光流體生醫元件與技術
Introduction of Optofluidics

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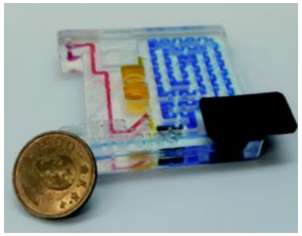
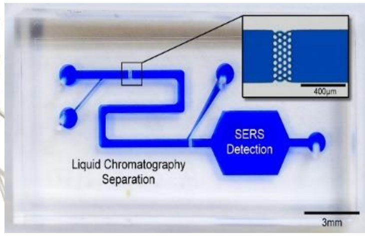
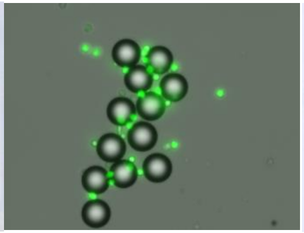
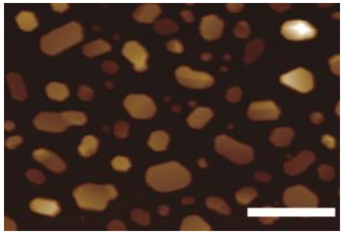
2018/11/02 Introduction to Lab on a Chip



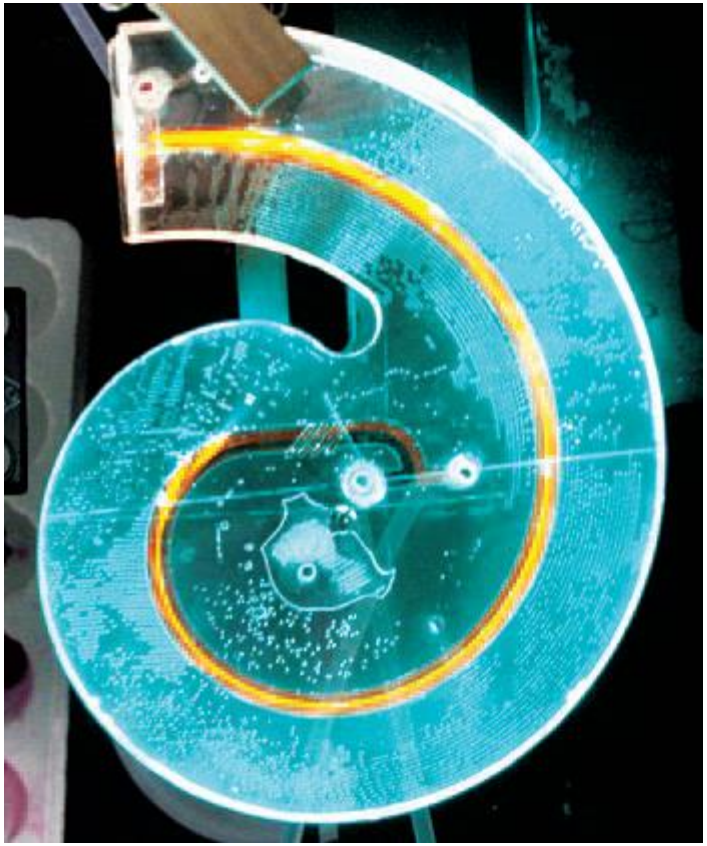






Outline

- What are Optofluidics?
- Why Optofluidics?
  - Optics
  - Microfluidics
- Optofluidics applications
  - Optical devices / components
  - Chemical/medical diagnosis
  - Energy applications

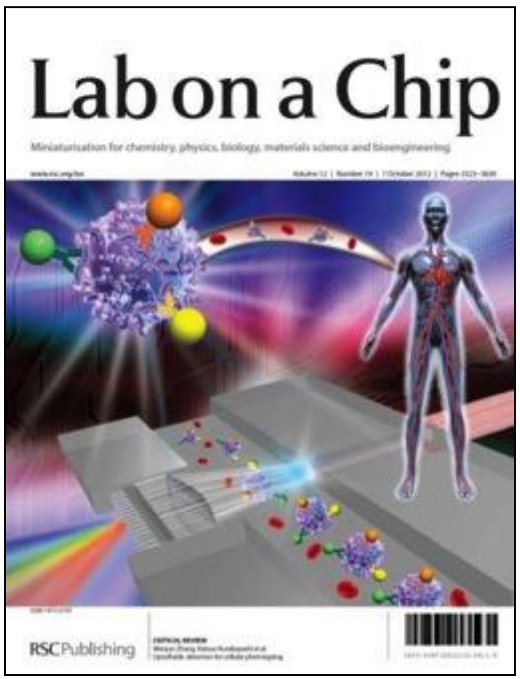


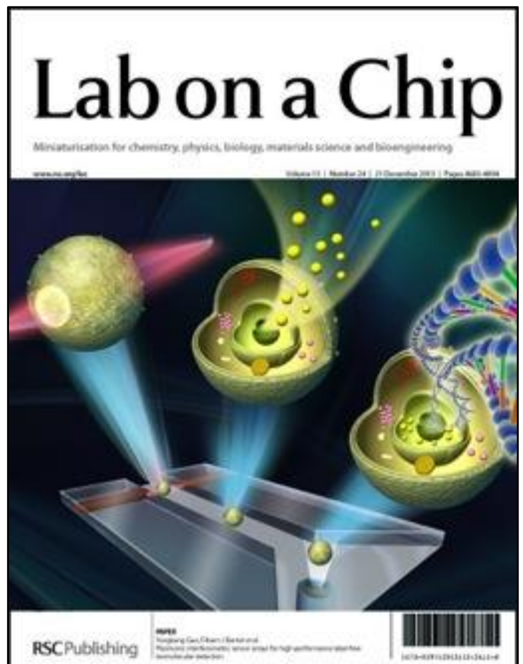
Navy Research Laboratory

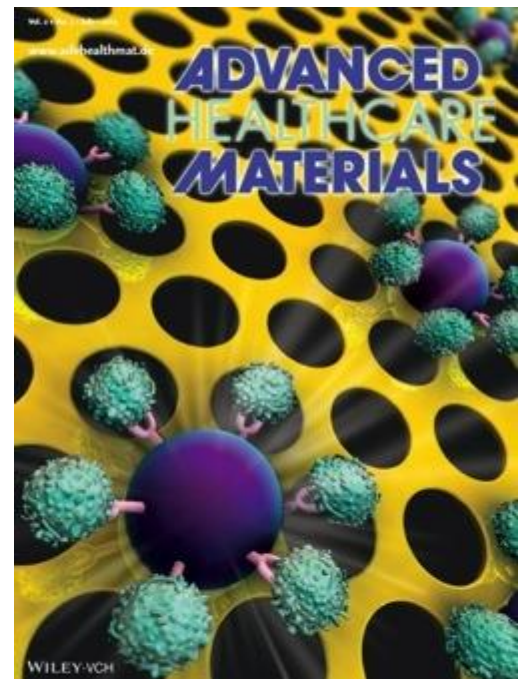
https://www.youtube.com/watch?v=G20GqND61ik

What are Optofluidics?

- A research area integrates optics and microfluidics
  - Emerging from microfluidics and nanophotonics in the mid-2000
- Optics: light source, detector, treatment, sample manipulation
- Microfluidics: sample manipulation, guiding, process







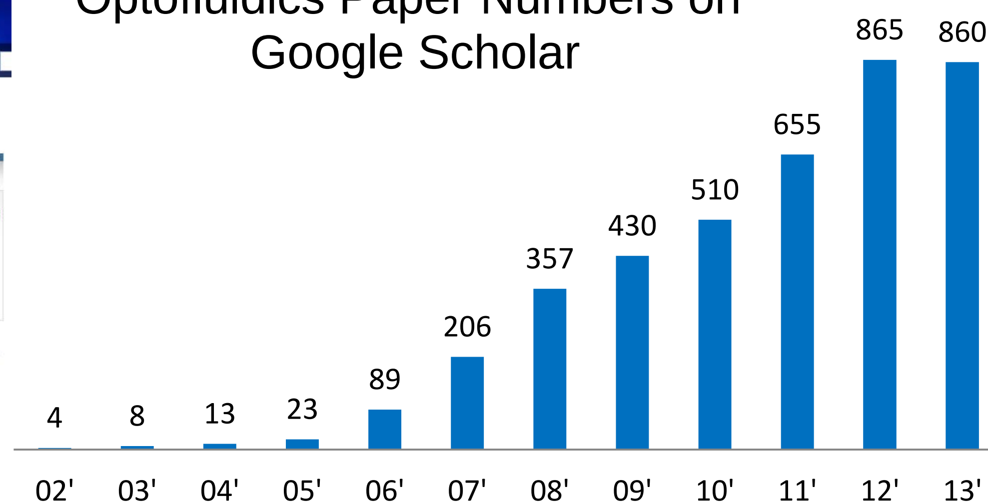
Research Activities of Optofluidics

Journals & Conferences

Company

Optofluidics

Optofluidics Paper Numbers on Google Scholar



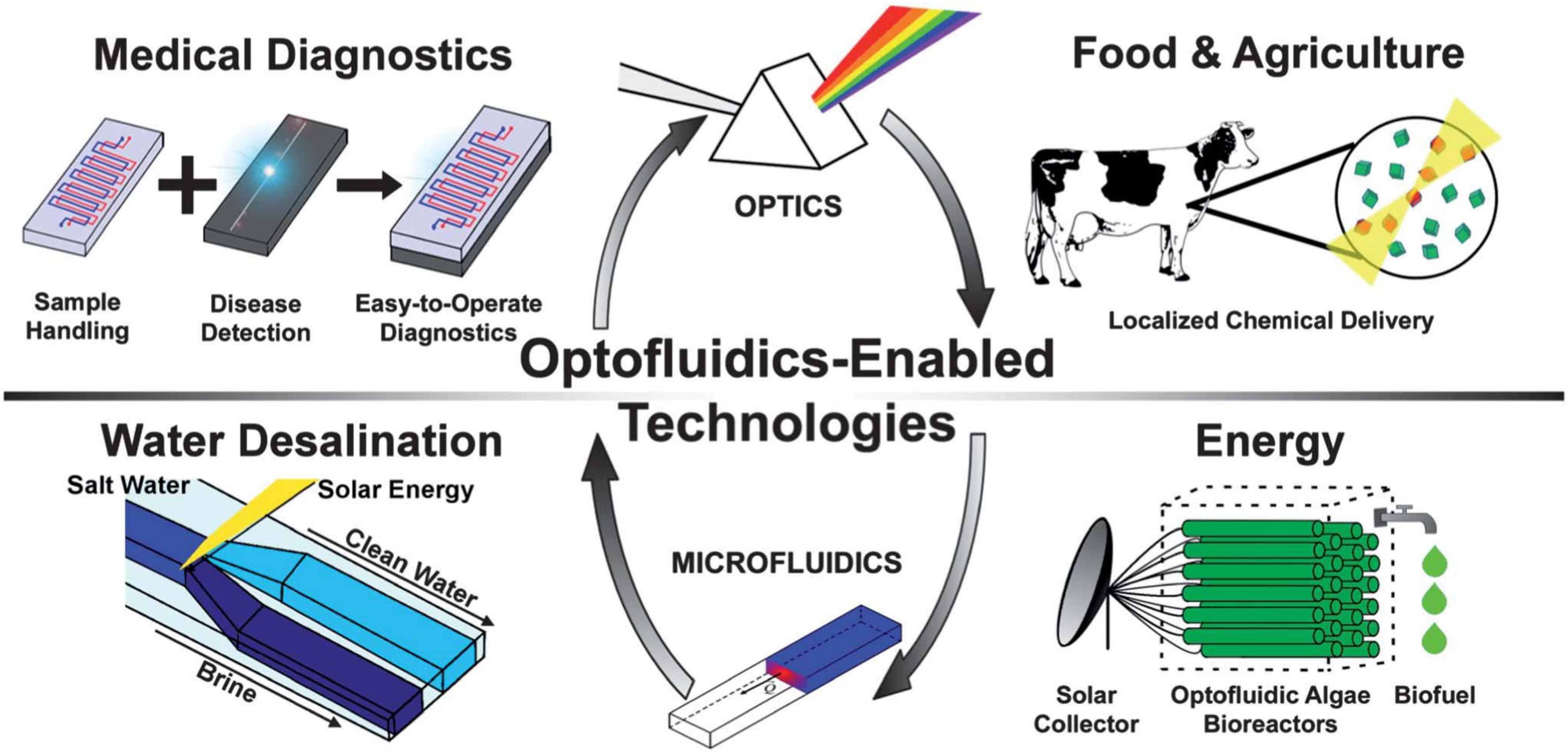
Current Research and Technologies [edit]

There are numerous research groups worldwide working on optofluidics, including those listed below.

Country	University / Institute	Group	Topic
Australia	University of Sydney	CUDOS (Eggleton)[5]	Photonic Crystals.
Austria	Johannes Kepler University Linz	Institute for Microelectronics and Microsensors (Jakoby)[6]	Fluidic sensors, Miniaturized IR sensor systems, microfluidic actuators.
Canada	University of Toronto	Sinton Group[7]	biosensors, energy.
Canada	University of Toronto	Biophotonics Group (Levy)[8]	Photonic crystals, sensors.
Canada	The University of British Columbia	MiNa Group[9]	Integrated optofluidics, sensors.
Canada	Queen's University	Escobedo Group[10]	Optical Diagnostics, Micro/Nano-devices.
Denmark	Danish Technical University	Kristensen Group[11]	Polymer optofluidics, lasers, single molecule analysis.
Israel	Hebrew University	NanoOpto Group (Levy)[12]	Optical Resonators, Plasmonics.
Iran	Sharif University of Technology	M.S. Saidi Group[13]	Optical Diagnostic Methods, Biofluids.
South Korea	Seoul National University	Biophotonics and Nano Engineering Lab (Kwon)[14]	Directed assembly, sensors, structural color.
South Korea	KAIST	Superlattice Nanomaterials Lab (Yang)[15]	Optofluidic materials, SERS sensors.
Germany	Technical University Berlin	Institute of Optics and Atomic Physics	Glass surface and volume structuring.
Germany	Karlsruhe Institute of Technology	Biophotonic Sensors Group (Mappes)[16]	Sensors, fabrication and integration techniques.
Germany	University of Münster	Nonlinear Photonics Group (Denz) [17]	Optical tweezing and its integration into optofluidic setups, direct-laser-writing of optofluidic components
Republic of China	National Taiwan University	Bio-Optofluidic System Lab [18]	optical sensing for dynamic cellular phenotyping.
Switzerland	EPFL	Psaltis Group[19]	optofluidic switches, imaging, energy.
Singapore	Nanyang Technological University	A.Q. Liu Group[20]	Optofluidic waveguides, lab-on-a-chip devices.
Singapore	Nanyang Technological University	N.T. Nguyen Group[21]	Diagnostics, Transport.
Template:ES	ICFO-The Institute of Photonic Sciences	Quidant group[22]	LSPR sensing, Plasmonic tweezers.
Turkey	Koç University	Nano-Optics Research Lab.[23]	Droplet resonators, optofluidic waveguides, optical trapping and manipulation.
United Kingdom	University of St Andrews	Optical Manipulation Group[24]	Optofluidic sensing, trapping, Raman spectroscopy, cell sorting, photoporation
United Kingdom	University of Strathclyde	Centre for Microsystems & Photonics[25]	Optofluidic components in photonic systems
United States	Purdue University	Steve Wereley Group[26]	Holographic optical tweezing, Optoelctrokinetic Patterning, Programmable Microfluidics, Micro-PIV.
United States	Cornell University	Erickson Group[27]	nanophotonic tweezing, optofluidic switches, biosensors, energy.
United States	UC Santa Cruz	Applied Optics Group[28]	Arrow waveguides, single molecule optofluidics.
United States	Brigham Young University	Hawkins Research Group[29]	Optofluidic waveguides, single molecule optical analysis.
United States	Caltech	Yang Biophotonics Group[30]	Optofluidic Microscopy, Imaging, OCT.
United States	UC San Diego	Ultrafast and Nanoscale Optics Group (Fainman)[31]	Nanoscale lasers, optofluidic switches, silicon devices.
United States	University of Michigan	Sherman Fan Lab[32]	Optofluidic lasers, SERS, ring resonators.
United States	University of Maryland	White Research Group[33]	Medical diagnostics, SERS, circulating tumor cells.
United States	Caltech	Nanofabrication Group (Scherer)[34]	Optofluidic Lasers, DNA detection, photonic crystals.
United States	Penn State	BioNEMS Laboratory (Huang)[35]	Optofluidic lenses, plasmonics.
United States	UC Berkeley	BioPOETS (Lee)[36]	Optofluidic transport, SERS, microfluidics.
United States	UC Berkeley	Berkeley Integrated Photonics Lab (Wu)[37]	Optoelectronic tweezers.
United States	UC San Diego	Lo Research Group[38]	Optofluidic flow cytometry.
United States	UIUC	Nano Sensors Group (Cunningham)[39]	Photonic Crystal Sensors, SERS.
United States	Harvard	Crozier Group[40]	Near Field Trapping, SERS
United States	Princeton University	Imaging Physics Group[41]	Microfluidic Tomography,[42] Deconvolution,[43] Superresolution[44]
United States	Iowa State University	Nastaran Hashemi Group[45]	Optofluidics, microfluidics, biosensors, diagnostics and therapeutics, energy.
United States	Iowa State University	Attinger Group[46]	Optofluidic transport
United States	Boston University	LINBS (Altug)[47]	Plasmonics, nanohole sensors, high throughput diagnostics
United States	University of Wisconsin, Madison	Micro/nano sensors and actuators group [48]	Liquid tunable microlenses.
Belgium	Vrije Universiteit Brussel	Brussels Photonics Team (B-PHOT) [49]	Polymer optofluidics, biosensors

https://en.wikipedia.org/wiki/List_of_optofluidics_researchers

Optofluidics Applications



(Nanoscale, 2012, 4, 4839–4857)

https://www.youtube.com/watch?v=m-eJOAx9DA4

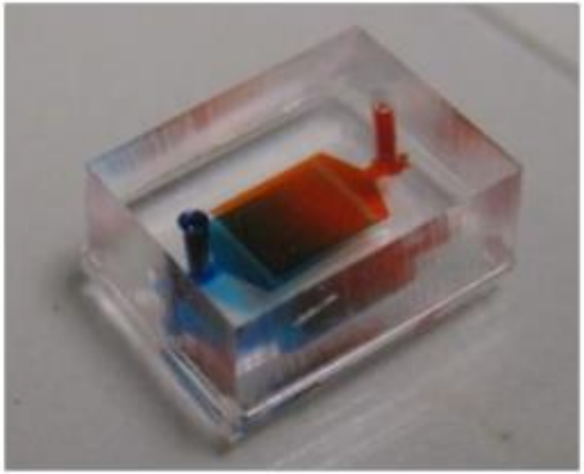
https://www.youtube.com/watch?v=-vwQ47TLJrA

Optofluidics for Optical Components

- Optical devices
  - Liquid waveguide, liquid lens, liquid mirror
- Optical manipulation
  - Cell, particle trapping, sorting and selection
- Optical sensing
  - Cell based analysis
  - Molecular imaging tools
  - Lab-on-chip devices

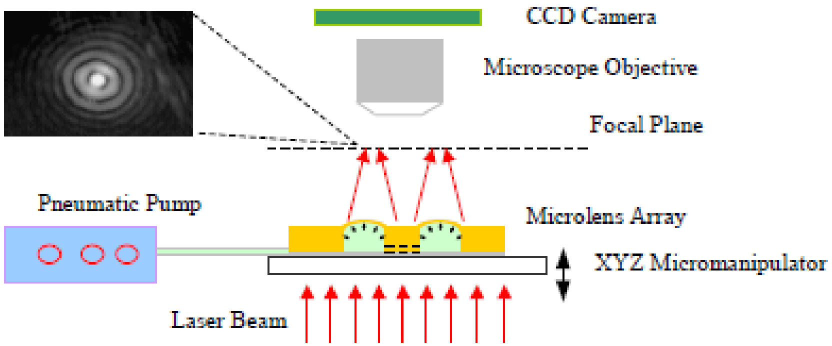
Liquid mirror telescopes

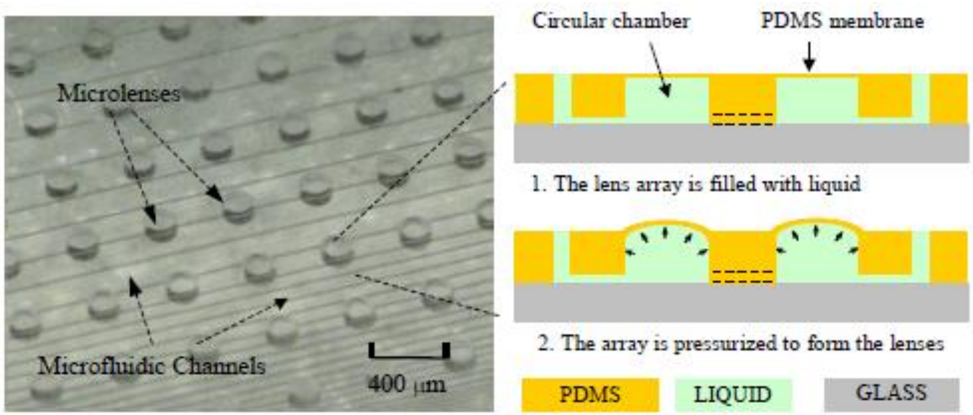
Materials? Advantages?



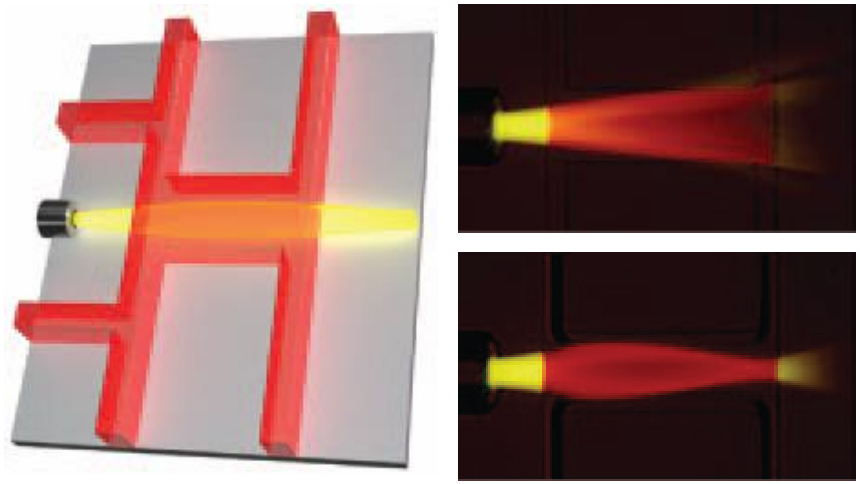
Optofluidics for Optical Components

Tunable curvature microlens

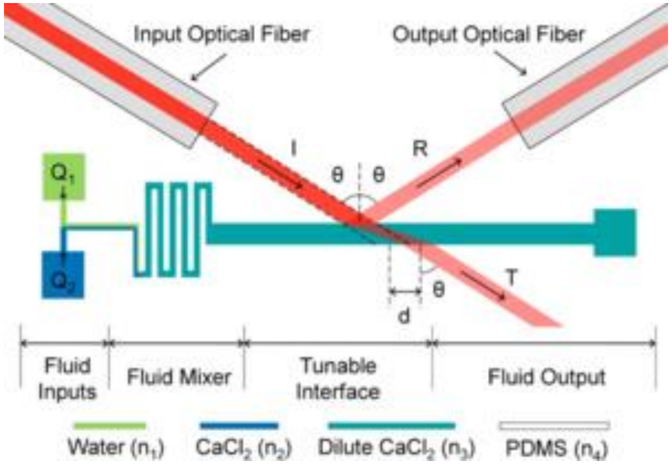




Luke Lee's group at UC Berkeley



Optical attenuator

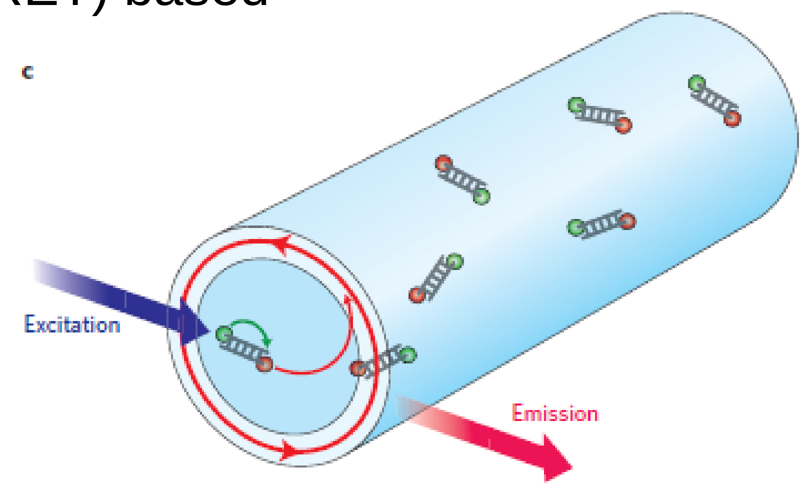


Tony Huang's group at PSU

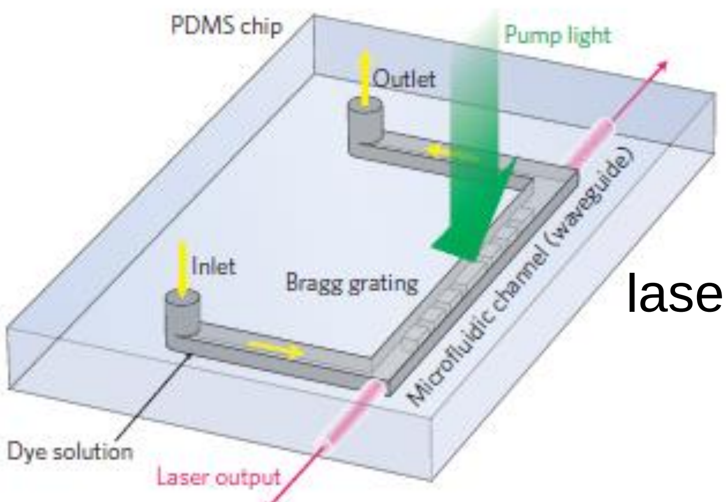
Optofluidics for Optical Components

- Dye laser
  - a laser which uses an organic dye as the lasing medium

Forster resonance energy transfer (FRET) based



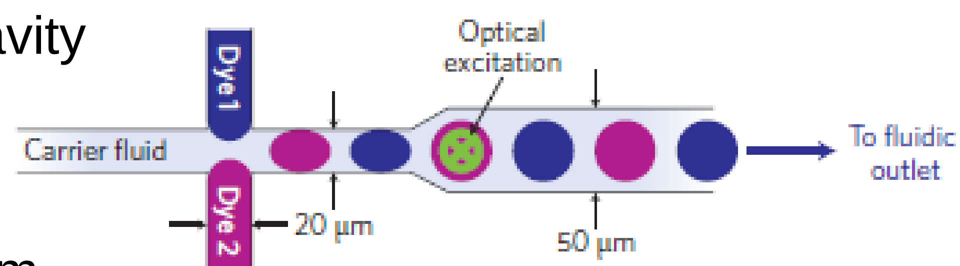
Grating based



laser cavity

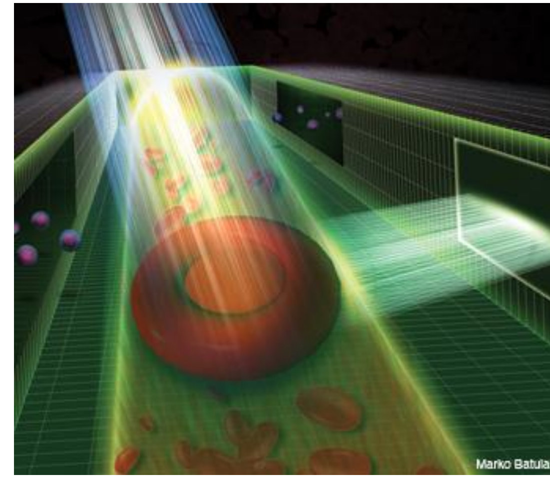
R6G as the fluid medium

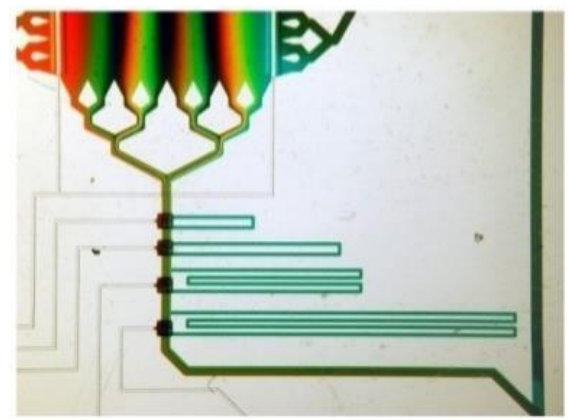
Microdroplet based



Optofluidics for Biological Analysis

- Optics for biological analysis
  - Non-invasive, less disturbing
  - High spatial resolution (~μm)
  - Fast response (real-time analysis)
  - Low biological damage
- Microfluidics for biological analysis
  - Laminar flow
  - Less sample and reagent requirement
  - Multi-functional analysis
  - Fast and uniform nutrition transfer

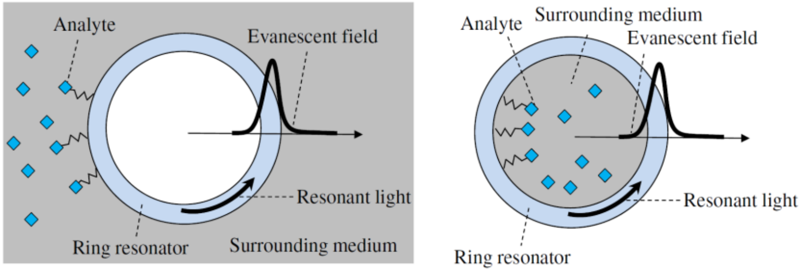


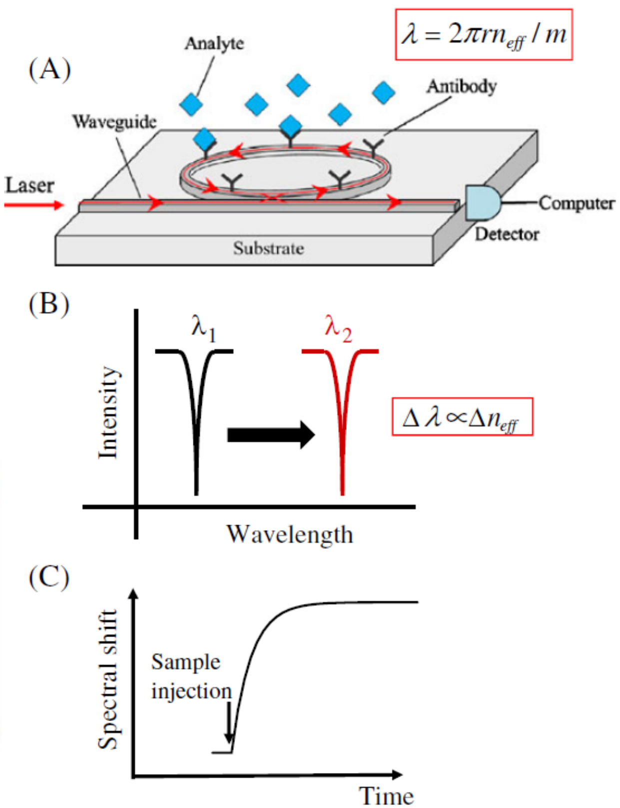


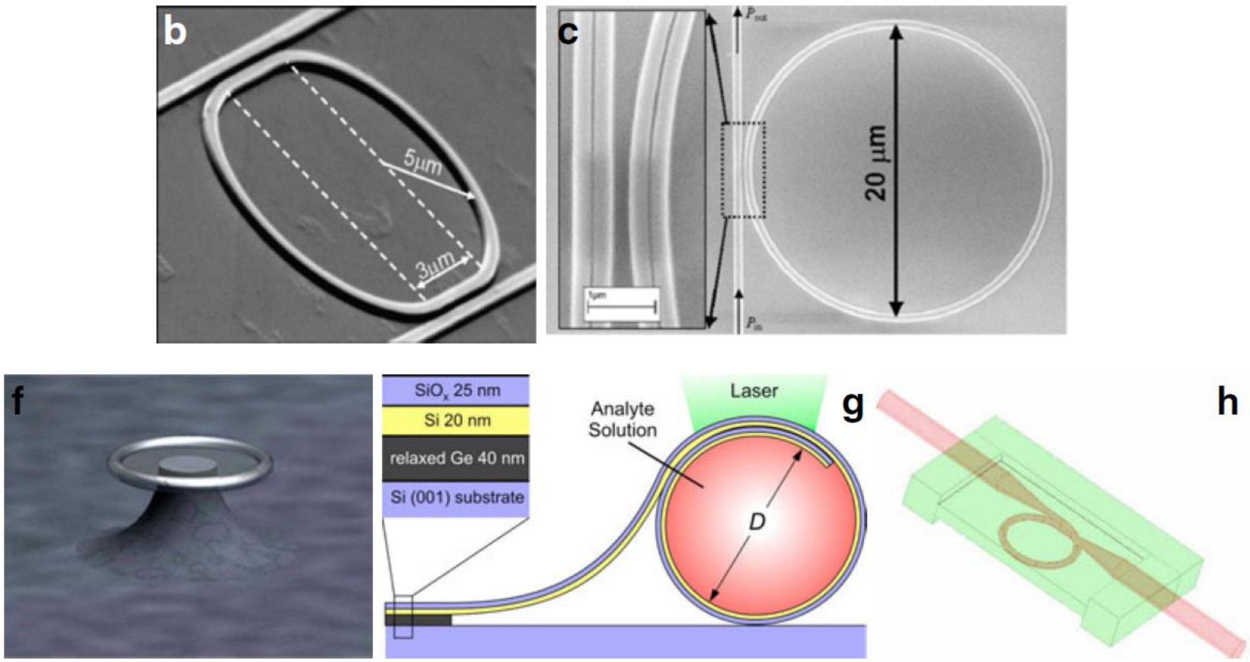
A. Folch Group at U Washington

Optofluidics for Biological Analysis

- Ring resonator sensor
  - Use the evanescent field to measure the analyte binding
  - Label-free detection



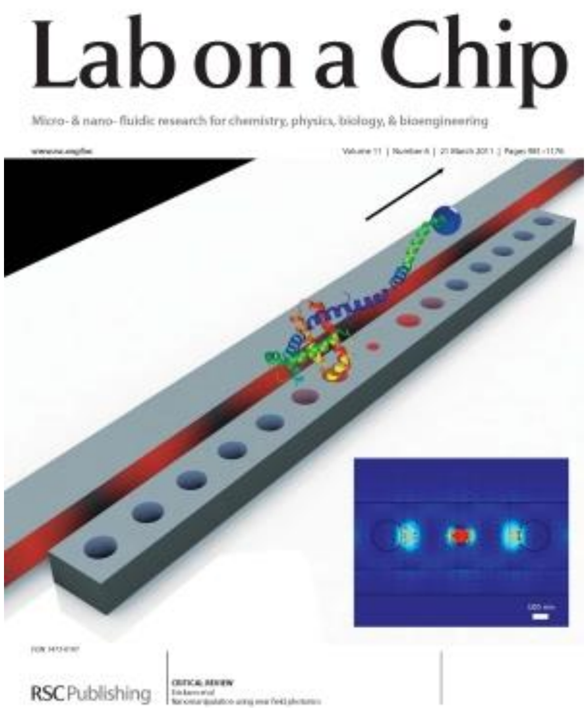




X. Fan Group, U Michigan

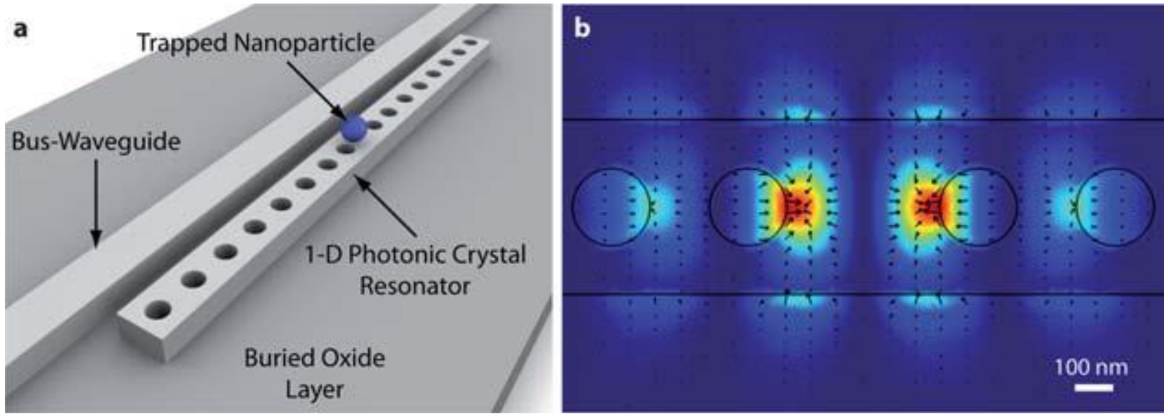
NanoTweezer

- First commercial product in optofluidic field
- Develop by Prof. Erikson at Cornell at Cornell University

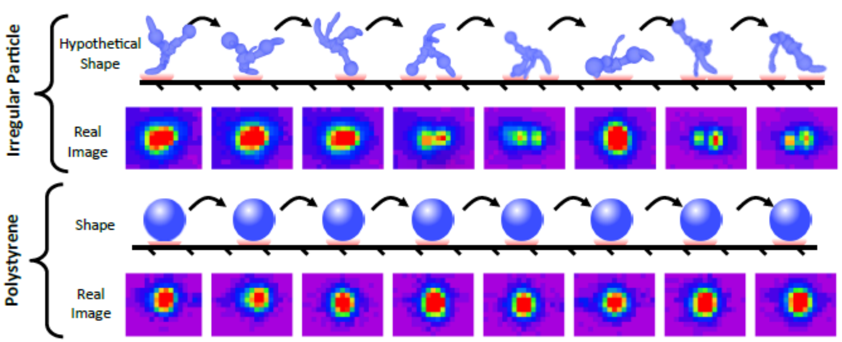


NanoTweezer

- Based on photonic crystal resonator to enhance scattering force



- Particle trapping, protein aggregation analysis, dynamic label- free particle shape analysis

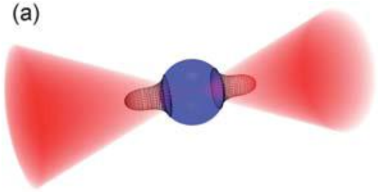


Optical Force to Manipulate Particles

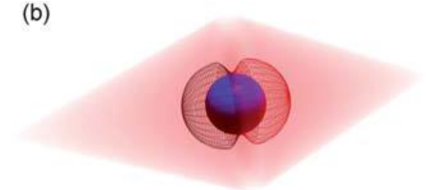
- Gradient force trapping
  - Pulling force: proportional to the gradient of light intensity

$$F_{grad} = \frac{2\pi \nabla I_o \alpha}{c}$$

(a)

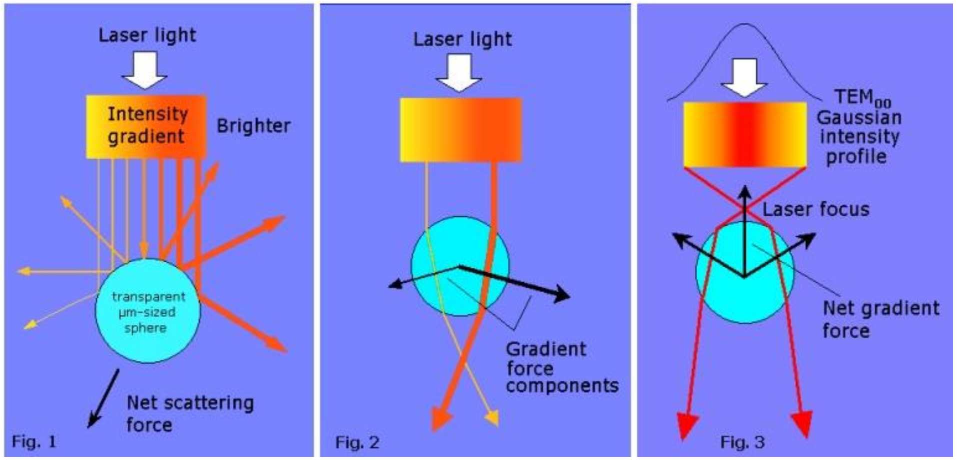


(b)



- Scattering force trapping
  - Weak repulsive force: along the propagation direction: proportional to the intensity of light
  - Less damage, suitable for stretching and rotating cells

$$F_{scat} = \frac{8\pi^3 I_o \alpha^2 \varepsilon_m}{3c\lambda^4}$$



http://optical-tweezers.com/RadiationPressure.htm

Next Steps of Optofluidics?

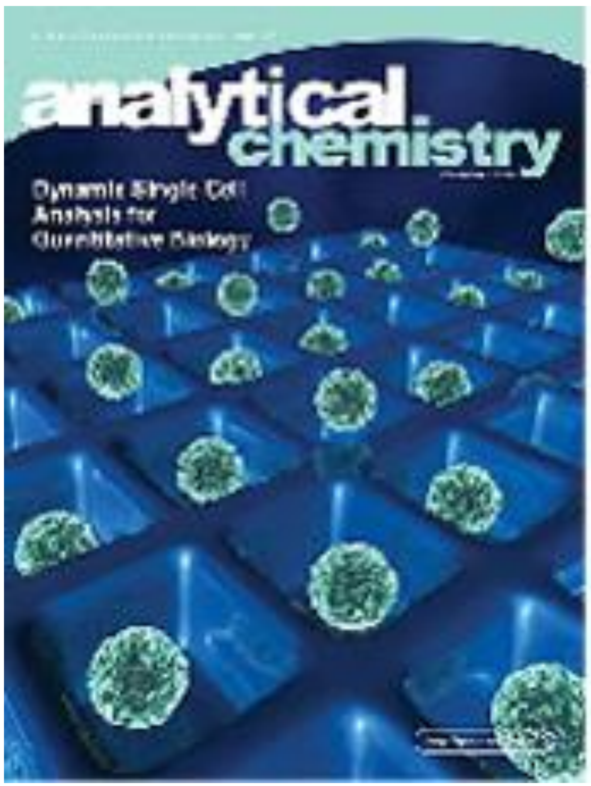
- Optofluidics should miniaturize optical components into one chip
  - A Lab-on-Chip device for point of care (POC) approach
- Why?
  - Less optical alignment
  - Small sample requirement
  - Fast response time
- How?
  - Reduce the size of optical components
  - Portable and disposable microfluidic chip

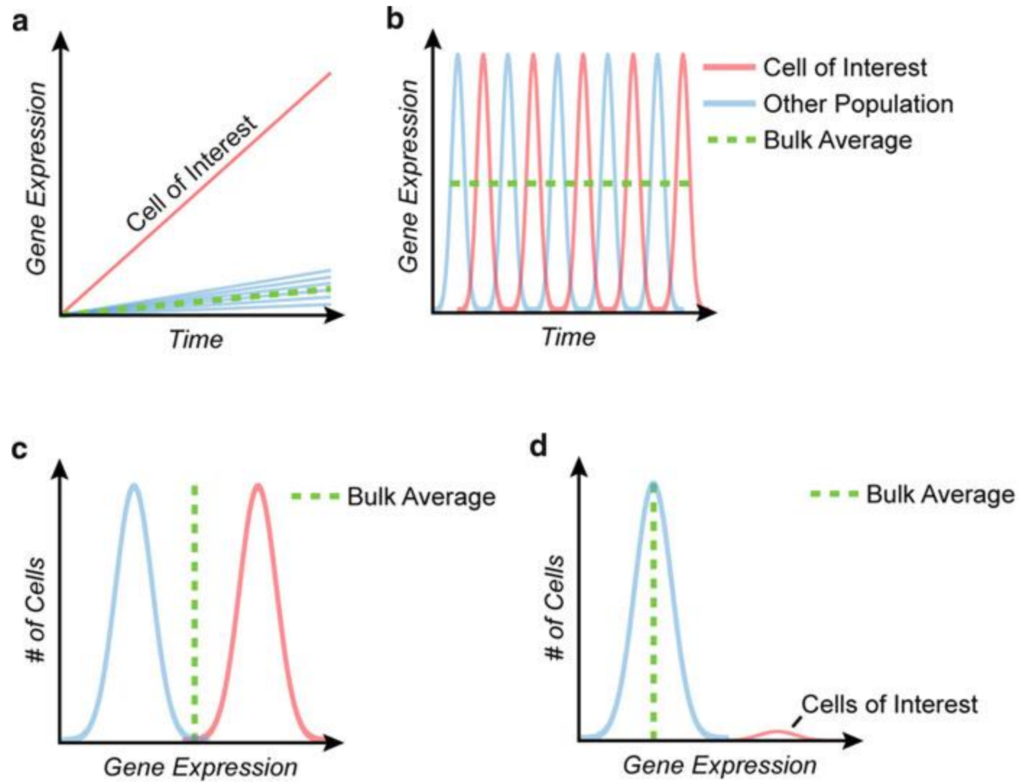
Next Steps of Optofluidics?

- Optofluidics should integrate multiple cell analysis functions into one chip
  - A Fully Optical Microfluidic (FOV) platform
- Why?
  - Simplicity of optical components (non-invasive)
  - Fast cellular operation
  - Flexibility toward to different cell types and applications
- How?
  - Dual wavelength light source
  - Better photo detectors (e.g. EMCCD, multi-anode PMT)

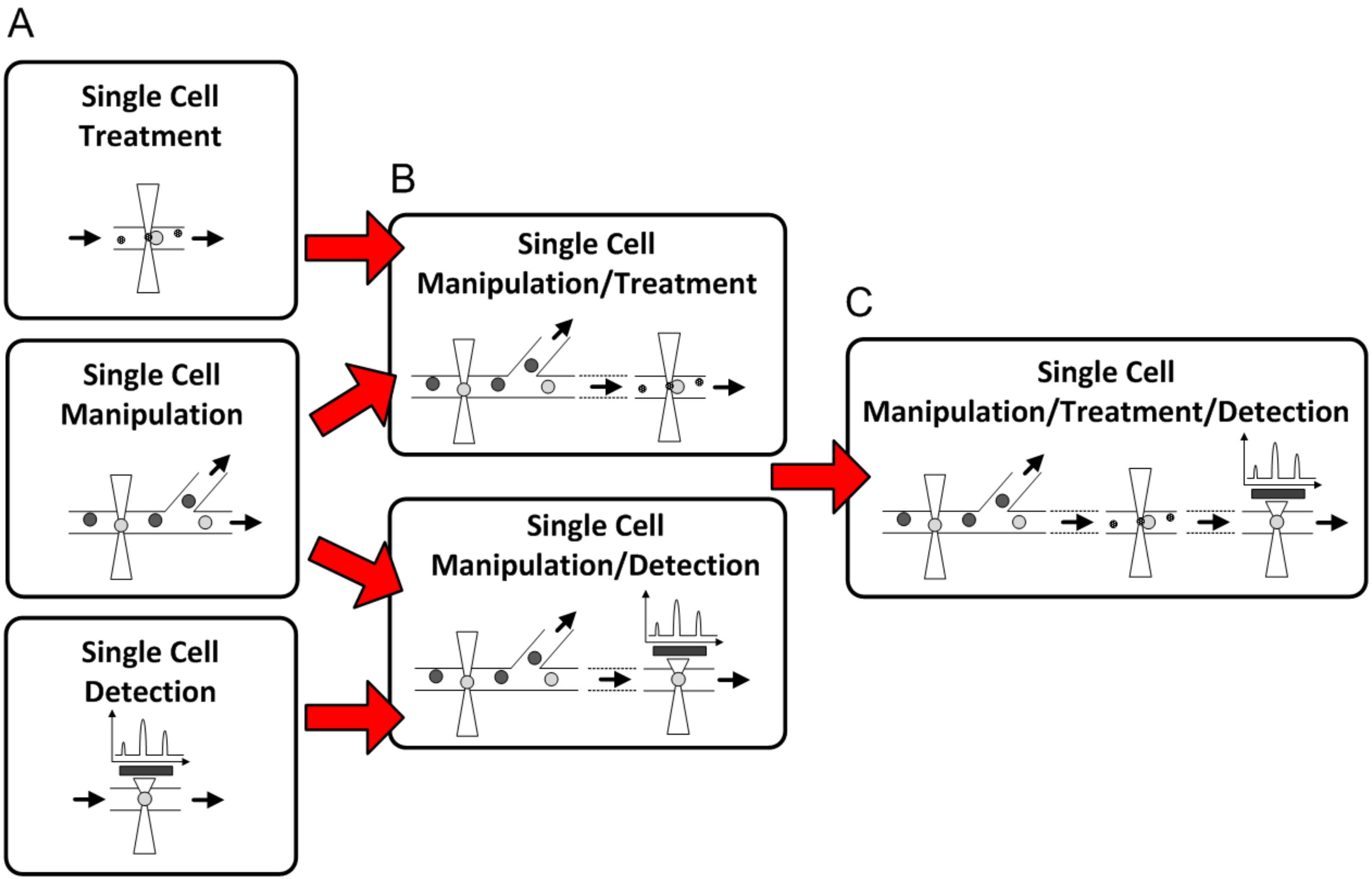
Optofluidics for Single Cell Analysis

- Why analyze single cells?
  - Cell heterogeneity



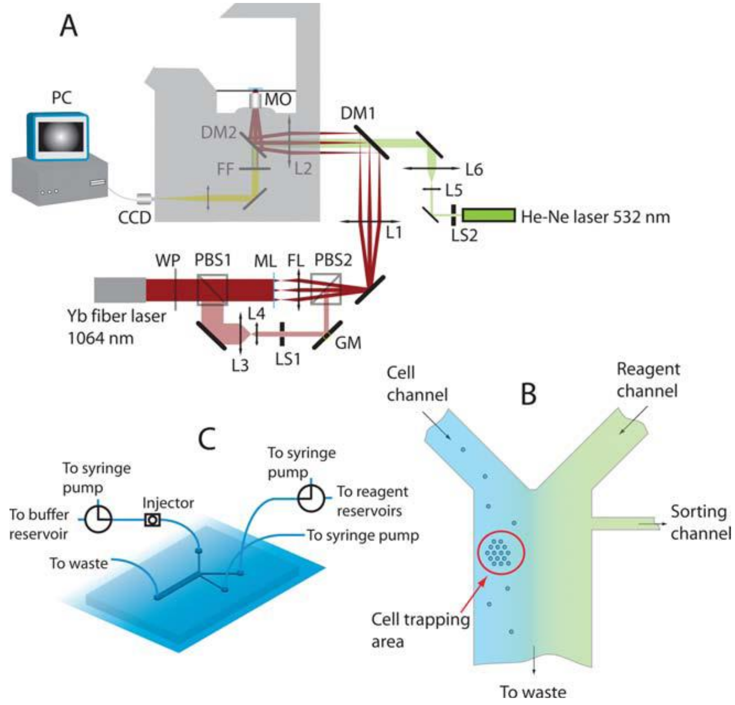


Optofluidics for Single Cell Analysis

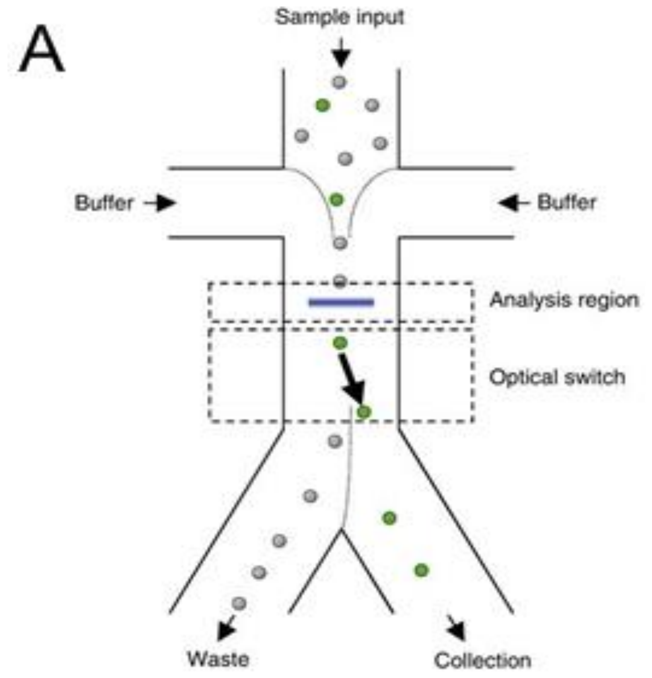


Single Cell Optical Manipulation

- Gradient Force
  - Cell detection / sorting
  - Microarray cell trapping



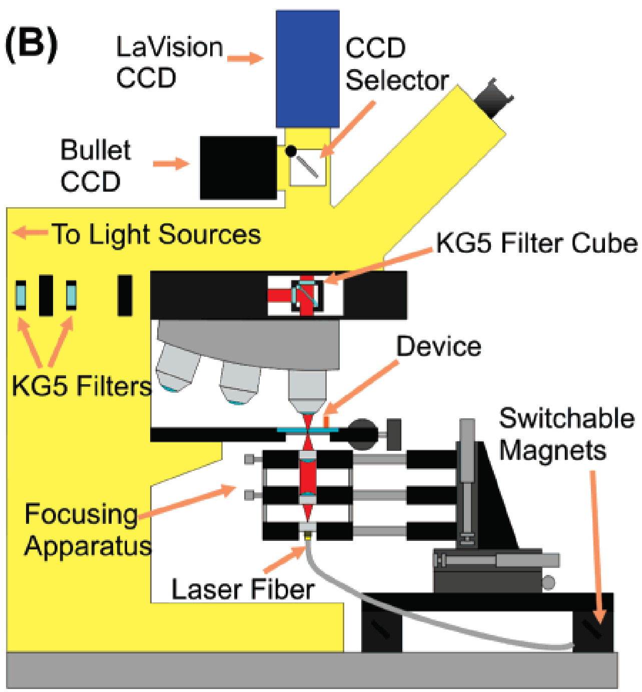
(Lab Chip, 2011, 11, 2432–2439)

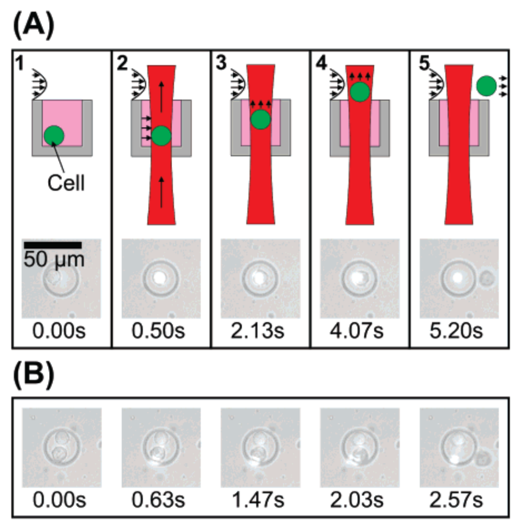


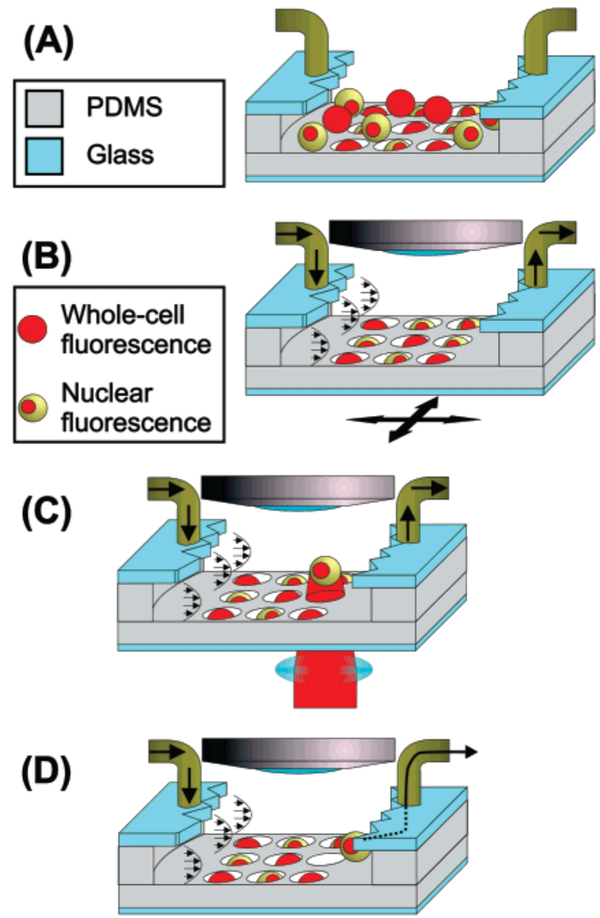
(NATURE BIOTECHNOLOGY VOLUME 23 NUMBER 1, 83-87, 2005)

Single Cell Optical Manipulation

- Scattering Force
  - Multi-parallel cell separation



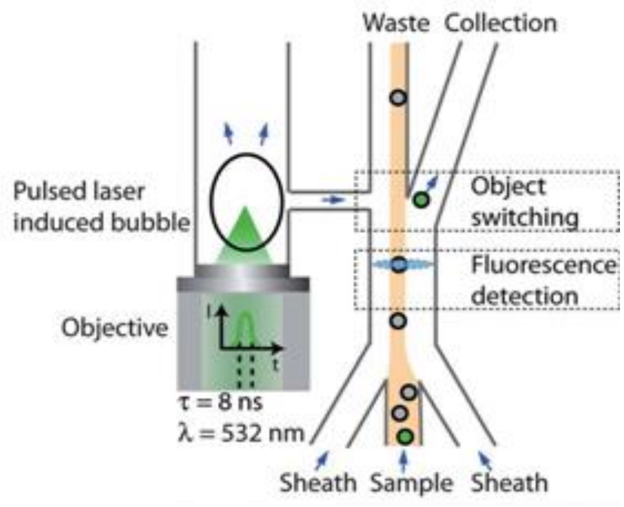




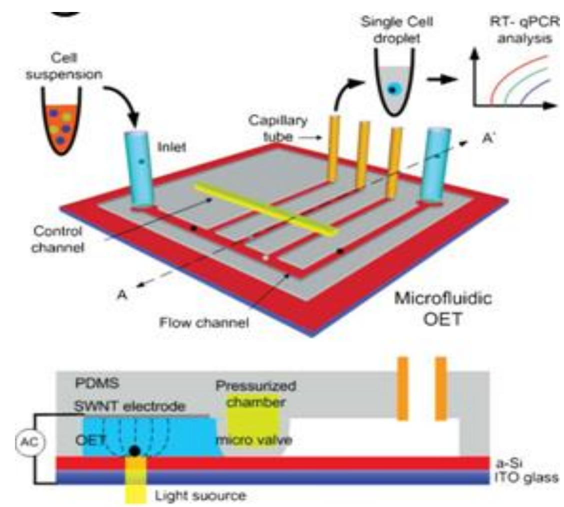
(Analytical Chemistry, Vol. 79, No. 24, 9321-9330, 2007)

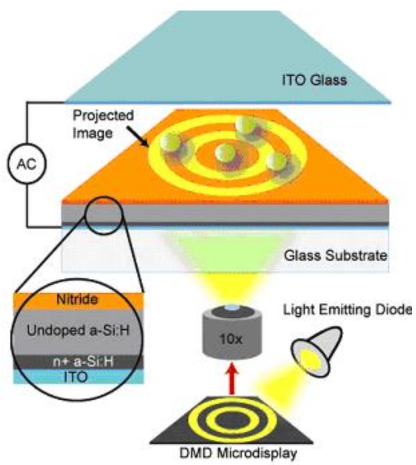
Single Cell Optical Manipulation

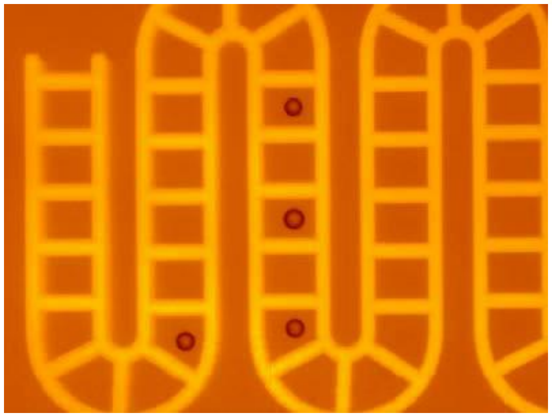
- Pulsed laser induced bubble



- Light induced electrical field
  - Optoelectronic Tweezers (OET)



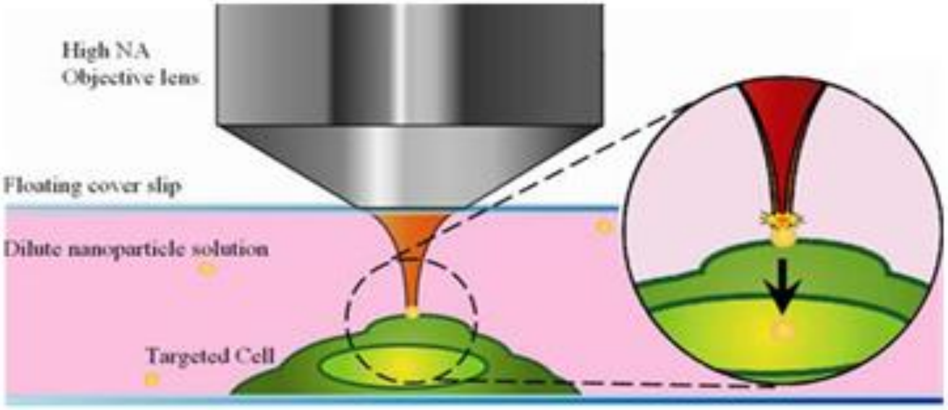


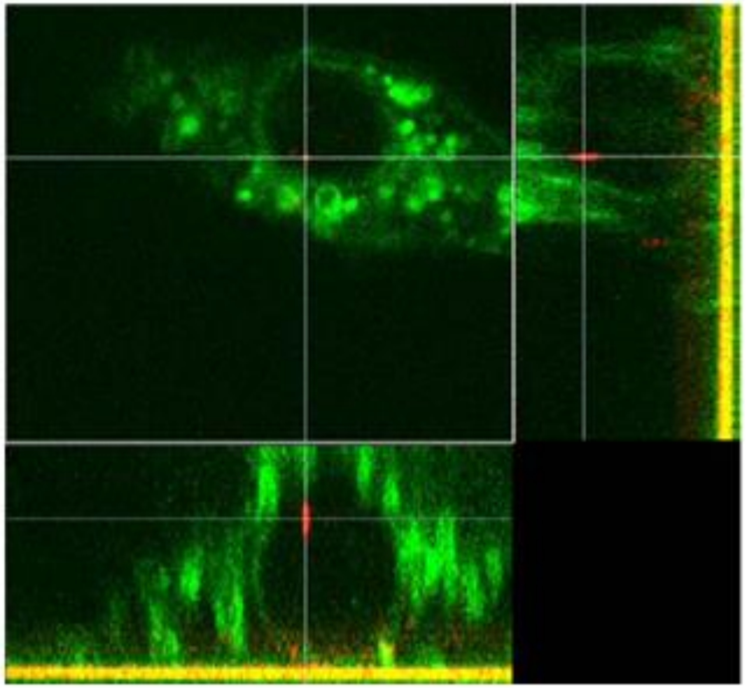


Ming Wu Group at U.C. Berkeley

Single Cell Optical Treatment

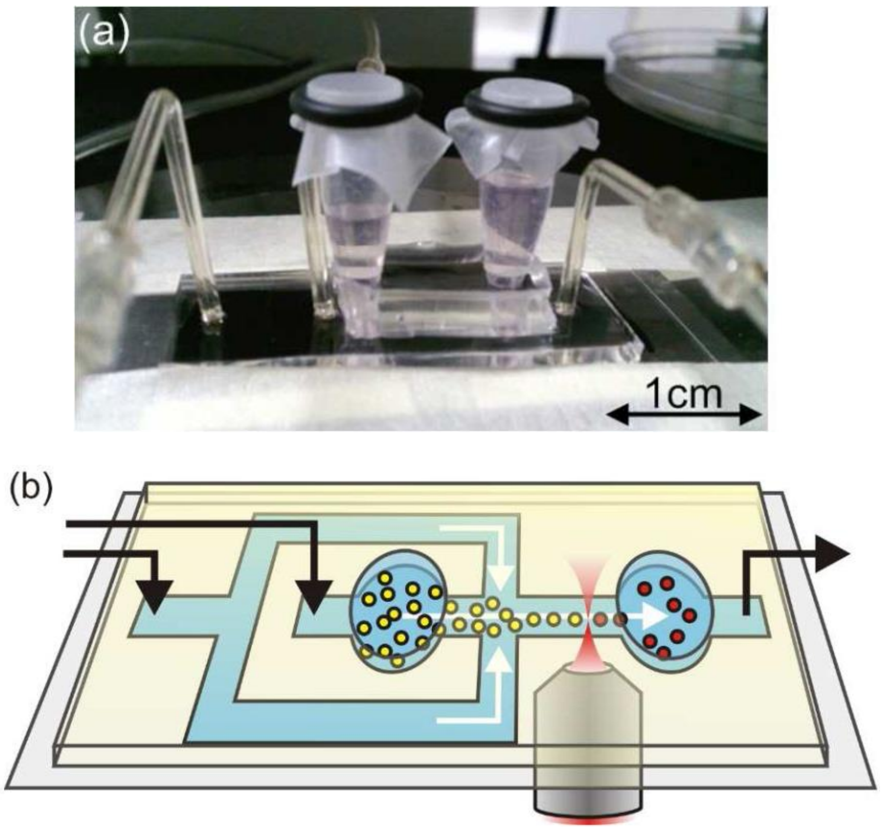
- Optical Transfection and injection
  - Transfection: DNA, RNA, Protein
  - Injection: gold nanoparticle

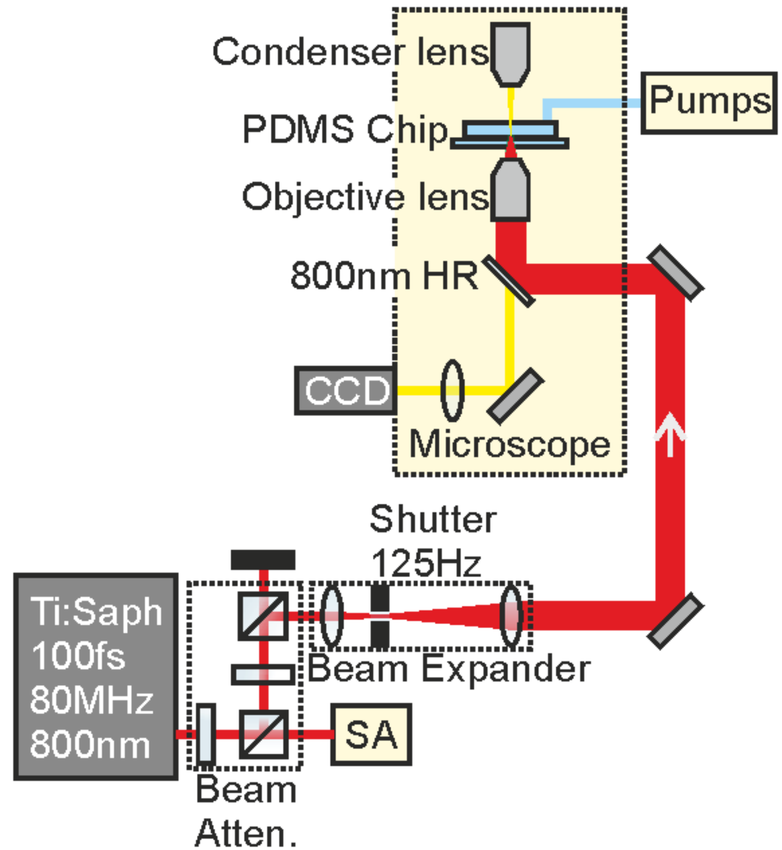




Single Cell Optical Treatment

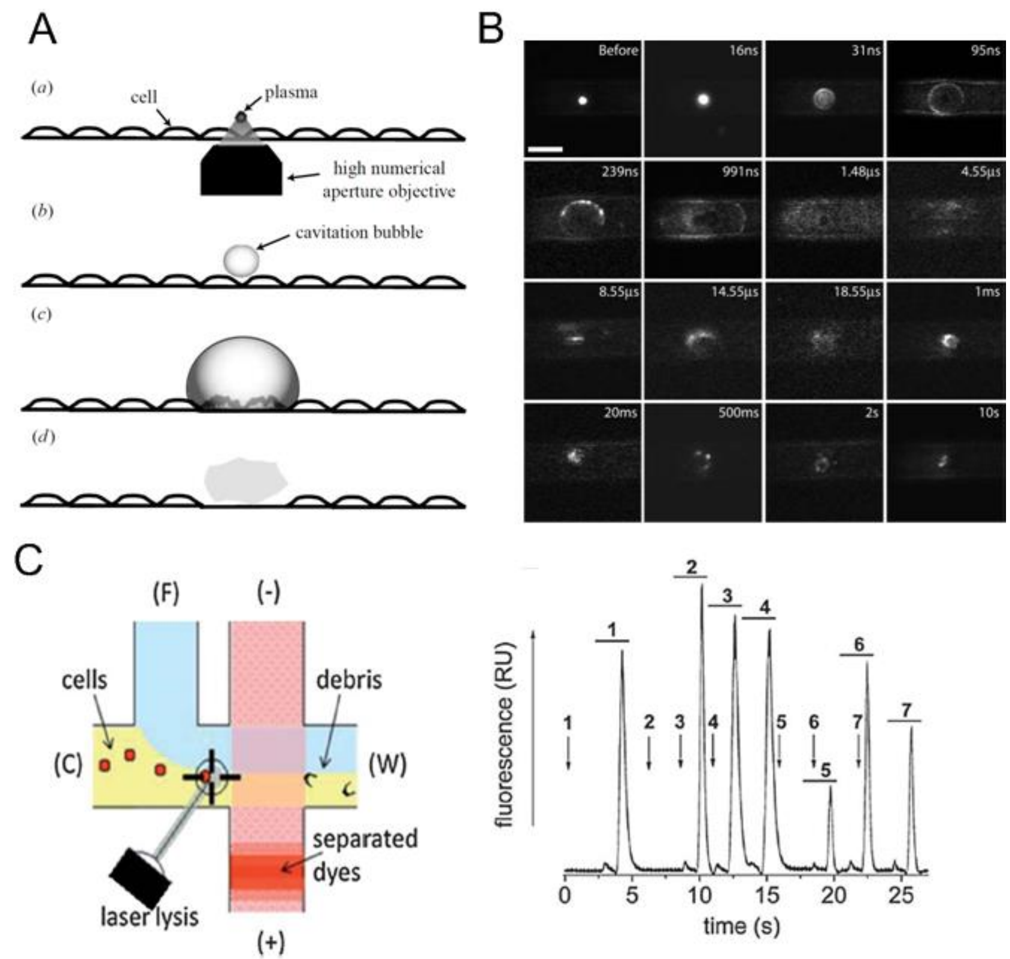
- High-throughput optical injection enabled by microfluidics





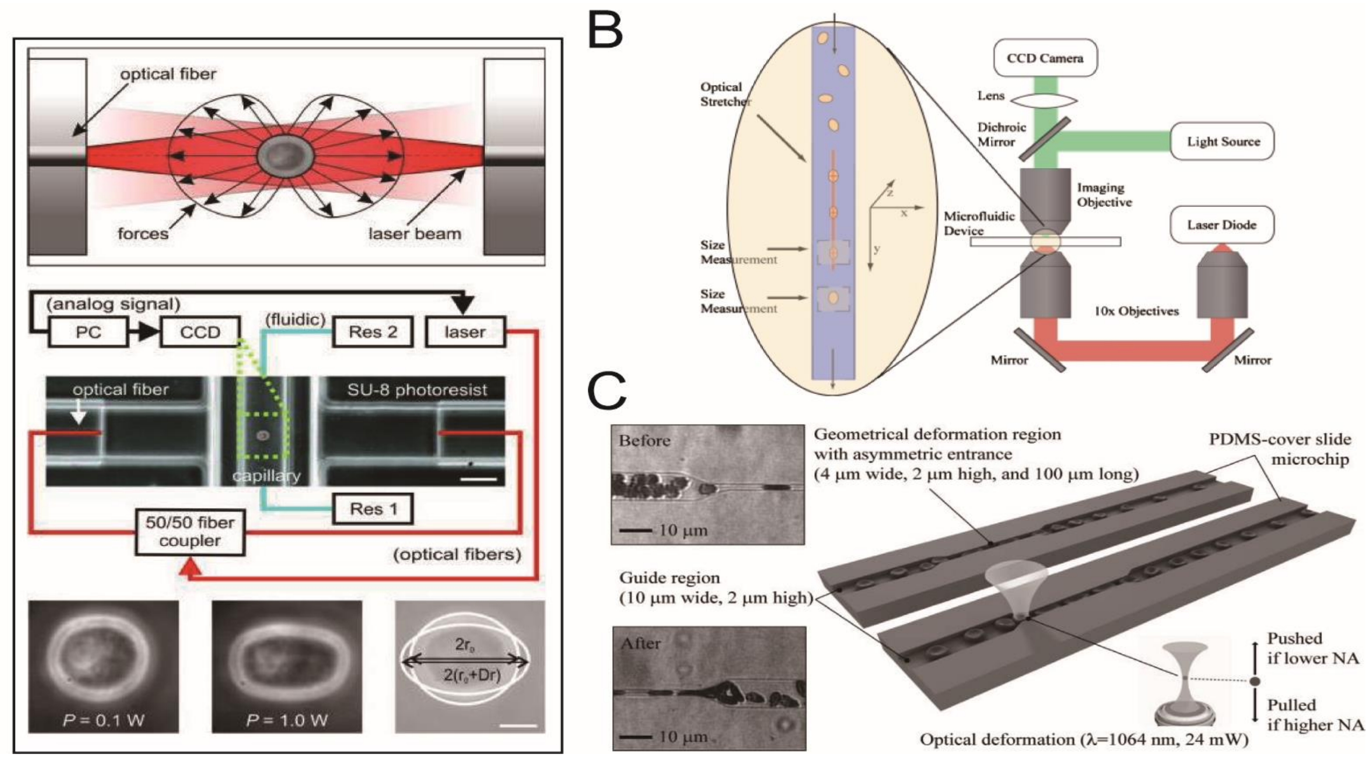
Single Cell Optical Treatment

- Steps of laser-induced cell lysis process
- Time-lapsed fluorescence images showing cell lysis dynamics in a microfluidic channel
- Optofluidic devices enabling cell lysis and electrophoresis separation of two fluorescent dyes inside cells.



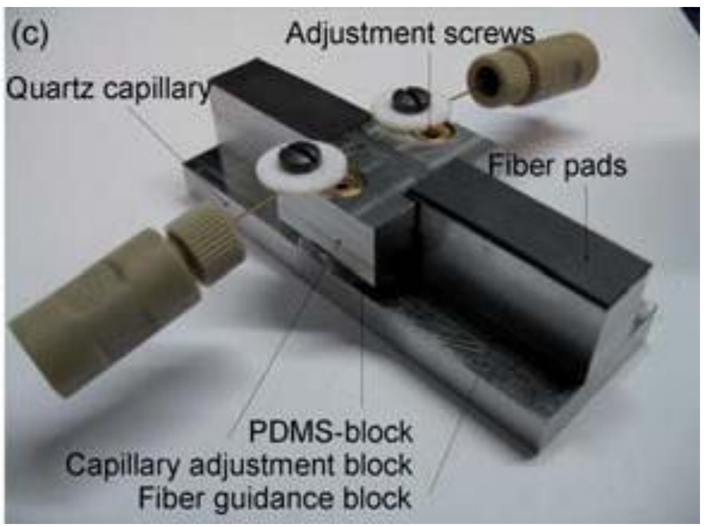
Single Cell Detection

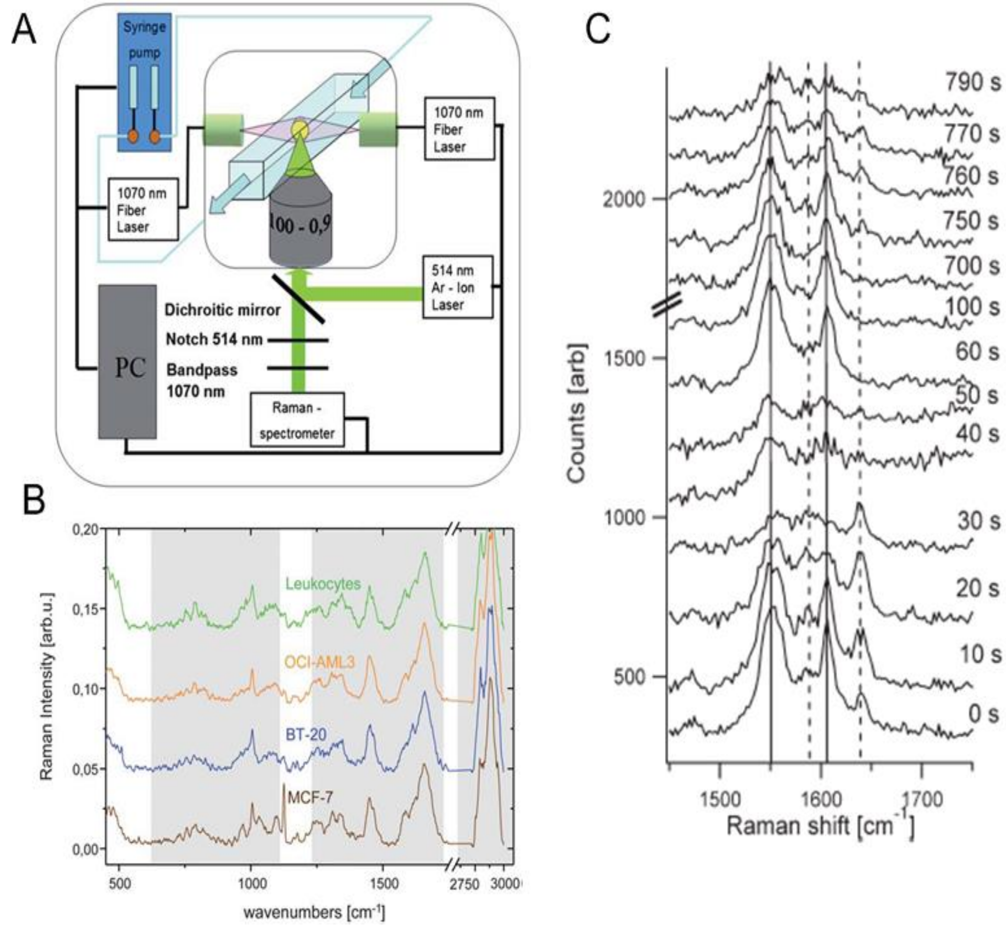
- Cell deformability detection
  - Use a optical stretcher with two laser beams from fiber
  - Normal cells v.s. cancer cell (more deformable)
  - Hematological disorder by measuring the deformability of RBC



Single Cell Detection

- Raman Tweezers
  - Cancer / normal cells
  - Oxygenation dynamics of single red blood cell





Bacteria Infection Diagnosis Method

- Current bacteria antibiotic susceptibility test (AST)

Plate culture
BacT/Alert

1day
1day-3day

- Two problems:
  1. complicated procedures and bulky instruments
  2. prolonged process time

Microfluidics for bacteria AST

- Standard AST

Biological samples (Ex: blood) → (Blood) Culture [1-3 days] → Plate culture [1 day] → Observation [~hrs]

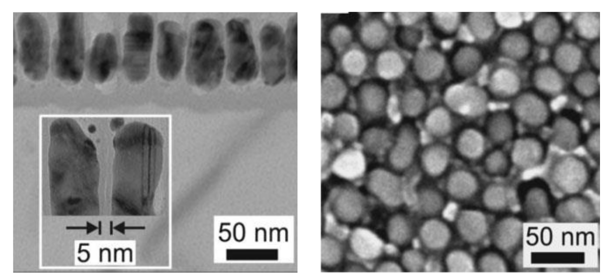
- Microfluidic AST

Biological samples (Ex: blood) → (Blood) half-time Culture → Broth/ microfluidics culture [~hrs] → LC separation [~mins] → SERS detection [~mins]

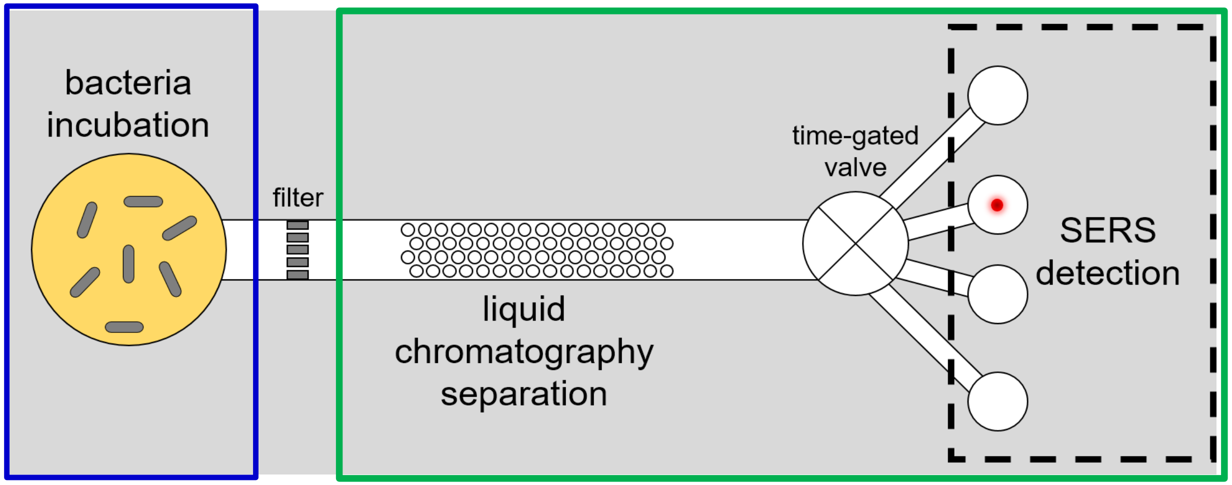
Sample pre-treatment | On-chip culture | Metabolite collection & SERS

- System integration:
  - Less manipulation error
  - Lower sample volume & process time
- Surface-Enhanced Raman Scattering (SERS)
  - Label-free and rapid detection

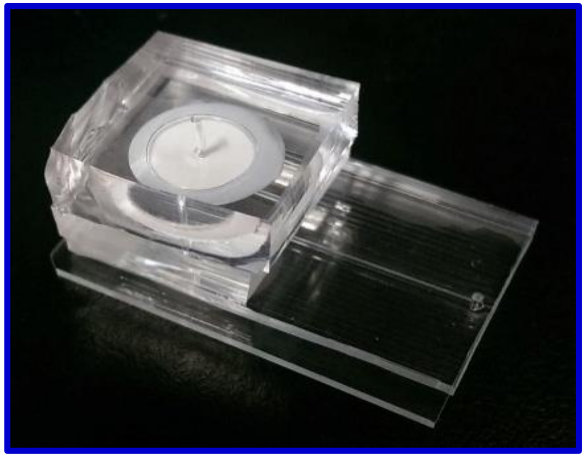
D=25nm W=5nm

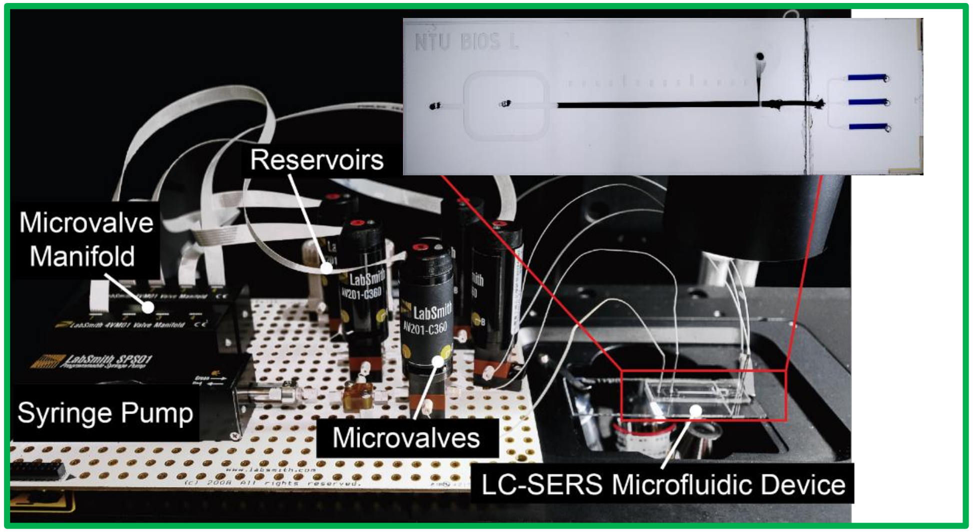


Microfluidics for bacteria AST



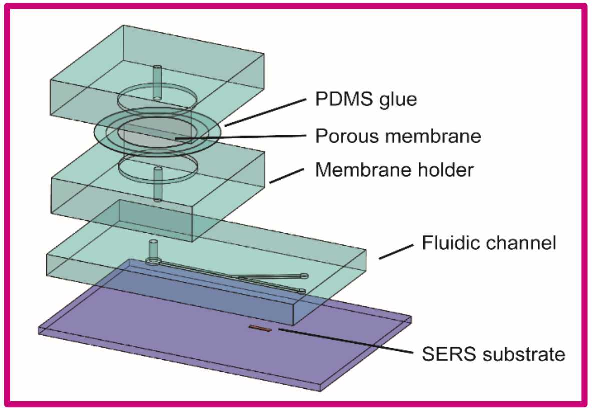
Sample preparation + Metabolite detection

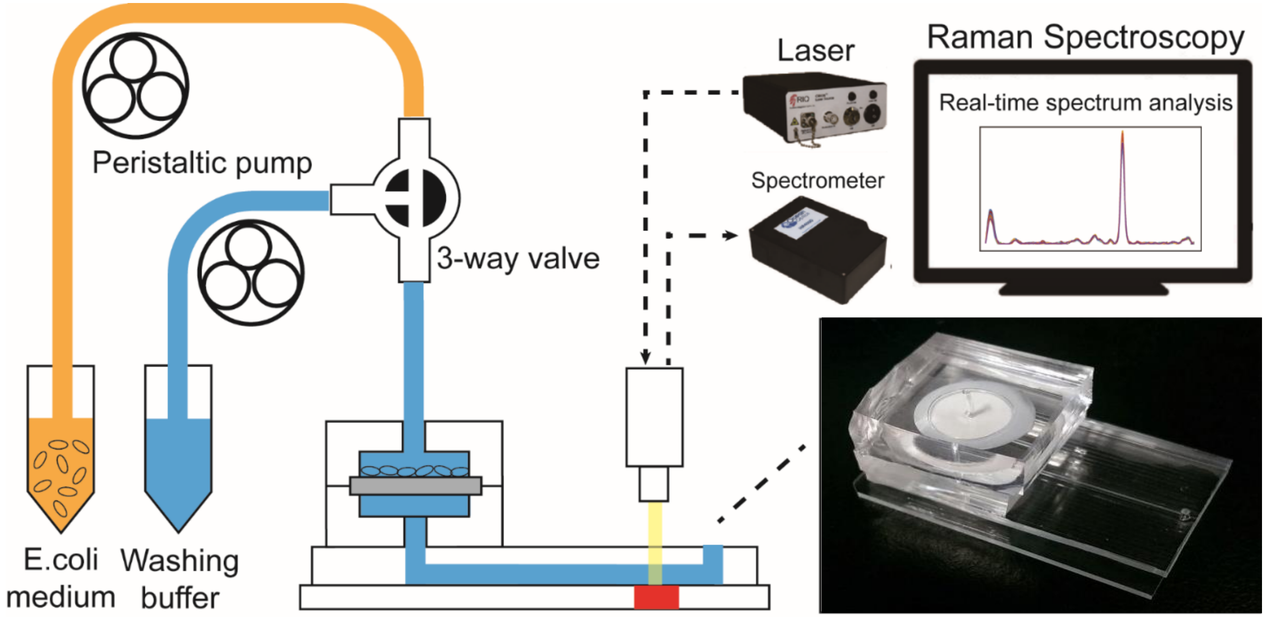




Microfluidic device for bacteria trapping

- Integrating a porous membrane in PDMS microfluidic device: enables bacteria filtration, buffer washing and culture
- Bacteria process timeless is than 5 minutes
- Low bacteria concentration requirement





(Chang et. al., in preparation)

Automated microfluidic control system

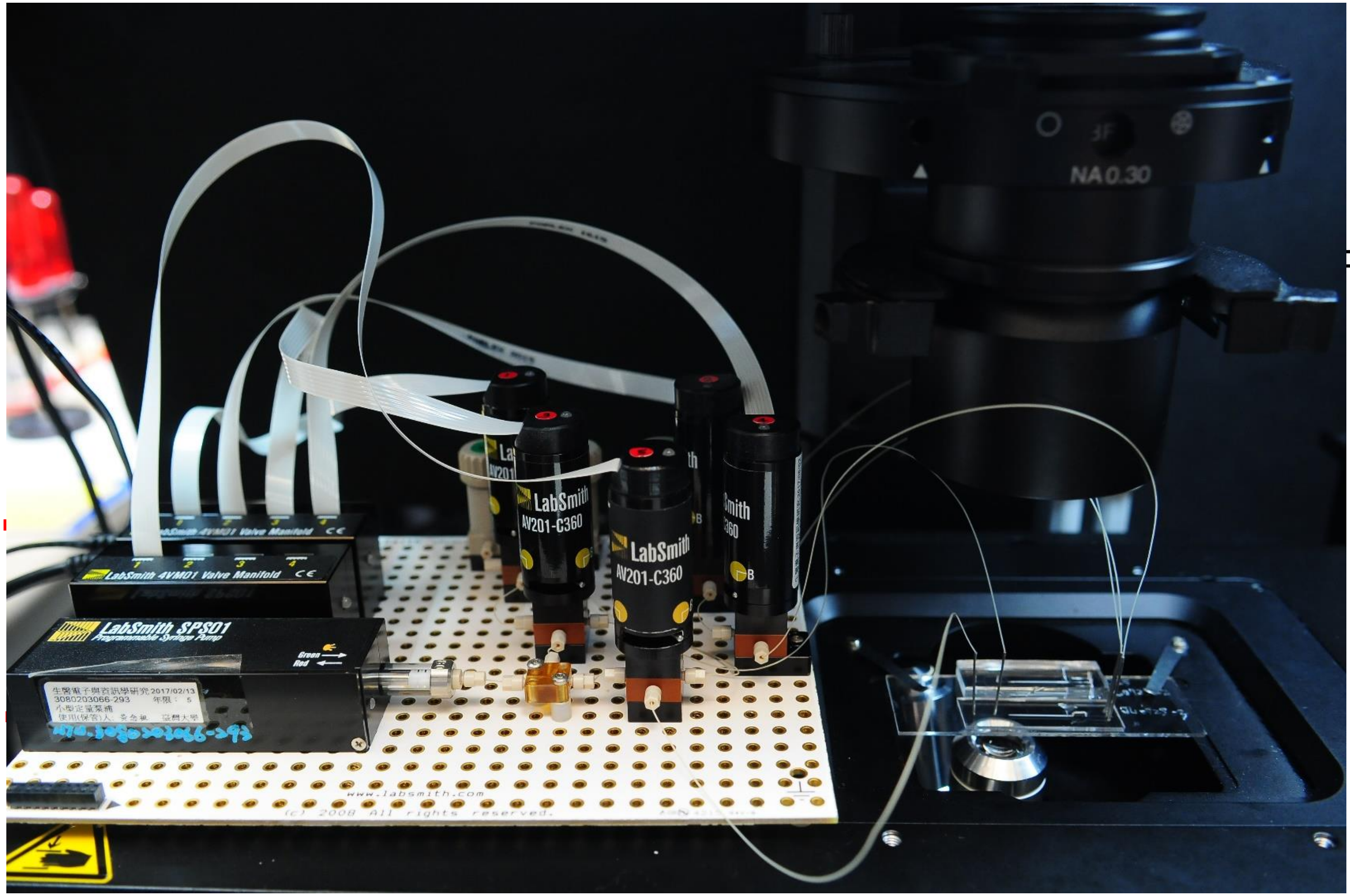
185 mm X 133 mm

Reservoirs

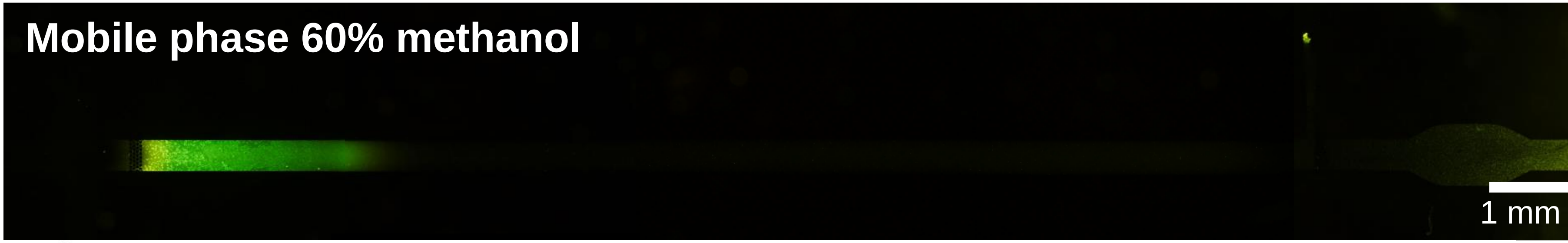
Valve Manifold

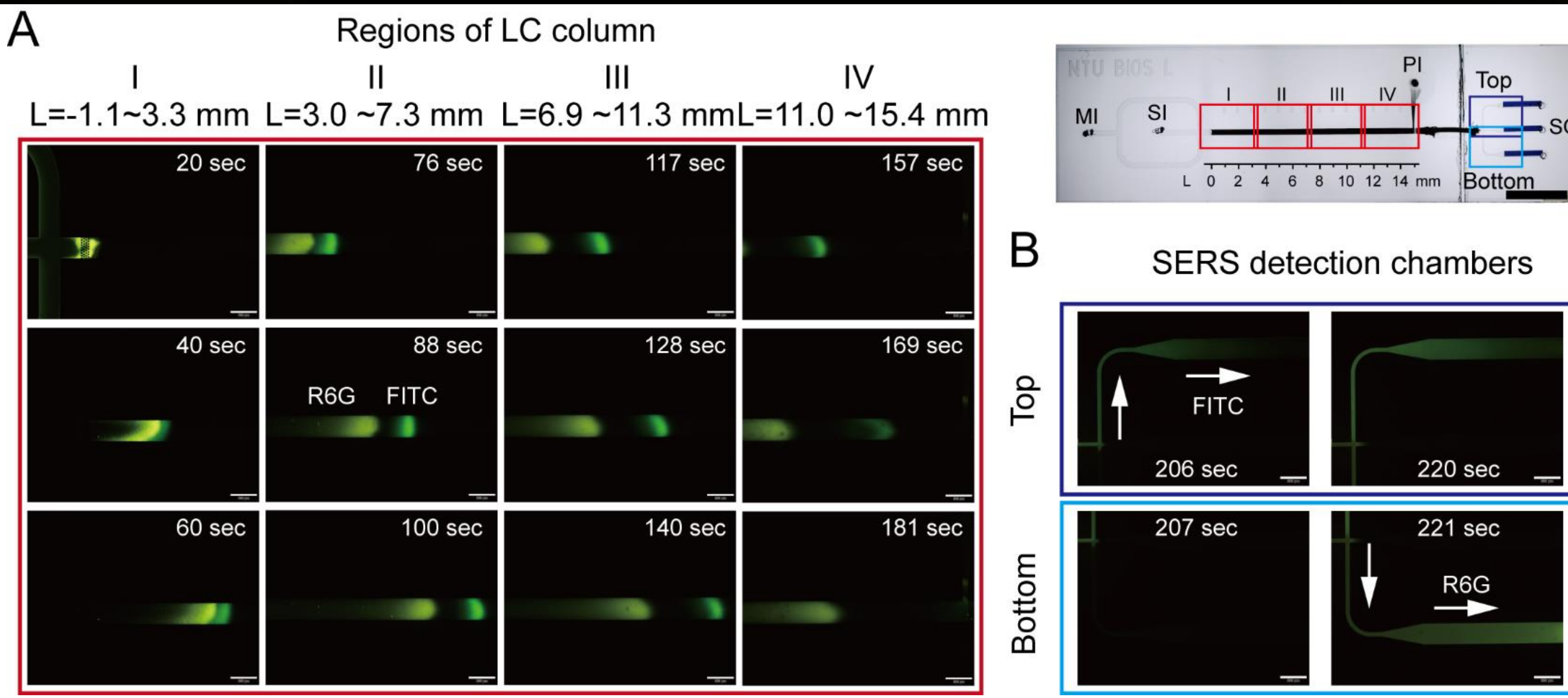
Valves

Micro-pump



On-chip LC separation of FITC and R6G

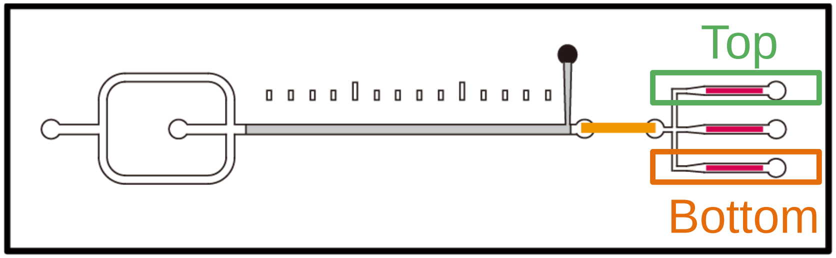


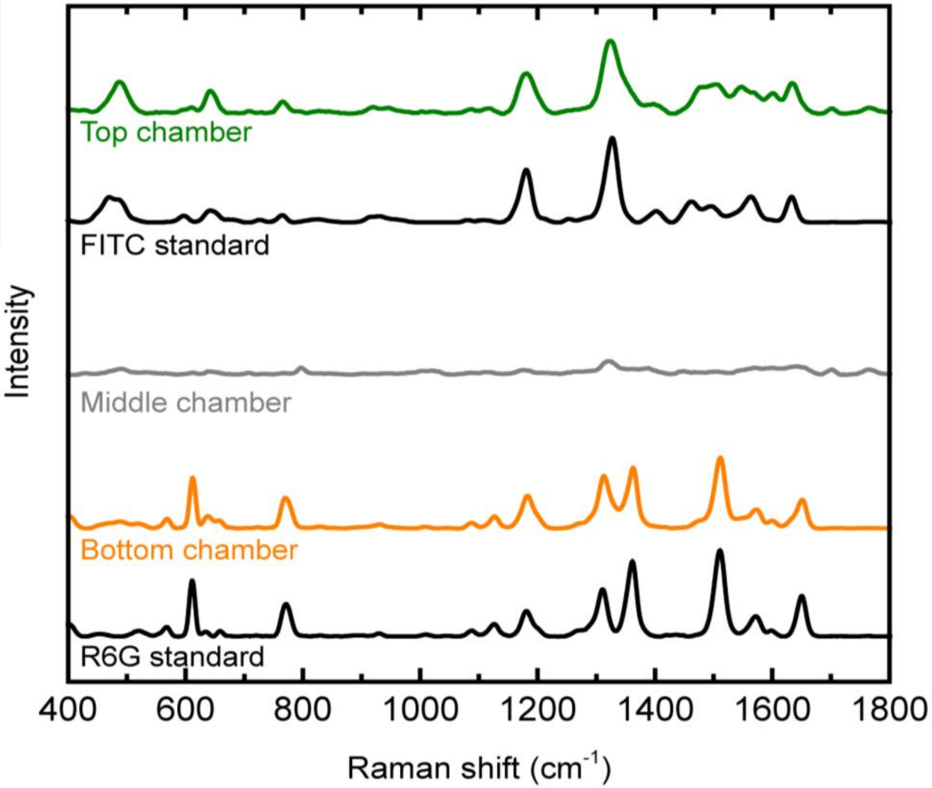


(Wang et. al., under review)

On-chip LC separation and SERS Detection

- Two fluorescent molecule (FITC and R6G) separation and in-situ SERS detection

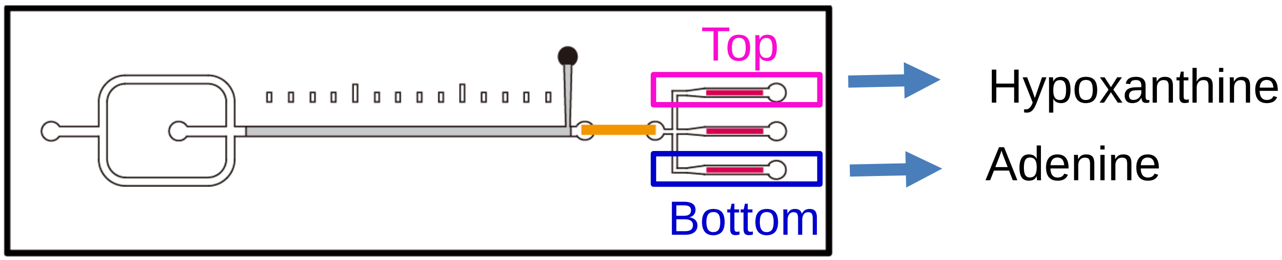


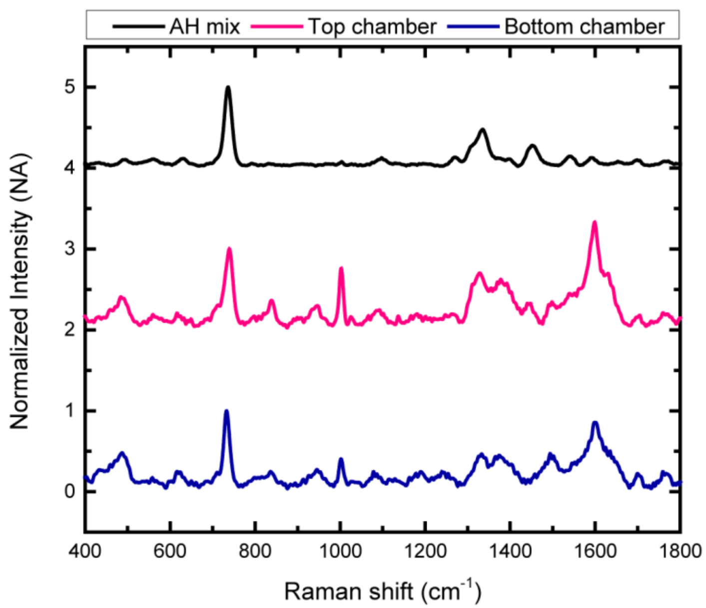


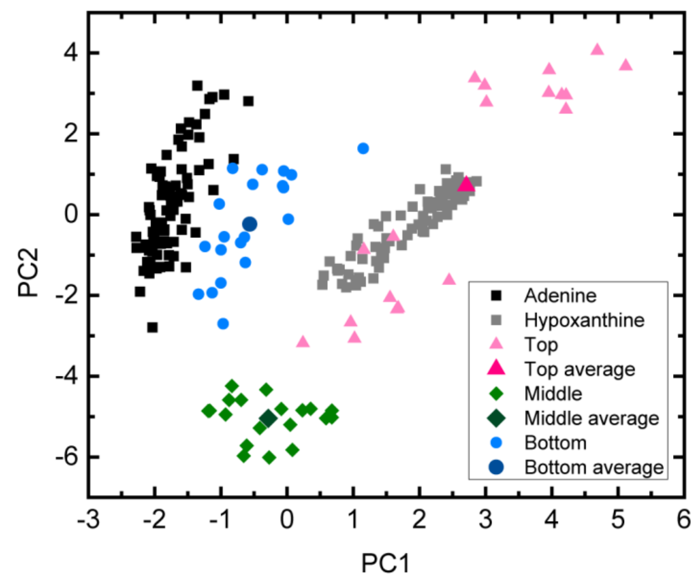
(Wang et. al., under review)

On-chip LC separation and SERS Detection

- Two bacteria metabolites (Adenine and Hypoxanthine) separation and in-situ SERS detection

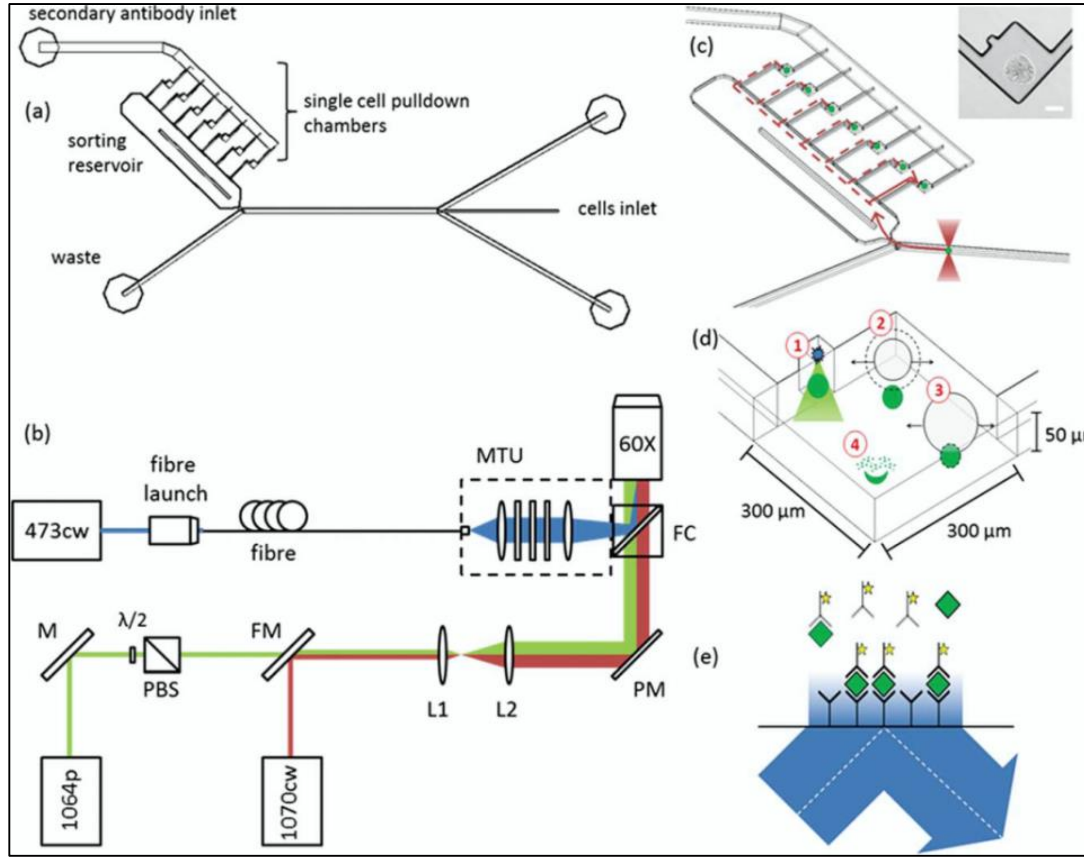






A Fully Optical Microfluidic (FOM) platform

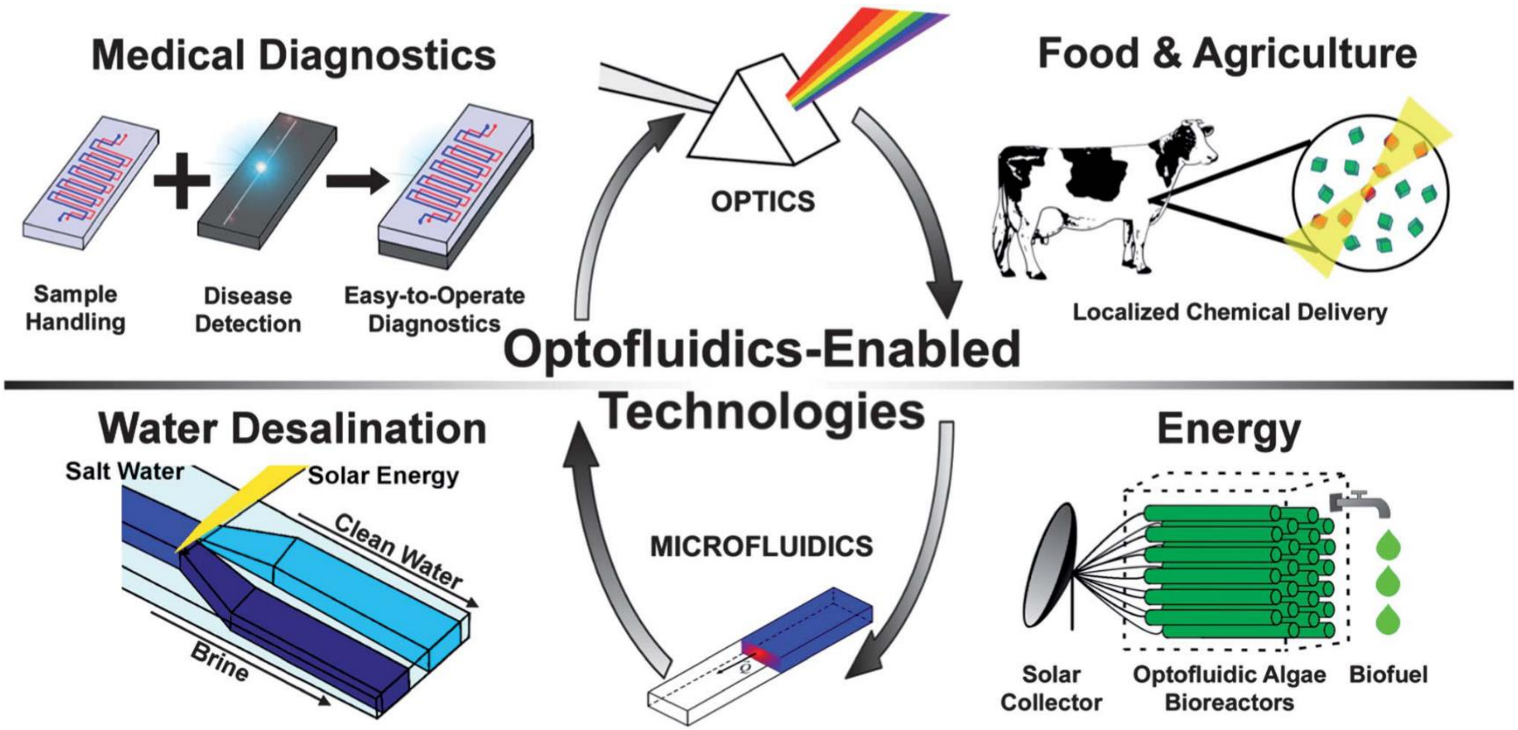
(*Lab Chip*, 2014, **14**, 1230-1245)



(*Lab Chip*, 2011, **11**, 1256-1261)

Conclusions

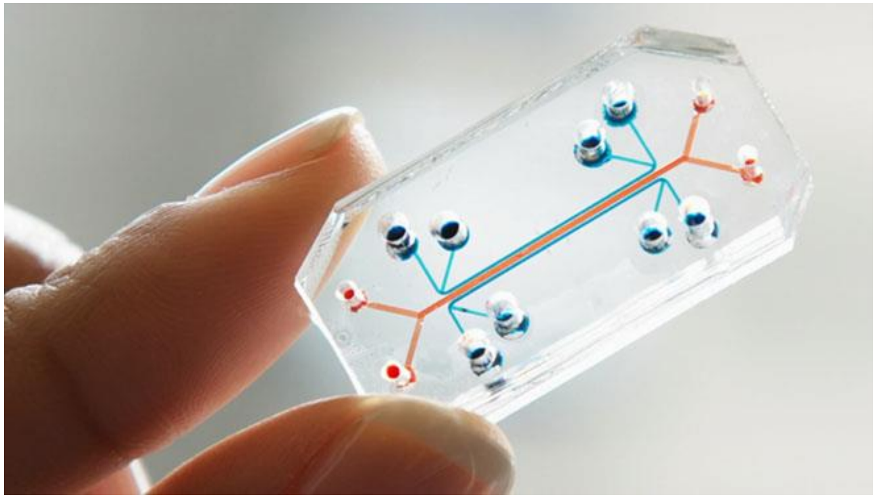
- Optofluidics can be applied for various applications
  - Optical component integration
  - Environmental applications: food and agriculture, water desalination, biofuel energy generation
  - Single cell manipulation, treatment and analysis
  - Medical devices for disease diagnosis



References

- Two TED video of two microfluidic related applications

Geraldine Hamilton: Body parts on a chip
https://www.youtube.com/watch?v=CpkXmtJOH84



Ultra low-cost medical diagnostics in a tiny box | Paul Yager | TED x Rainier
https://www.youtube.com/watch?v=isTlzL0fxtw