

---

---

---

---

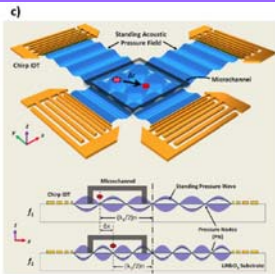
---

---

---

---

## Effect of Altering Frequency...



c) For moving a trapped cell in a node in 2D pattern, the resonance frequency is shifted to the next resonance frequency which produces different nodal points.

The trapped cells move to the adjacent nodes produced by a new frequency. (Note the  $\text{LiNbO}_2$  substrate.)

Ding, X., Lin, S.-C.S., Kraljic, B., Yun, H., Li, S., Chiang, I.-K., Shi, J., Benkovic, S.J., Huang, T.J., 2012a. PNAS 109 (28), 11105–11109.

Steven S. Sallerman

---

---

---

---

---

---

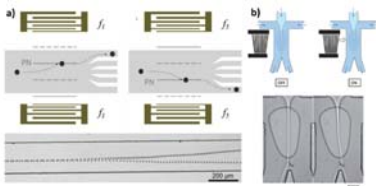
---

---

---

---

## Acoustic Cell Sorting – Ding et. al...



a) Acoustic based-device for sorting the cells in different lines across the channel. By changing the nodal line, cells are sorted in different positions across the channel.

b) Pushing the fluid, carrying the cells toward the desired outlet by acoustic force.

Ding, X., Lin, S.-C.S., Lapsley, M.I., Li, S., Guo, X., Chan, C.Y., Chiang, I.-K., Wang, L., McCoy, J.P., Huang, T.J., 2012b. Lab. Chip 12, 4228–4231.  
Frohn, T., Braunmüller, S., Schmidt, L., Wotzsch, A., Weitz, D.A., 2010. Lab. Chip 10, 789–794.

Steven S. Sallerman

---

---

---

---

---

---

---

---

---

---

## Dielectrophoresis

- Motion of polarized (uncharged) particles in a nonuniform electric field.
- Dielectrophoretic forces depend on:
  - Charge of the particle (may be uncharged).
  - Geometry of the device.
  - Dielectric constant of the medium and particle.
  - Physiology of the particle.
- Uses:
  - Trapping, sorting, focusing, filtration, patterning, and assembly particles from 10nm to 100um.
  - Separating biological entities/particles suspended in a buffer medium.

Steven S. Sallerman

Jubery, TZ and P. Dutta. A new design for efficient dielectrophoretic separation of cells in a microdevice. Electrophoresis 2013, 34, 643–650

---

---

---

---

---

---

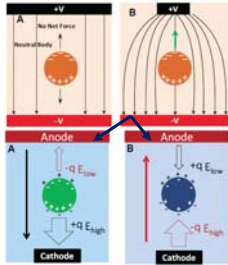
---

---

---

---

## Dielectrophoresis...



- A. Uniform electric field  
B. Nonuniform electric field
- A. Particle is more polarizable than the medium and it experiences net force toward the higher electric field ( $E_{high}$ ) region. This process is known as pDEP.
- B. Particle is less polarizable than the medium, and the net force on the particle acts toward the lower electric field ( $E_{low}$ ) region. This type of particle motion is known as nDEP.

Steven S. Sallierman

Jubery, TZ and P. Dutta. A new design for efficient dielectrophoretic separation of cells in a microdevice. *Electrophoresis* 2013, 34, 643-650

---

---

---

---

---

---

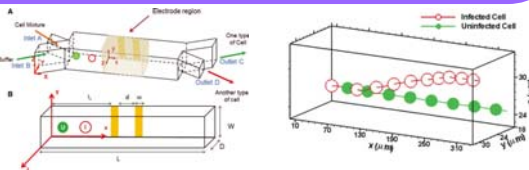
---

---

---

---

## Proposed Device – Jubery et. al...



- A. A mixture of cells is introduced through inlet A and buffer is introduced through inlet B. The bulk fluid flow velocity through these inlets is 200 m/s.
- B. Computational domain for simulation-considering particles. This domain is considered from the shaded region in the actual device.
- C. Translocation path of cells in actual domain.

Steven S. Sallierman

Jubery, TZ and P. Dutta. A new design for efficient dielectrophoretic separation of cells in a microdevice. *Electrophoresis* 2013, 34, 643-650

---

---

---

---

---

---

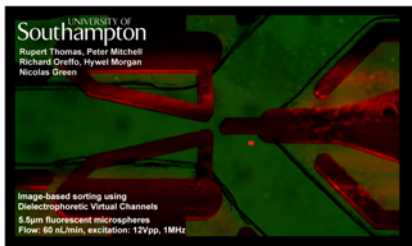
---

---

---

---

## Dielectrophoresis Separation...



Steven S. Sallierman

<https://youtu.be/9O4V242X2I>

---

---

---

---

---

---

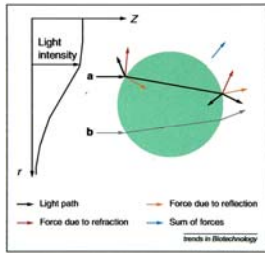
---

---

---

---

## Optical Forces on a Dielectric Particle...



- Laser light of intensity ( $z$ ) varies across space ( $r$ ) as shown in the graph and is reflected and refracted at the interface of the particle.
- Photons have momentum and so their redirection by interacting with the particle results in a momentum transfer to the particle.
- Light is strongest at a (a) resulting in movement towards the beam axis. The net result is shown by the blue arrow.

Steven S. Sallterman

Odde, DJ and MJ Renn. Laser-guided direct writing for applications in biotechnology. *Trends in Biotechnology* 17(1), pp 385-389 (1999)

---

---

---

---

---

---

---

---

---

---

## Optical Tweezers and Scissors



Steven S. Sallterman

Munce, NJ 2005

---

---

---

---

---

---

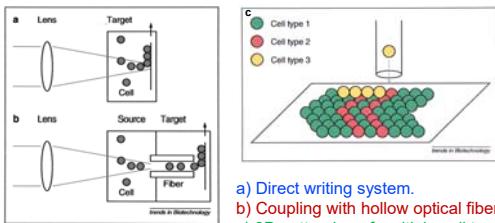
---

---

---

---

## Applications...



- Direct writing system.
- Coupling with hollow optical fiber to target surface.
- 3D patterning of multiple cell types.

Steven S. Sallterman

Odde, DJ and MJ Renn. Laser-guided direct writing for applications in biotechnology. *Trends in Biotechnology* 17(1), pp 385-389 (1999)

---

---

---

---

---

---

---

---

---

---

## Electrowetting

- **Young's equation** (after Thomas Young who first proposed it in 1805) describes the simple balance of force between the liquid-solid, liquid-vapor, and solid-vapor interfacial surface energies of a droplet on a solid surface:

$$\gamma_{LG} \cos \theta + \gamma_{SL} = \gamma_{SG}$$

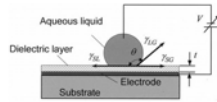
where

$\gamma_{LG}$  (gamma liquid-gas) is the liquid-gas interfacial tension,  
 $\gamma_{SL}$  (gamma solid-liquid) is the solid-liquid interfacial tension,  
 $\gamma_{SG}$  (gamma solid-gas) is the solid-gas interfacial tension, and  
 $\theta$  (theta) is the contact angle.

**Know this!**



Thomas Young lived from 1773 to 1829 and was an English scientist and researcher. Discovered interference of light.



Steven S. Satterman

Cho, SK, et al., "Creating, transporting, cutting and merging liquid droplets by electrowetting-based actuation for digital microfluidic circuits." *Journal of Microelectrochemical Systems* 12(1) pp. 70-80 (2003)

---

---

---

---

---

---

---

---

---

---

- **Surface tension** is a property of the liquid and is dependent on **temperature** and the **other fluid** it is in contact with.
- At the **interface** between a liquid and a gas, or between two immiscible liquids, forces develop in the liquid surface that causes the surface to behave as if a "membrane" were stretched over it.
- This phenomenon is due to **unbalanced cohesive forces** acting on the liquid molecules at the fluid interface.
- **Surface tension** is the **intensity of molecular attraction per unit length** along any line in the surface.

Steven S. Satterman

---

---

---

---

---

---

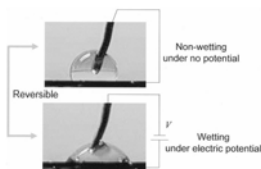
---

---

---

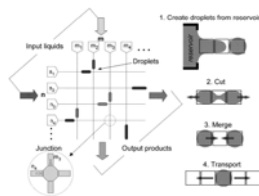
---

## Digital Manipulation...



Electrowetting and electrocapillarity - an externally added electrostatic charge will modify the surface tension or capillary forces at the fluid-surface interface.

Steven S. Satterman



Digital microfluidic circuit for manipulating samples and reagents. Division, transport and merging.

Cho, SK, et al., "Creating, transporting, cutting and merging liquid droplets by electrowetting-based actuation for digital microfluidic circuits." *Journal of Microelectrochemical Systems* 12(1) pp. 70-80 (2003)

---

---

---

---

---

---

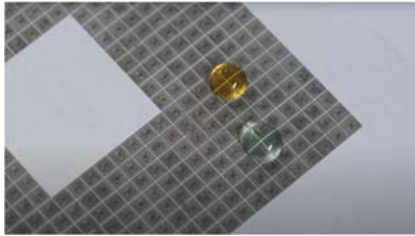
---

---

---

---

## Digital Microfluidics...



Steven S. Sallierman

<https://youtu.be/z0NBsyhApvU>

---

---

---

---

---

---

---

---

- The effect of a potential  $V$  on the contact angle is then determined by the following:

$$\cos\theta_{(V)} - \cos\theta_o = \frac{\epsilon_r \epsilon_o V^2}{2\gamma_{LG}t}$$

where

$\theta$  (theta) is the contact angle at the applied potential,

$\theta_o$  (theta-nought) is the equilibrium contact angle at  $V = 0$ ,

$V$  is the electric potential across the interface (V),

$\epsilon_r$  (epsilon) the dielectric constant of the dielectric layer,

$\epsilon_o$  (epsilon) is the permittivity of a vacuum ( $8.85 \times 10^{-12}$  F/m),

(where F = farad per m),

$t$  is its thickness (m) and

$\gamma_{LG}$  (gamma liquid-gas) is the liquid-gas interfacial tension.

**Know this!**

Steven S. Sallierman

---

---

---

---

---

---

---

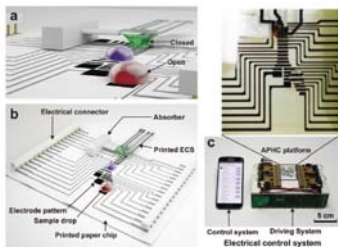
---

## Paper-Based Microfluidic Chip – Ruecha et. al...

A printed, paper-based active microfluidic chip actuates drops by electrowetting.

- Partially open (blue and red drops) and closed (green drop) forms.
- A modularly assembled platform.
- An integrated portable electrical control system consisting of the chip platform, the driving system, and the mobile-based wireless control system.

This system was able to detect glucose, dopamine and uric acid with its electrochemical sensors.



Ruecha, N., Lee, J., Chae, H., Cheong, H., Seum, V., Preechakasedki, P., Chailapakul, O., Tanev, G., Madsen, J., Routhongkum, N., 2017. Adv. Mater. Technol. 2 (3), 1600207.

Steven S. Sallierman

---

---

---

---

---

---

---

---



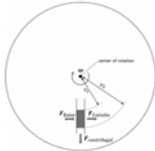
## Centrifugal Microfluidics – CD Size Disks

### ● Applications

- Clinical chemistry.
- Immunodiagnosics
- Protein analysis.
- Cell handling.
- Molecular diagnostics.
- Food, water, and soil analysis.

### ● Features

- Pneumatic energy for switching or pumping "inward"
- Pre-storage and release of reagents.
- No external pumps.
- Volumes from nL to mL.
- Channels, chambers and sensor matrices.
- Bubble removal.
- Metering and mixing.
- Parallel operations.



Steven S. Sallerman

Strohmeier O, Keller M, Schwemmer F, et al. Centrifugal microfluidic platforms: advanced unit operations and applications. *Chemical Society Reviews*. 2015;44(17):6187-6229.

---

---

---

---

---

---

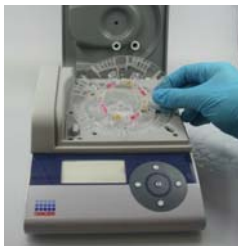
---

---

---

---

## Lab-on-a-Disk: DNA – Mark et. al...



### Example:

Nucleic acid based detection of pathogenic microorganisms and the immunoassay based detection of toxins.

### Process:

1. Storage of liquids and lyophilized reagents on the LabDisk and their time-controlled release.
2. Transfer of sample material by the use of antibody-coated microbeads.
3. Aliquoting of sample material for simultaneous analysis on one LabDisk.

Steven S. Sallerman

Mark, D., et al. 2012. Automated and miniaturized detection of biological threats with a centrifugal microfluidic system. *Smart Biomedical and Physiological Sensor Technology* 3:367-336792.

---

---

---

---

---

---

---

---

---

---



Steven S. Sallerman

1:09 m, <https://youtu.be/XXUVtpP6Q8>

---

---

---

---

---

---

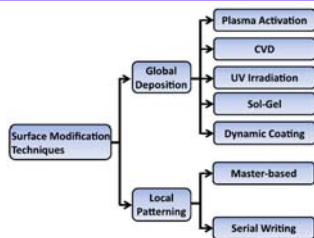
---

---

---

---

## Surface Modification - Polymers



Steven S. Sallterman

Kisara, Maria, and Jens Ducree. 2013. Integration of functional materials and surface modification for polymeric microfluidic systems. *Journal of Micromechanics and Microengineering* 23, no. 3:033001.

---

---

---

---

---

---

---

---

## Functions of Surface Layers...

- Change of contact angle.
- Provision of functional groups for surface.
- Lowering surface energy.
- Immobilization (of molecular capture probes).
- Suppression of non-specific absorption/biofouling.
- Establishment of barrier properties to prevent swelling/dissolution.
- Gas permeability.
- Tuning of optical and thermal properties, dirt protection.
- Scratch resistance.

Steven S. Sallterman

Kisara, Maria, and Jens Ducree. 2013. Integration of functional materials and surface modification for polymeric microfluidic systems. *Journal of Micromechanics and Microengineering* 23, no. 3:033001.

---

---

---

---

---

---

---

---

## Global Deposition...

- **Plasma Activation.** (Ar, Ne, He, H<sub>2</sub>, NH<sub>2</sub>, CO, CO<sub>2</sub>, O<sub>2</sub>, H<sub>2</sub>O, N<sub>2</sub>, NO<sub>2</sub> and F<sub>2</sub>)
  - e.g. Oxygen gas induces the formation of *hydrophilic* groups on the surface. (Although transient, as they quickly revert back.)
- **Chemical Vapor Deposition.**
  - Solvent-free integration of thin films and nanostructures.
- **UV Irradiation**
  - Short-wavelength radiation in this range can be applied to the surface modification of fluorocarbon polymers.
  - In UV light at low wavelengths (180–190 nm) acidic groups are created on the polymer surfaces that are available for patterned protein binding and cell adhesion.
- **Sol-Gel**
  - Low reaction temperature
  - May provide improved bonding, barriers, corrosion protection.
- **Dynamic Coatings**
  - Surfactant solutions are pumped at a certain constant speed through the channel and physisorb to the channel surface. Eventual desorption from the surface.

Steven S. Sallterman

Kisara, Maria, and Jens Ducree. 2013. Integration of functional materials and surface modification for polymeric microfluidic systems. *Journal of Micromechanics and Microengineering* 23, no. 3:033001.

---

---

---

---

---

---

---

---

## Hydrophobic & Hydrophilic Surfaces...



Steven S. Sallerman

[https://youtu.be/FLegmQ8\\_dHg](https://youtu.be/FLegmQ8_dHg)

---

---

---

---

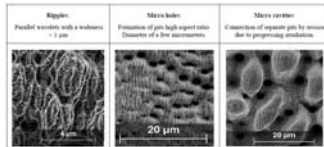
---

---

---

---

## Ultra Short Laser Pulse Modification...



Steven S. Sallerman

Hildenbagen, J. et al. 2013. Simultaneous Micro Structuring and Functionalization of Surfaces with Picosecond Laser. International Conference on Optics in Precision Engineering and Nanotechnology (IOPEN2013), 8769, 87691D. <https://youtu.be/xyxPgiEjkk>

---

---

---

---

---

---

---

---



Steven S. Sallerman

<https://youtu.be/clyxPgiEjkk>

---

---

---

---

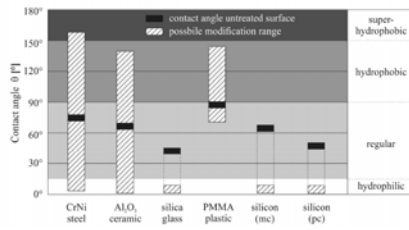
---

---

---

---

## Obtained Contact Angle Modification...



Hidenhagen, J. et al. 2013. Simultaneous Micro Structuring and Functionalization of Surfaces with Picosecond Laser. International Conference on Optics in Precision Engineering and Nanotechnology (IOPEN2013) 8769, 87691D.

Steven S. Sallerman

---

---

---

---

---

---

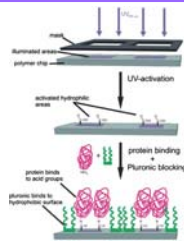
---

---

---

---

## Biofunctionalization...



Schulte J, Freudigmann C, Benz K, Bolliger J, Gebhardt R and Stöble M 2010 A method for patterned in situ biofunctionalization in injection-molded microfluidic devices Lab Chip 10, 2551-8

Steven S. Sallerman

---

---

---

---

---

---

---

---

---

---

## Selective Protein Adsorption...

- **Biofouling** occurs as platelets, fibrinogen, IgG and albumin bind to sensors and other surfaces.
- **Foreign body giant cells (FBGC)** may envelope surfaces in response to macrophages being drawn to areas of inflammation.
- **Poly(ethylene glycol) (PEG)**:
  - A nontoxic, non-immunogenic and non-antigenic polymer may prevent these phenomena.
  - Stable, non-fouling surfaces may be created by:
    - Chemical coupling reactions,
    - UV-induced graft polymerizations,
    - Self assembled monolayers (SAMs).

Steven S. Sallerman

---

---

---

---

---

---

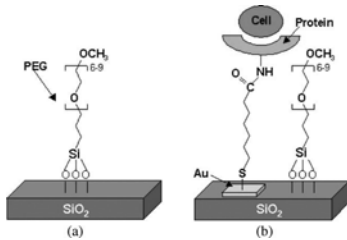
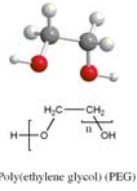
---

---

---

---

## PEG and Gold Surface Modification...



Lan, SM et al. "Surface modification of silicon and gold-patterned silicon surfaces for improved biocompatibility and cell patterning selectivity." *Biosensors and Bioelectronics* 20(9), pp. 1697-1708 (2005).

Steven S. Satterman

---

---

---

---

---

---

---

---

---

---

## Recommended Reading

Wang et al. *Optics Express* 2019, 27(12), 17331-17340. https://doi.org/10.1364/OE.27.17331

SINTEF INDUSTRIAL MEDICAL RESEARCH

Cancer Res Treat 2018; doi:10.1007/s12220-018-0210-0

**REVIEW** Open Access

**Microfluidics-based strategies for molecular diagnostics of infectious diseases**

Yu Wang<sup>1</sup>, Jian-Da Wang<sup>1</sup>, Wei-Li Chen<sup>1</sup>, Jing-Jing He<sup>1</sup>, Wang-Jing Chen<sup>1</sup> and Bi-Hong Liu<sup>1</sup>

**ABSTRACT** Microfluidic diagnosis strategies for infectious disease detection require identifying components that are representative for a panel of pathogenic (POT) antigens, microfluidics, single treatment, automatic, and improved without any external detection method, such as colorimetric, optical, or electrochemical, and so on. However, this is a challenge because the molecular weight of a pathogen is too small to be detected by conventional methods. Here, we introduce the typical on-chip microfluidic and microfluidics-based strategies for infectious disease diagnosis, including sample preparation, amplification and detection. First, the preparation of microfluidics systems for infectious disease diagnosis, second, the detection of infectious disease diagnosis, and third, the application of the microfluidics-based strategies to infectious disease diagnosis. Both this basic and advanced microfluidics-based strategies for infectious disease diagnosis are summarized in a panel of the current study of this study, and proposed future directions for microfluidics-based infectious disease diagnosis.

**KEYWORDS** Microfluidics; Molecular diagnostics; infectious disease; Point-of-care testing (POCT); Digital assay

**REVIEW**

**Advances in isolation and detection of circulating tumor cells based on microfluidics**

Chen-Duo, Ding-Feng, Cao

**ABSTRACT** Circulating tumor cells (CTCs) are the cancer cells that migrate to the peripheral blood after escaping from the original or primary tumor. CTCs could be used as an early marker of clinical relapse as well. Despite the great importance of CTCs, the current clinical experiments for CTCs are very difficult because of their low numbers and heterogeneity. In this review, we summarize the recent advances in CTCs detection strategies based on microfluidics. We have found that some advances have been made that could drive robust strategies for cancer diagnosis. The current study summarizes the state-of-the-art progress in CTCs detection strategies based on microfluidics, such as microfluidics-based CTCs isolation, CTCs detection, and CTCs enumeration. We also discuss the research trends, approaches, advantages, limitations, and challenges with an eye on identifying clinical demand in developing microfluidics-based CTCs detection technology.

**KEYWORDS** Circulating tumor cells; cancer; isolation and detection; microfluidics

Steven S. Satterman

---

---

---

---

---

---

---

---

---

---

## Key Points

- Cell and molecule manipulation can be accomplished with optical, acoustic, electrical centrifugal, hydrodynamic magnetic and surface modification techniques.
- DRIE can be used for high-aspect ratio nanofabrication.
- Coulter counter impedance cell sizing is commonly used for RBC counts and volume measurement.
- Surface acoustic waves can be used for cell manipulation.
- Dielectrophoresis, the motion of polarized (uncharged particles) in a nonuniform electric field, depends on the charge of the particle, geometry of the device, dielectric constant of the medium and particle, and physiology of the particle.
- Laser light can impart optical forces on a dielectric particle by photon momentum transfer.

Steven S. Satterman

---

---

---

---

---

---

---

---

---

---

### Key Points...

- Electrowetting depends on Young's equation describing the simple balance of force between the liquid-solid, liquid-vapor, and solid-vapor interfacial surface energies of a droplet on a solid surface.
- Digital microfluidics is possible because of the effect of a potential  $V$  on the contact angle of a droplet.
- Centrifugal force-based "lab-on-a-disk" is an advanced implementation of lab-on-a-chip based on a spinning CD-like device.
- Global deposition techniques include plasma activation, chemical vapor deposition, UV irradiation, sol-gel and dynamic coatings.
- Biofunctionalization uses lithography techniques and biological, polymer and metal materials to functionalize polymer chips.

Steven S. Satterman

---

---

---

---

---

---

---

---

### Key Points...

- Surface modification and functionalization of surface layers include:
  - Change of contact angle.
  - Provision of functional groups for surface.
  - Lowering surface energy.
  - Immobilization (of molecular capture probes).
  - Suppression of non-specific absorption/biofouling.
  - Establishment of barrier properties to prevent swelling/dissolution.
  - Adjusting gas permeability.
  - Tuning of optical and thermal properties, dirt protection.
  - Addition of scratch resistance.

Steven S. Satterman

---

---

---

---

---

---

---

---

### Appendix

- LOC material comparison.
- Plasma, CVD,
- UV & sol-gel coating techniques.
- More Lab-on-Disk.

Steven S. Satterman

---

---

---

---

---

---

---

---

## LOC Materials...

Table 3. Comparison of Typical Materials Used for the Fabrication of LOC Systems

material	characteristics
silicon	rigid, high temperature resistance, ease of surface modification (silane), biocompatible, low aqueous leaching, not gas-permeable, active fluidic system requires polymer hybrid device
ceramics	rigid, good mechanical, thermal and electrical properties
glass	rigid, transparent, ease of surface modification
poly(methyl methacrylate) (PMMA)	rigid, transparent, low water absorption
epoxy, silica copolymer (COC)	rigid, transparent, low water absorption
polystyrene (PS)	rigid, transparent
polycarbonate (PC)	rigid, transparent, highly heat resistant
polydimethylsiloxane (PDMS)	flexible, transparent, biocompatible, chemically inert, highly gas permeable
Whisker chromatography paper	rigid, pure cellulose, homogeneous, reproducible, biocompatible

Steven S. Sattlerman

Wongkaew N, Simsek M, Griesche C, Baumann AJ. Functional Nanomaterials and Nanostructures Enhancing Electrochemical Biosensors and Lab-on-a-Chip Performances: Recent Progress, Applications, and Future Perspective. *Chemical Reviews*. 2019;119(1):120-194.

## Fabrication Costs...



Table 4. Evaluation of Practicability of LOC Materials for Use in Biosensor-Related Applications<sup>71</sup>

applications	silicon/ glass	elastomers	thermoplastics	paper
electrochemical detection	good	limited	moderate	moderate
cost of production	high	medium	low	low
reusability	yes	no	yes	no
disposable device use	expensive	good	good	good
online monitoring	yes	yes	yes	no

Steven S. Sattlerman

Wongkaew N, Simsek M, Griesche C, Baumann AJ. Functional Nanomaterials and Nanostructures Enhancing Electrochemical Biosensors and Lab-on-a-Chip Performances: Recent Progress, Applications, and Future Perspective. *Chemical Reviews*. 2019;119(1):120-194.

## Plasma and CVD Techniques...

Table 1. Characteristics of plasma treatment techniques in polymer microfluidics.

Research group	Polymeric substrate	Type of gas and contact angle	Stability of the coating
Tsang et al [98]	PMMA, PEEK	O <sub>2</sub> , C <sub>2</sub> F <sub>4</sub>	20 days (PMMA), 60 days (PEEK)
Tsang et al [99]	PDMS	C <sub>2</sub> F <sub>4</sub> , SF <sub>6</sub>	Months to years
Vanderhoff et al [100]	PMMA + Si containing fluorocarbon	O <sub>2</sub> , C <sub>2</sub> F <sub>4</sub>	Not evaluated
He et al [101]	PMMA	O <sub>2</sub> + CF <sub>4</sub> 120°	Not evaluated
Subramanian et al [102]	PMMA, COC, PC	O <sub>2</sub> + CF <sub>4</sub> 120° O <sub>2</sub> + hydrocarbons (1,2,2,2-tetrafluoroethyl methacrylate, HFE-TM, >140°)	Not evaluated
Makris et al [103]	PDMS	O <sub>2</sub> + Ar, 132°	85% recovery after 5 days
Ray and Yoo [104]	COC	O <sub>2</sub> , 7° Ar, 10° N <sub>2</sub> , 3°	Stable for >30 days
Wang et al [105]	PDMS	Ar + APFES, 100° Ar + APFES + aPPEG, 64°	Not evaluated 4 weeks

Table 2. Characteristics of CVD techniques in polymer microfluidics.

Research group	Polymeric substrate	Deposited material	Stability of the coating
Chen and Lakshmi [106]	PDMS	Poly(2-methyl-2-silylene-oxo-p-styrene)	Not evaluated
Richter et al [107]	PDMS	Poly(PTDA-co-EGDA)	Not evaluated
Delek et al [110]	COP	SiO <sub>2</sub>	27 weeks
Gambhir et al [111], [112]	COP	APTES, APTES + EDA, DEGDME, MPTMS	Not evaluated
Eichler et al [113]	PC, COC	HMDSO, TMDS, TEOS, SiH <sub>4</sub>	20 days
Iskovic et al [114]	SiO <sub>2</sub>	Amino groups due to the pyrolytic dissociation of ammonia	Not evaluated

Steven S. Sattlerman

Kitara, Maria, and Jens Ducreux. 2013. Integration of functional materials and surface modification for polymeric microfluidic systems. *Journal of Micromechanics and Microengineering* 23, no. 3:033001.

## UV Irradiation and Sol-Gel...

Table 3. Characteristics of UV irradiation techniques in polymer microfluidics.

Research group	Polymeric substrate	Wavelength (nm)	Stability of the coating
Schütte <i>et al</i> [119]	COC	185	Acid groups' density decrease to 25% within 19 weeks
Pflieger <i>et al</i> [120]	PS	Laser: 193 Mercury lamp; 185, 248	Not evaluated
Nagai <i>et al</i> [121]	PDMS	172	Not evaluated
Hosomi <i>et al</i> [122, 123]	PMMA, PS	172	PMMA: not evaluated PS: only 100 kPa remains stable after 30 days

Table 4. Characteristics of sol-gel techniques in polymer microfluidics.

Research group	Polymeric substrate	Deposited material	Stability of the coating
Yang <i>et al</i> [126]	PDMS	Glass layer from TEOS	No available data
Ahate <i>et al</i> [125]	PDMS	Glass layer from TEOS and MTES	
Roman and Culbertson [127]	PDMS	Glass layer from isopropoxide, zinc-oxim, isopropoxide and vanadium triisobutoxide oxide	

Kitsara, Mania, and Jens Ducrec. 2013. Integration of functional materials and surface modification for polymeric microfluidic systems. *Journal of Micromechanics and Microengineering* 23, no. 3:033001.

Steven S. Sallerman

## Carrier for Immunoassay...



Disposable test carrier for immunoassay: reagents are stored in aluminium pouches. If centrifugal force is applied, the pouches burst due to the increased hydrostatic pressure of the liquid.

Mark, D., et al. 2012. Automated and miniaturized detection of biological threats with a centrifugal microfluidic system. *Smart Biomedical and Physiological Sensor Technology* 4, 030702.

Steven S. Sallerman

## Transfer of Magnetic Beads...



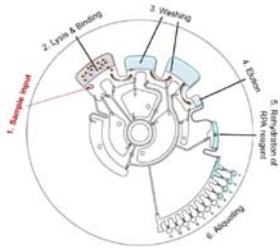
The transfer of magnetic beads is automated by rotating the disk over a magnet.

Mark, D., et al. 2012. Automated and miniaturized detection of biological threats with a centrifugal microfluidic system. *Smart Biomedical and Physiological Sensor Technology* 4, 030702.

Steven S. Sallerman



## Nucleic Acid Analysis...



Process for the nucleic acid analysis.

After extraction and amplification the sample is divided into multiple chambers.

Steven S. Satterman

Mark, D., et al. 2012. Automated and miniaturized detection of biological threats with a centrifugal microfluidic system. *Smart Biomedical and Physiological Sensor Technology* 4: 8367-8370E.

---

---

---

---

---

---

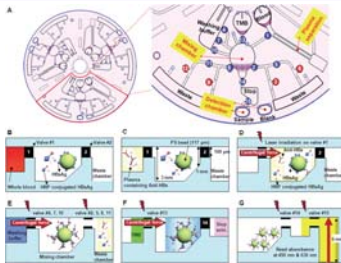
---

---

---

---

## Lab-on-a-Disk: ELISA – Lee et al...



Automated enzyme-linked immunosorbent assay (ELISA) system.

Starting with whole blood, this microbead based system can measure the concentrations of the antigen and the antibody of Hepatitis B virus (HBV), HBsAg and Anti-HBs.

Compared to conventional ELISA, time was reduced from 2 hrs. to 30 min.

Steven S. Satterman

Lee, B. et al. A fully automated immunoassay from whole blood on a disc. *Lab Chip*, 2009, 9, 1548-1555

---

---

---

---

---

---

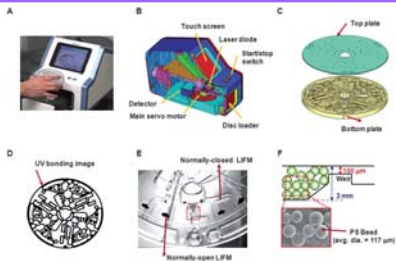
---

---

---

---

## ELISA...



Steven S. Satterman

Lee, B. et al. A fully automated immunoassay from whole blood on a disc. *Lab Chip*, 2009, 9, 1548-1555

---

---

---

---

---

---

---

---

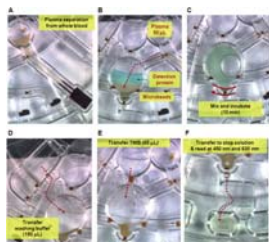
---

---

## Spin "Program" and Images

Table 1 Spin program

Spin No.	Speed (rpm)	Time (sec.)	Operation
1	3600	180	Plasma separation
2	2400	20	Transfer plasma into mixing chamber
3	+250—250	600	Mix beads, plasma & detection probe
4	2400	35	Remove residual to waste chamber
5	—	2	Close 1 <sup>st</sup> waste channel
6	2400	20	Transfer 1 <sup>st</sup> washing buffer (150 $\mu$ L) to mixing chamber
7	+250—250	20	Mixing beads and washing buffer
8	2400	35	Remove 1 <sup>st</sup> washed residue
9	—	2	Close 2 <sup>nd</sup> waste channel
10–17	—	170	Repeat 6–9 twice for 2 <sup>nd</sup> and 3 <sup>rd</sup> washing step (each 100 $\mu$ L)
18	2400	20	Transfer TMB to mixing chamber
19	+250—250	600	Mixing beads and TMB
20	2400	20	Transfer to stopping solution chamber
21	+250—250	20	Mixing with stopping solution
22	2400	20	Transfer to detection chamber
23	—	20	Detection



Steven S. Satterman

Lee, B. et al. A fully automated immunoassay from whole blood on a disc. Lab Chip, 2009, 9, 1548–1555

---



---



---



---



---



---



---



---