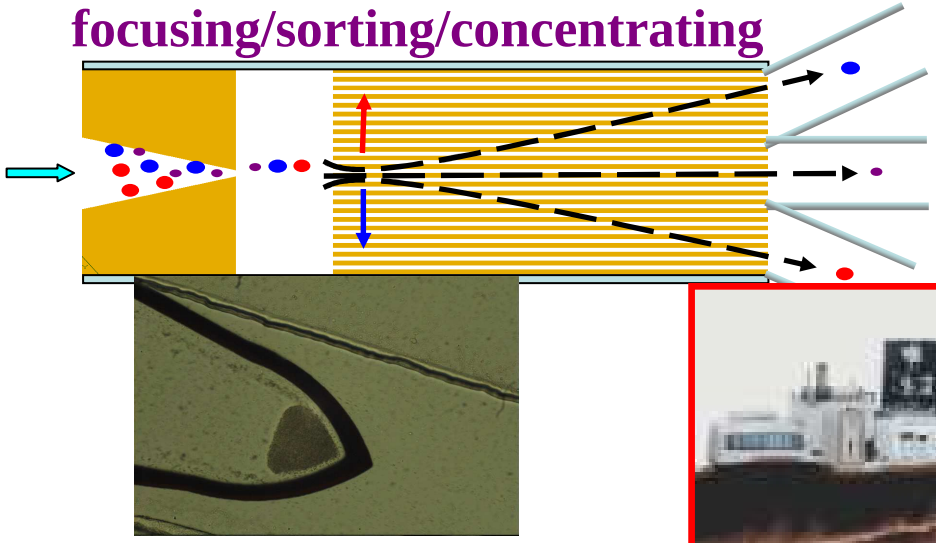
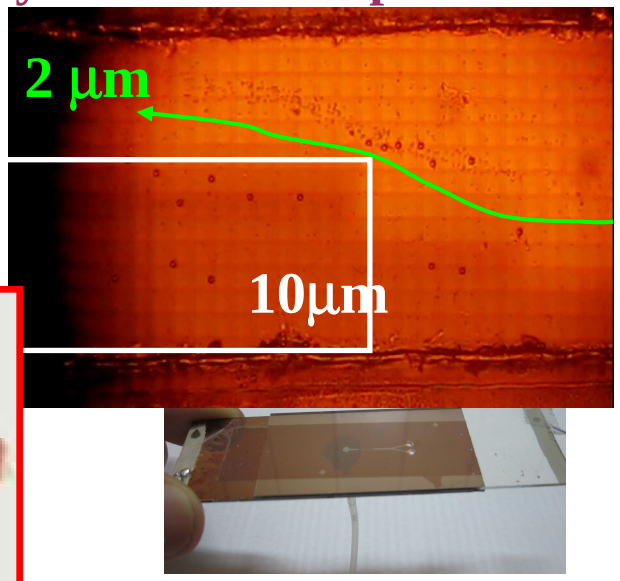
COMSOL CONFERENCE
TAIPEI2013

COMSOL Multiphysics for the Designs and Applications on Biomicrofluidic Chips

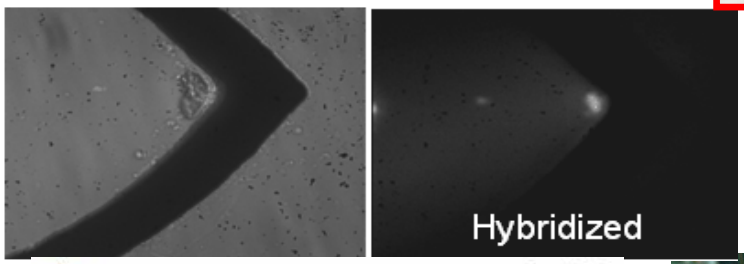
High-throughput focusing/sorting/concentrating

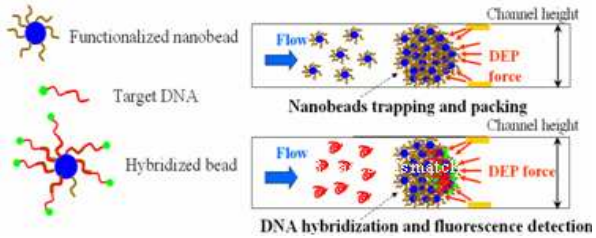


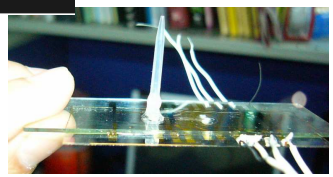
Optically-induced manipulation



On- chip DNA/immuno-assay

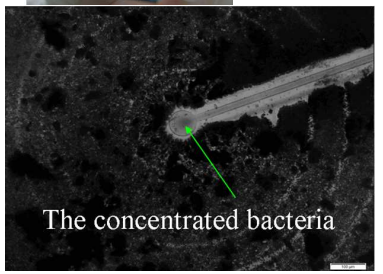


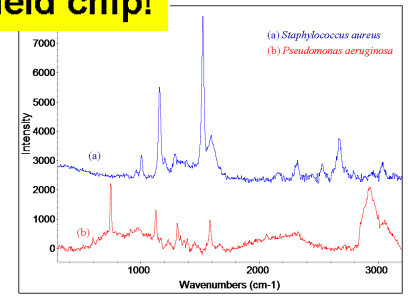




On-chip identification

Hand-held chip!





Presenter: I-Fang Cheng, Ph.D 2013/10/25

Curriculum Vitae

◆**Education:**

Ph.D degree, Institute of Nanotechnology and Microsystems Engineering, National Cheng Kung University (2010/07).

M.S. degree, Institute of Biomedical Engineering, National Cheng Kung University (2007/05).

◆**Research interest:** 1. Micro/Nano-Electrokinetics 2. Biosensors and Nanobiotechnology
3. Biomicrofluidics 4. Optically-Induced Biosensor Systems
5. MicroElectroMechanical Systems (MEMS)

◆**Experience**

1. Assistant researcher in National Nano Device Laboratories (NDL), National Applied Research Laboratories, 2011/12 to present. (**Current position**)
2. Postdoctoral fellow in Institute of Biomedical Engineering, National Cheng Kung University, 2010/08 to 2011/12.
3. Visiting student, University of Notre Dame, Department of Chemical Engineering. (2006/07/05~2006/08/20), (2007/06/20~2007/08/10), (2008/06/25~2008/08/25) and (2009/05/15~2009/08/15).

Diagnostic Chip for Microbe/Virus Infection

Molecular detection
(tens pg/ml, in 5 min)

Whole cell
assay/identification
(minute-level)

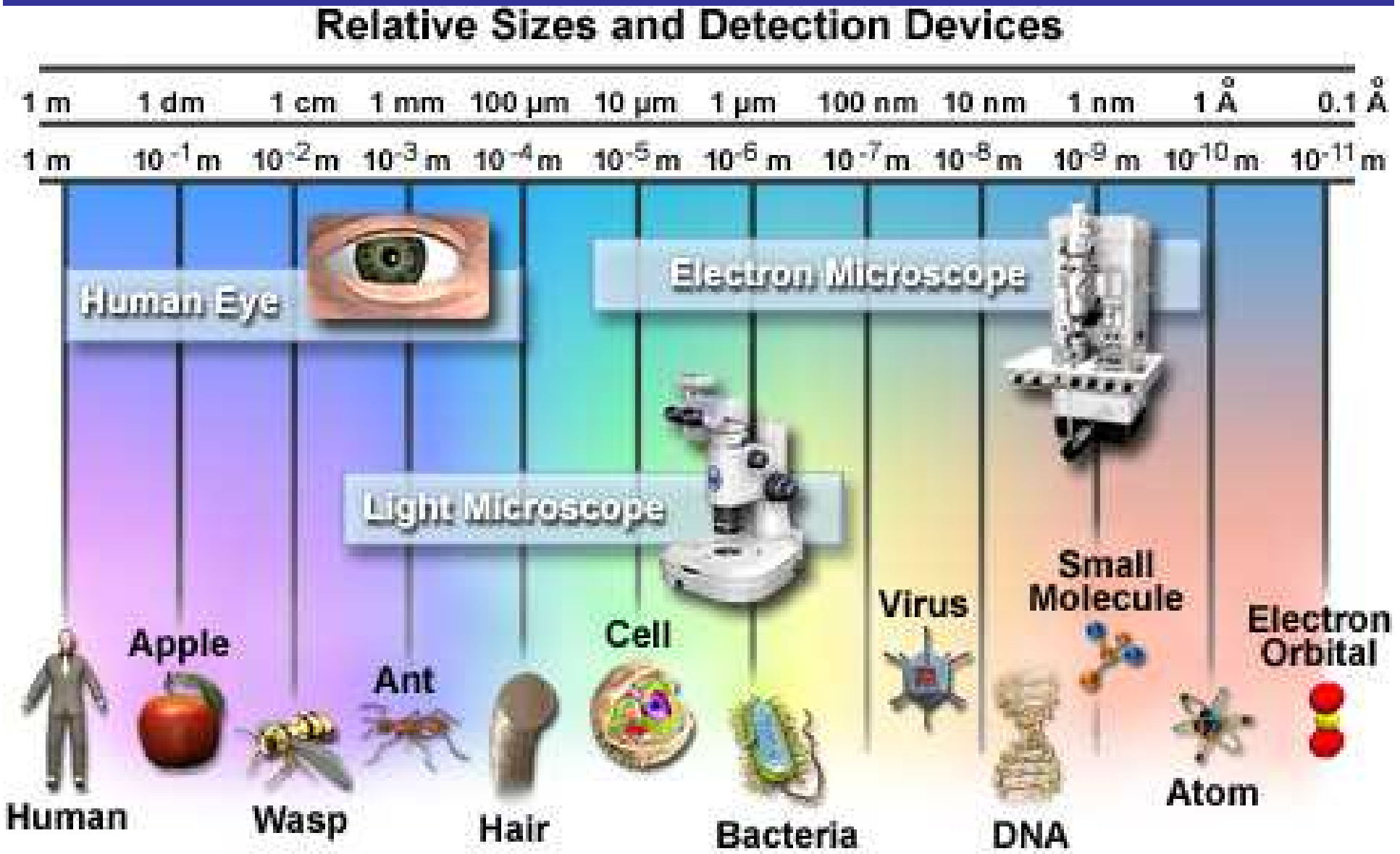
Early detection of cancer cell

Sorting/isolating
CTC in Blood
(1-1000 cells/ml)
(1.2 ml/hr)

Rapid
Analysis/determination
of cancer cell
(minute-level)

Scales

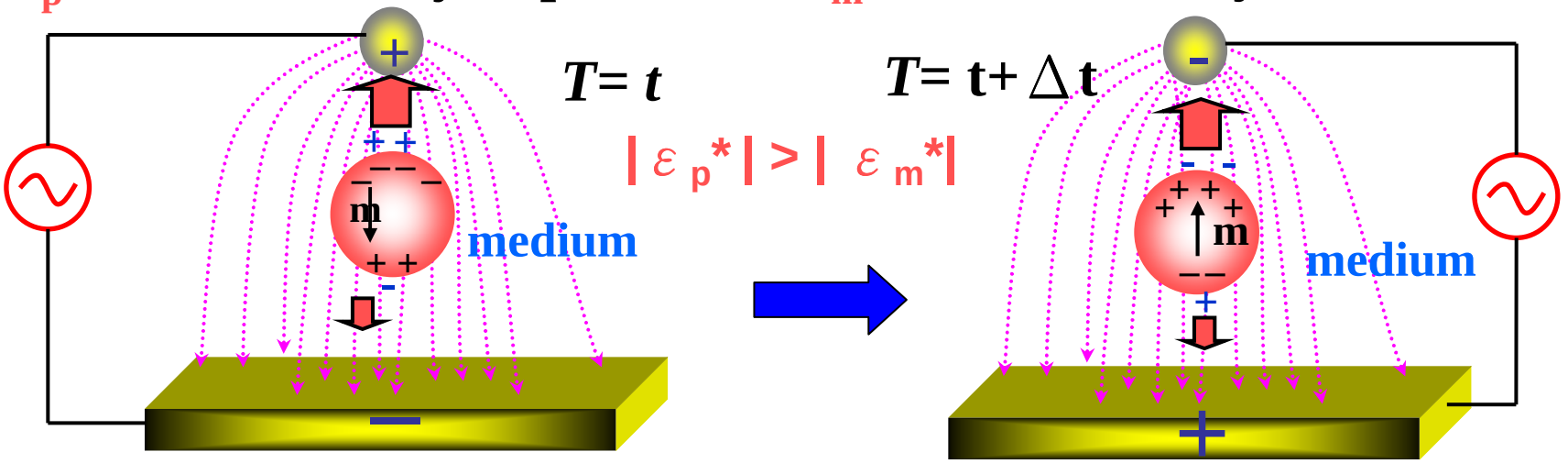
http://micro.magnet.fsu.edu/cells/index.html



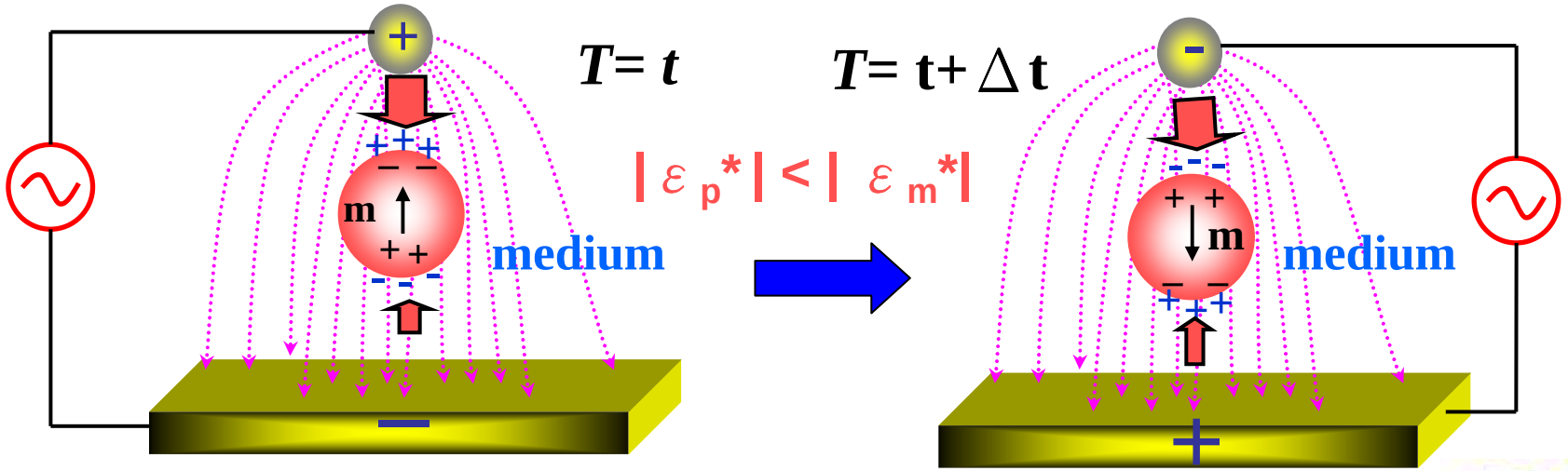
Micro/Nano Electrokinetics

Directions of Dielectrophoretic Force

ε_p^*: Polarisability of particle ε_m^*: Polarisability of medium



❖A cell is attracted toward the strong field region



❖A cell is repelled toward the weak field region

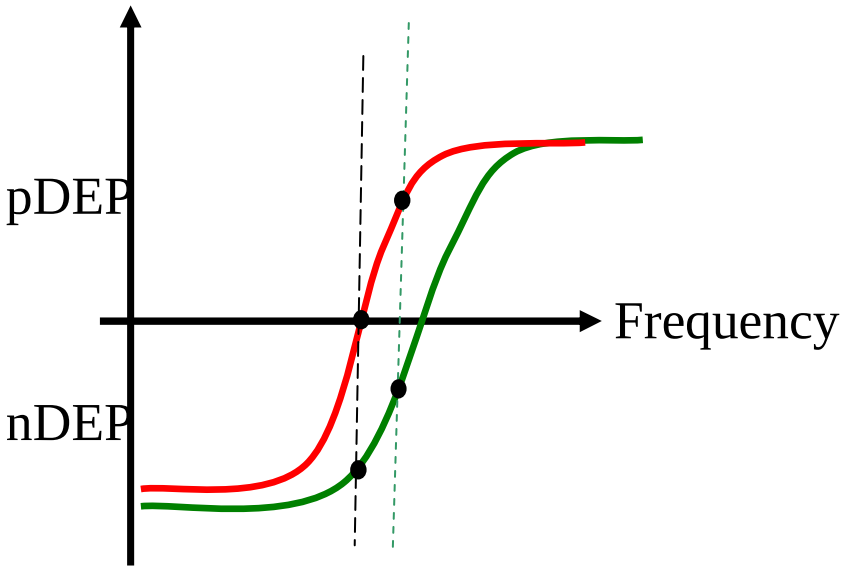
Theory of Dielectrophoretic Force

$$F_{DEP} = 2\pi\varepsilon_m r^3 \mathrm{Re}[f_{CM}(\omega)]\nabla E^2$$

r: particle radius

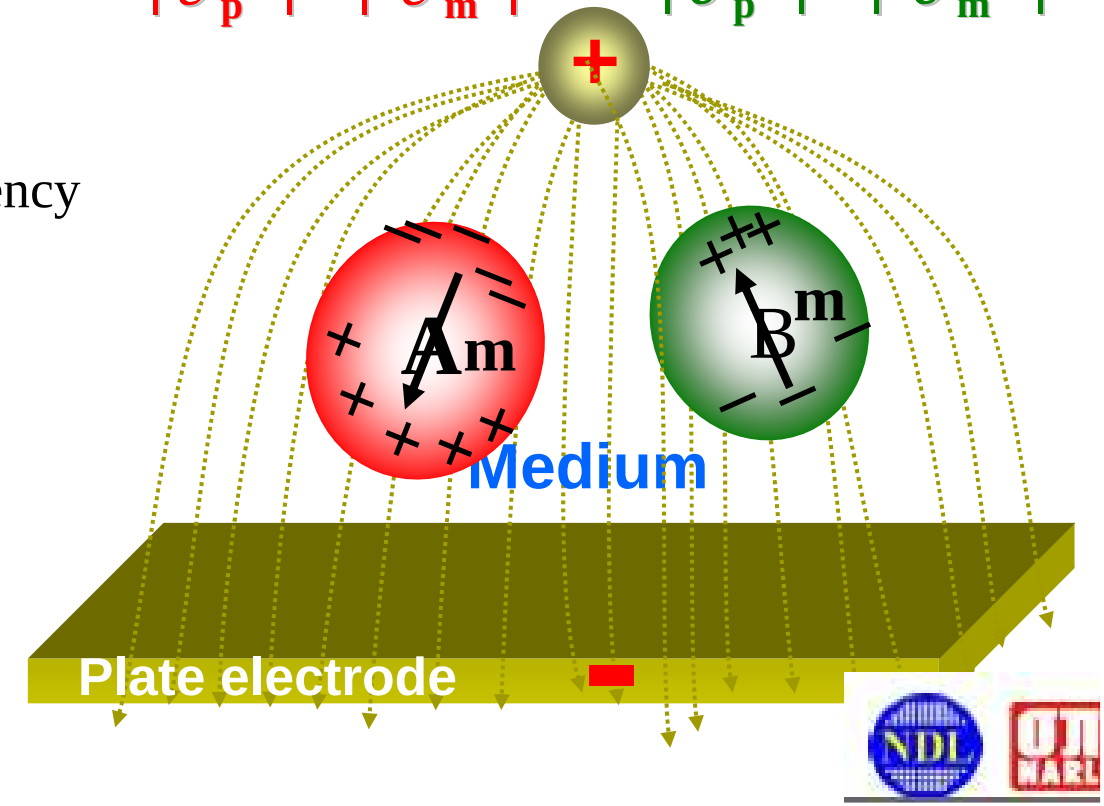
$f_{CM}(\omega) = (\varepsilon_p^* - \varepsilon_m^* / \varepsilon_p^* + 2\varepsilon_m^*)$: Clausius - Mossitti factor

$\varepsilon^* = \varepsilon - j\sigma/\omega$, σ : conductivity, ε : permittivity , $\omega = 2\pi f$, f : frequency



$E = \nabla\Psi = \triangle V/d$

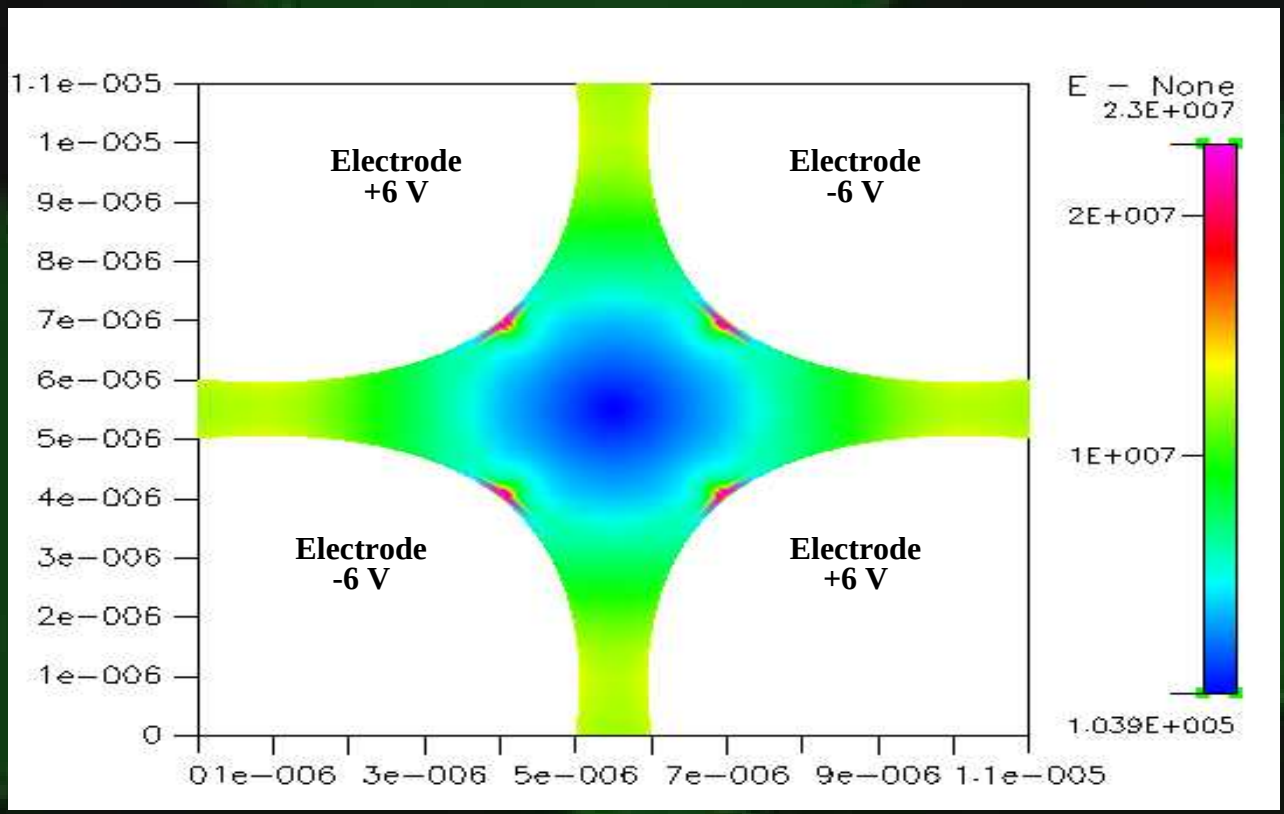
$|\varepsilon_p^*| > |\varepsilon_m^*|$ $|\varepsilon_p^*| < |\varepsilon_m^*|$



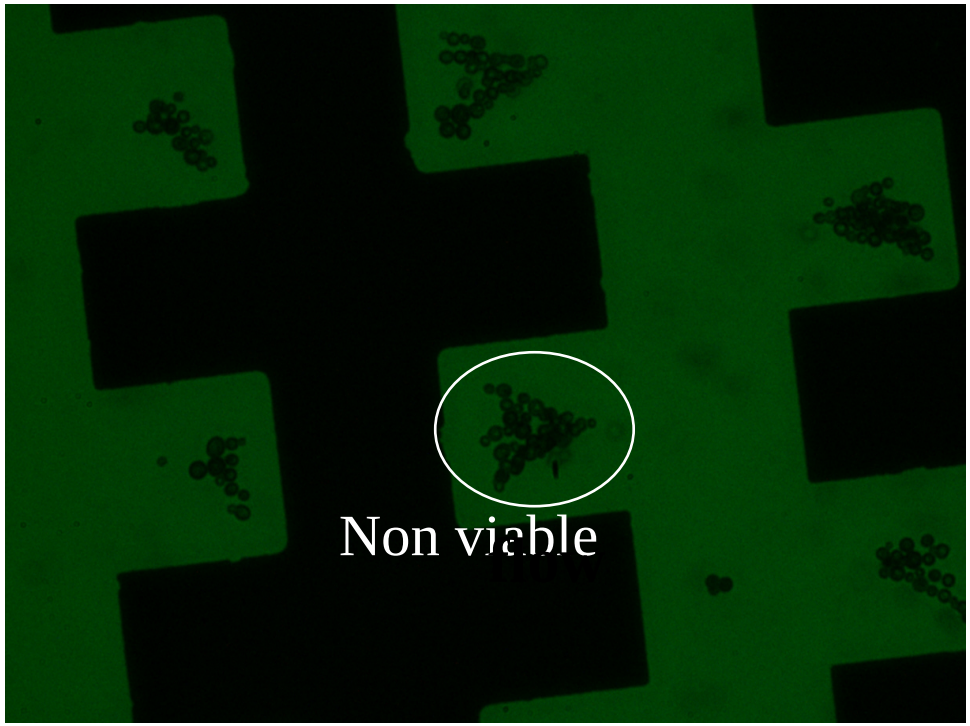
$\mathrm{Re}[f_{CM}(\omega)] > 0$: positive DEP

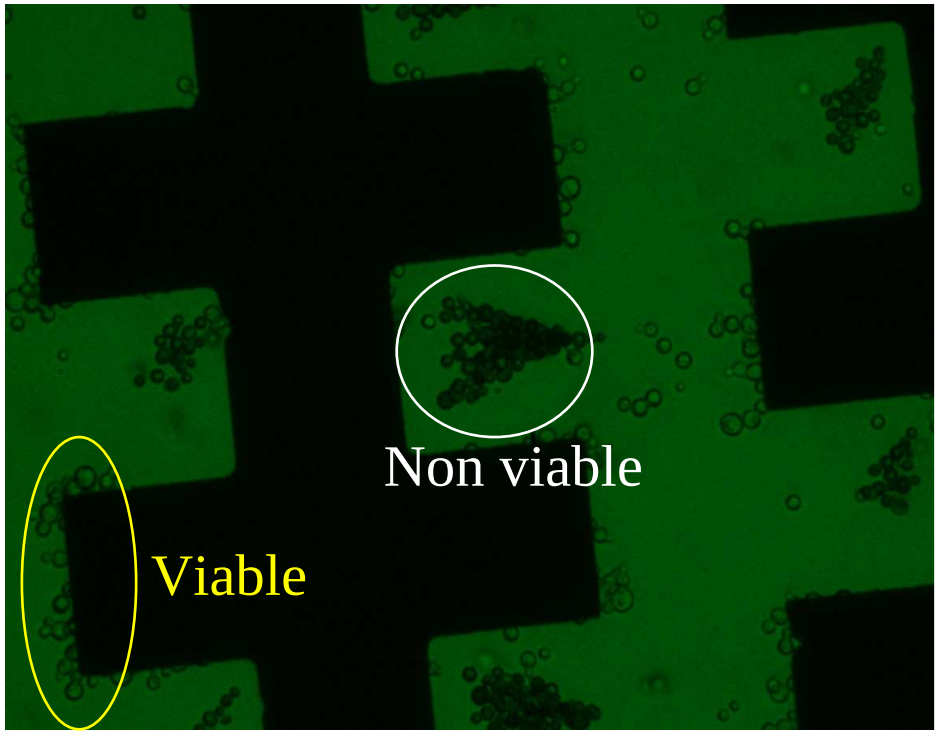
$\mathrm{Re}[f_{CM}(\omega)] < 0$: negative DEP

The Phenomena of DEP



Separation of Viable and non-Viable *Candia albicans*





Medium:10 mM KCl

Frequency (Hz) / Bacteria	500 k	1 M	5 M	10 M	15 M
Live	N	wp	P	sP	P
Death	wN	N	N	N	N

Detection of microorganism/cells/virus/molecules

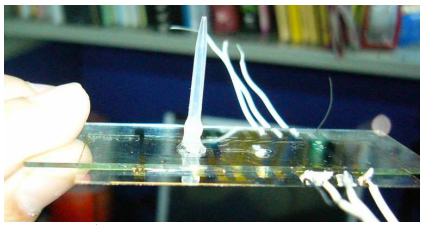
Sample preparation:

- Separation, isolation
- Concentration

Gold standard culture
Instruments
Biochemistry kits
Microdevices

Target identifications:

- Identification
- Discrimination
- Quantification

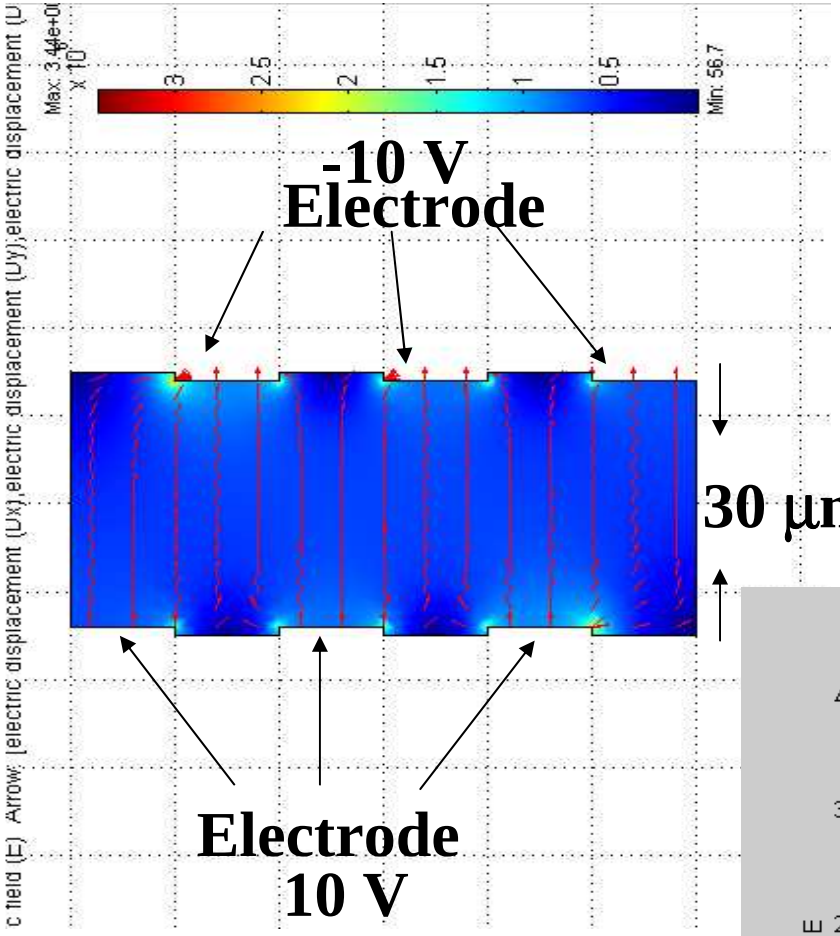


MEMS
Microfluidics
Electrokinetics
Optics

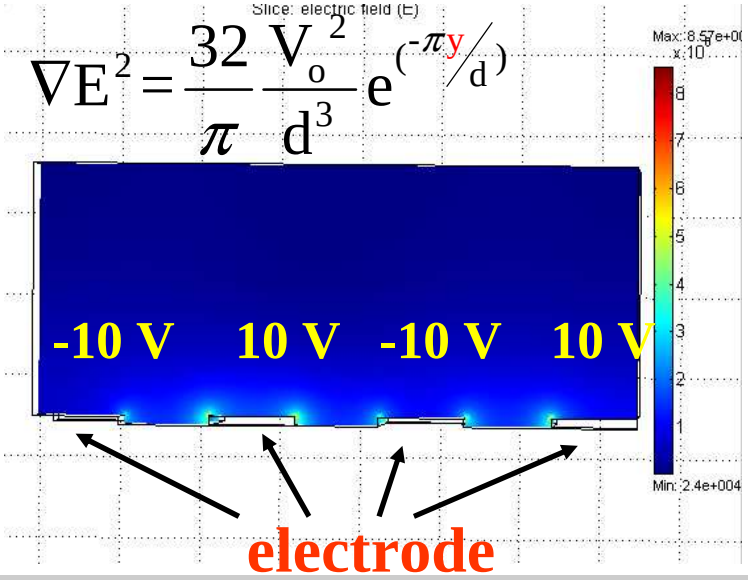
→

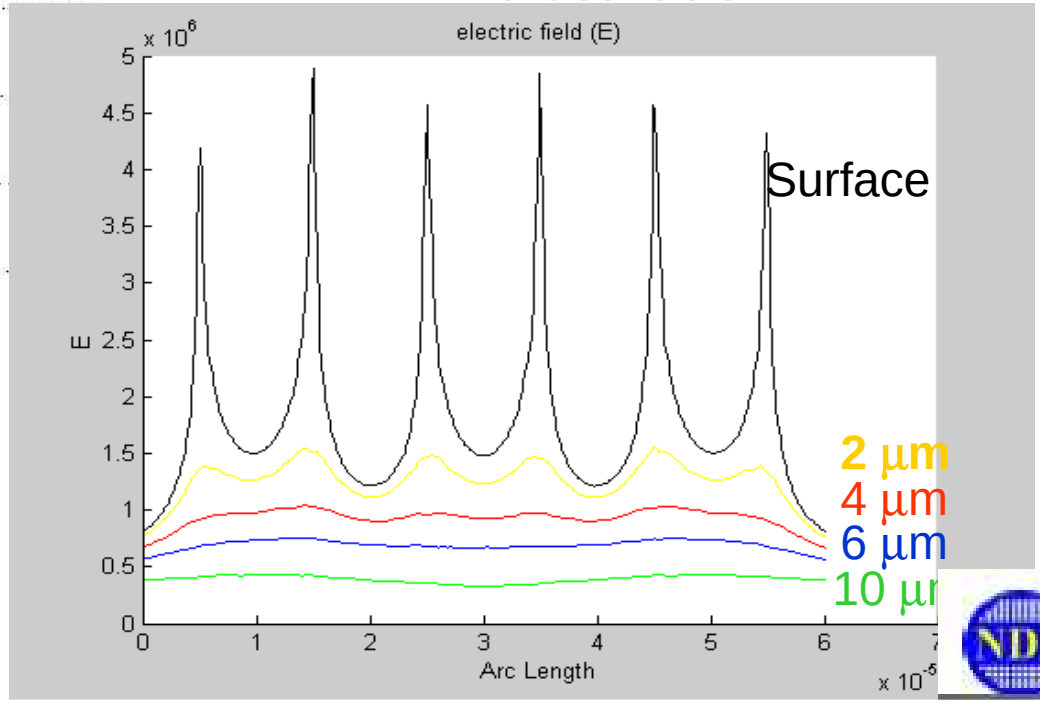
Rapid! (within a few minutes)
High sensitivity! (< nM, or 10^4 particles/ml)
High specificity !
Portable!
Low cost!
Field usable (Point-of-care)!

Simulation of Dual Layer Electrodes

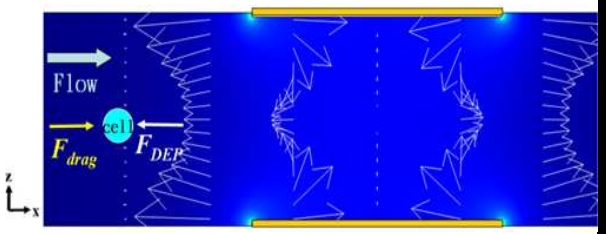


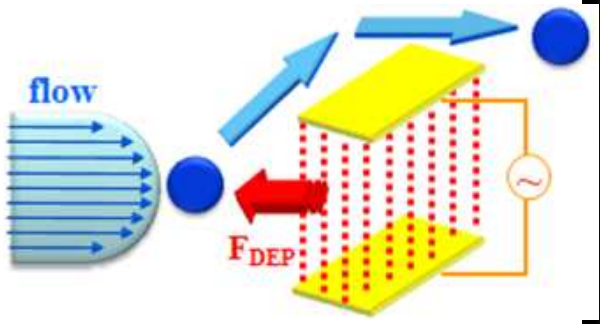
$$\nabla E^2 = \frac{32}{\pi}\frac{V_o^2}{d^3} e^{(-\pi y/d)}$$



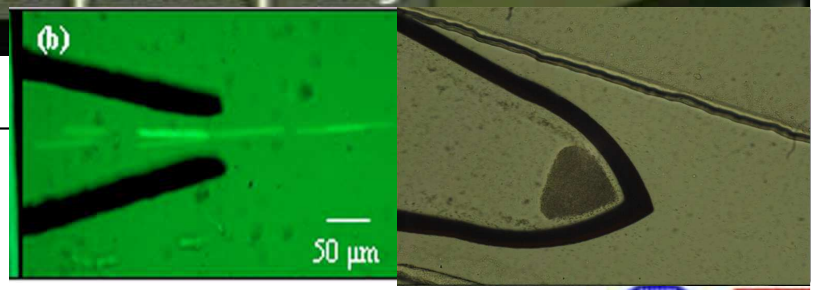


Sorting of Particles based on Different Magnitudes of DEP Force





$$F_{drag} = 6\pi\eta r v \sin\theta \qquad V_{DEP} = \frac{9\varepsilon_m r^2 \,\mathrm{Re}(f_{CM}(\omega))\mathrm{V}_{\mathrm{rms}}{}^2}{64\eta a^3 \sin\theta}$$

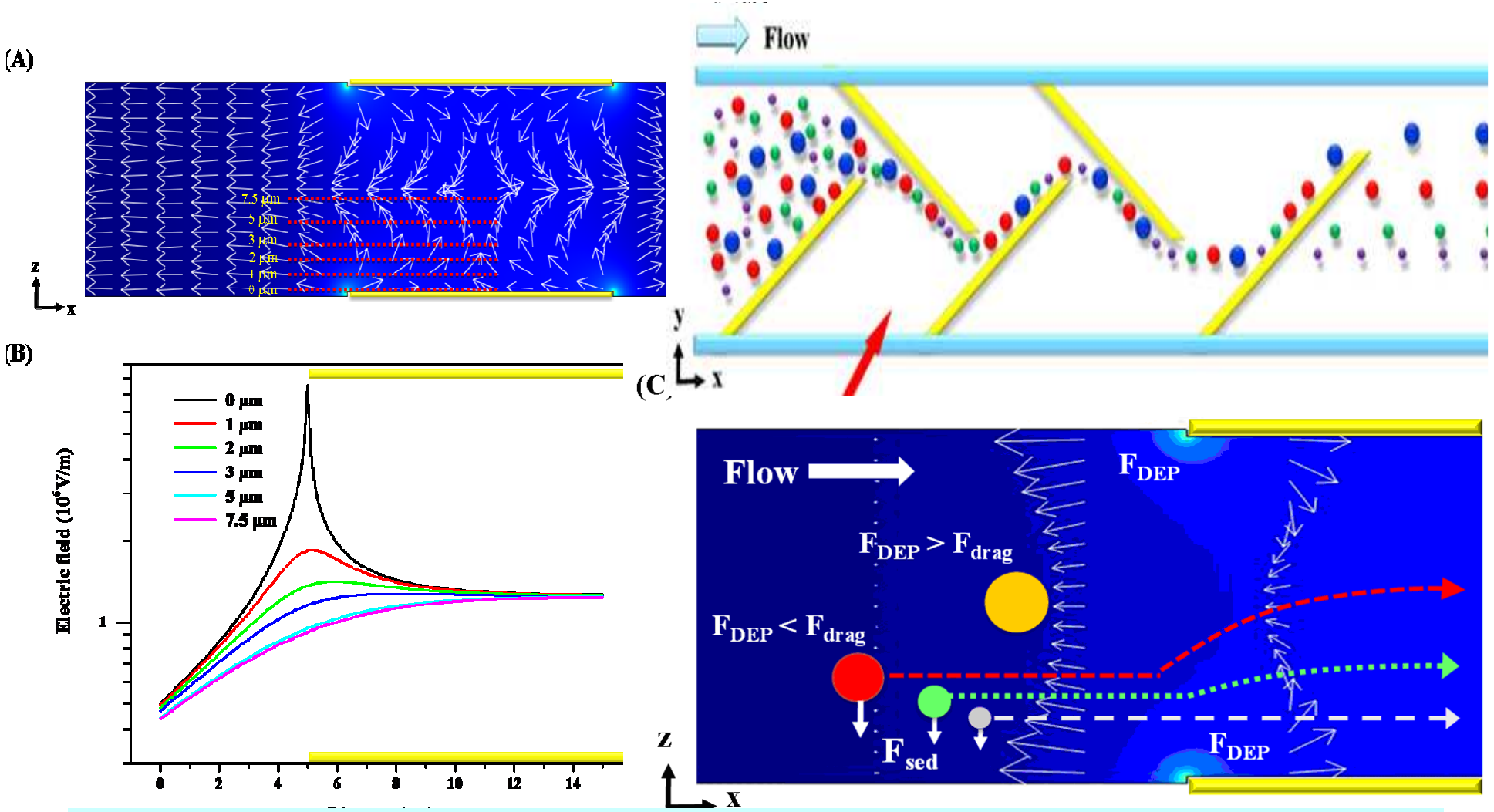


$F_{DEP} > F_{drag}$ deflection

$F_{DEP} < F_{drag}$ penetration

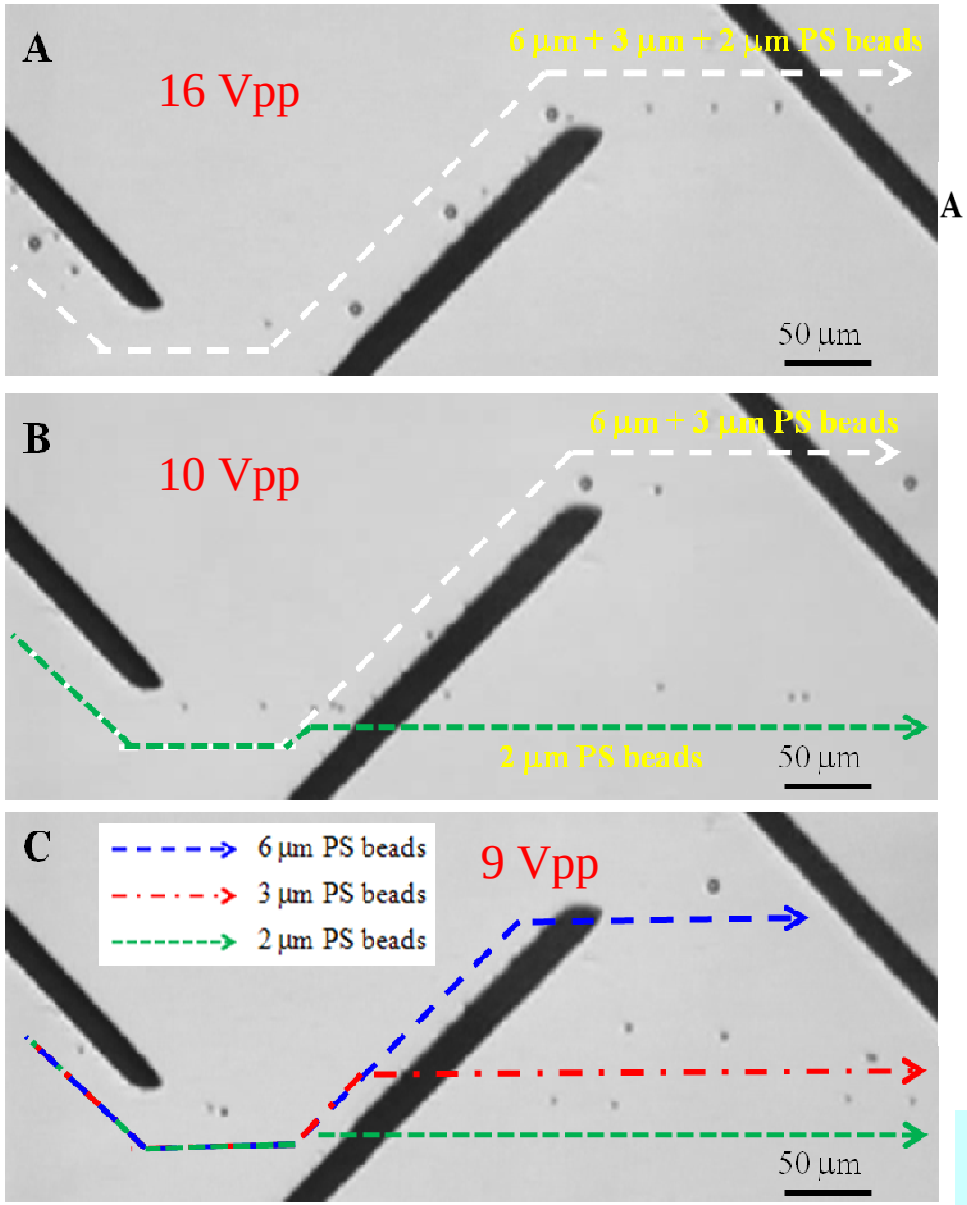
I-F Cheng et al., *Biomicrofluidics*, 1(2007) 021503.

Precisely sized separation of multiple particles based on the DEP gradient in the z-direction

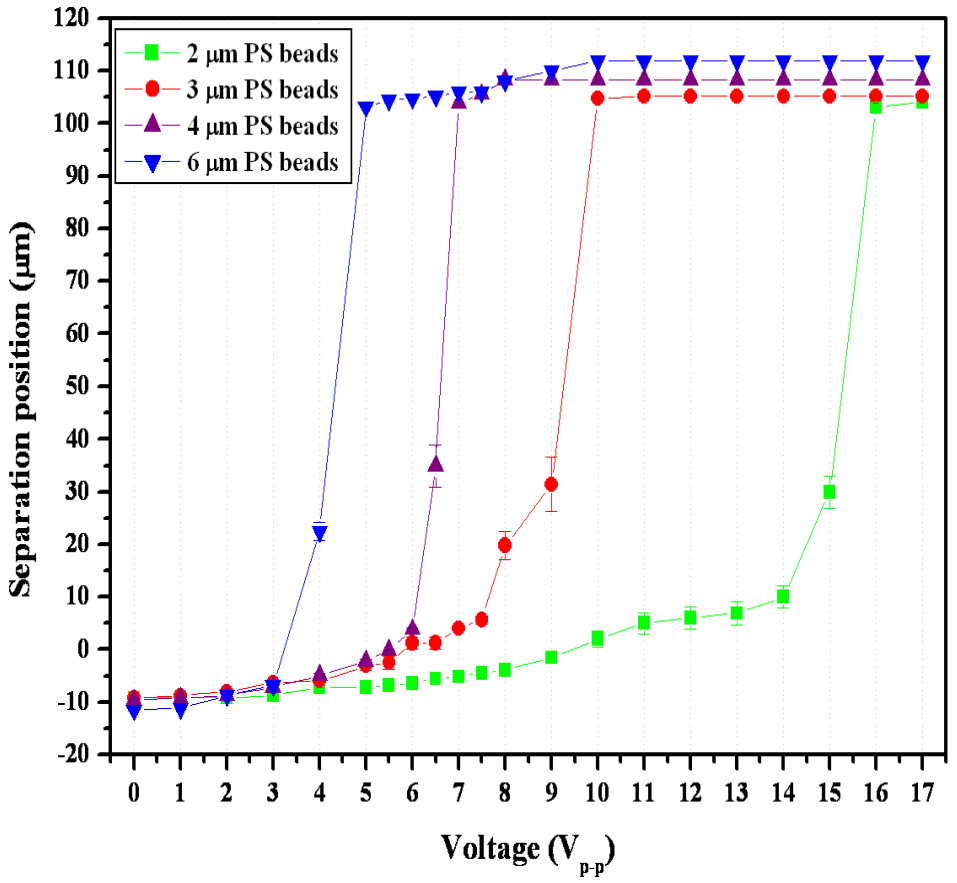


S-H Liao† , **I-F Cheng†** , H-C Chang, *Microfluid Nanofluid*, (2011)**12**, 201
(† **equal contribution**)

Field Fraction of multiple particles by tuning AC voltage

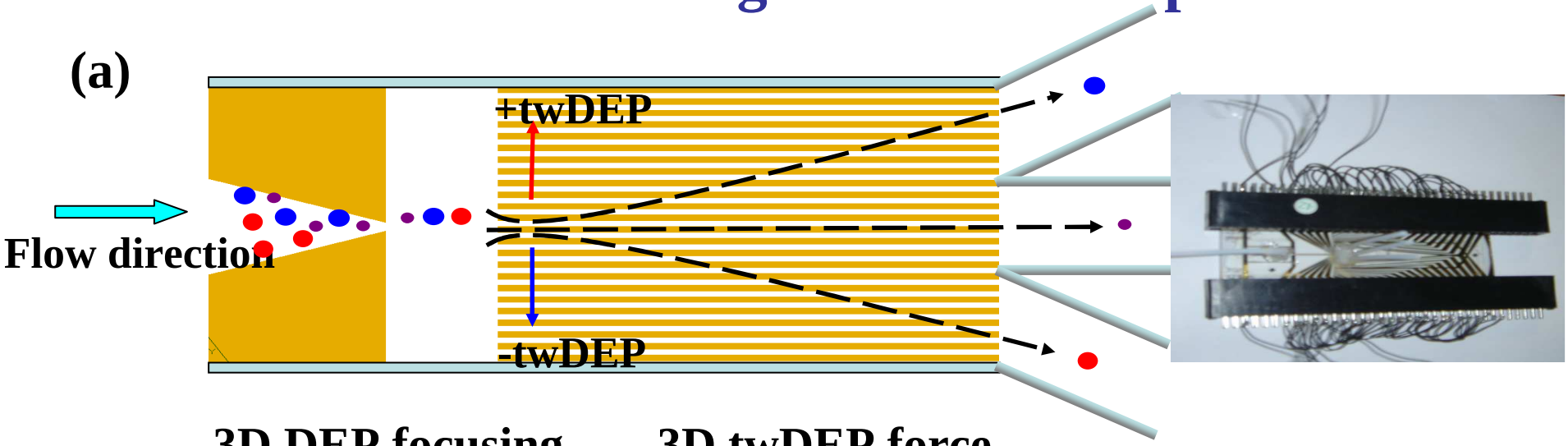


A

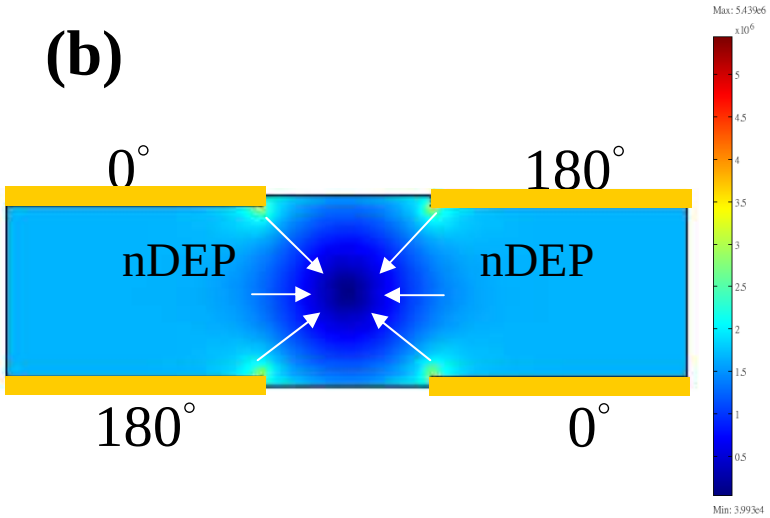


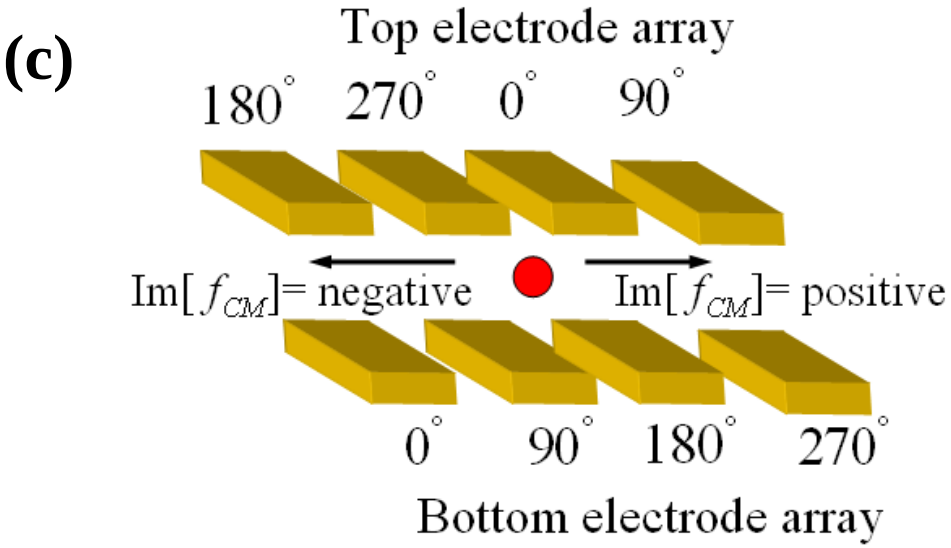
S-H Liao† , **I-F Cheng†** , H-C Chang, *Microfluid Nanofluid*, (2011)**12**, 201 († **equal contribution**)

A continuous high-throughput bioparticle sorter based on 3D traveling-wave dielectrophoresis



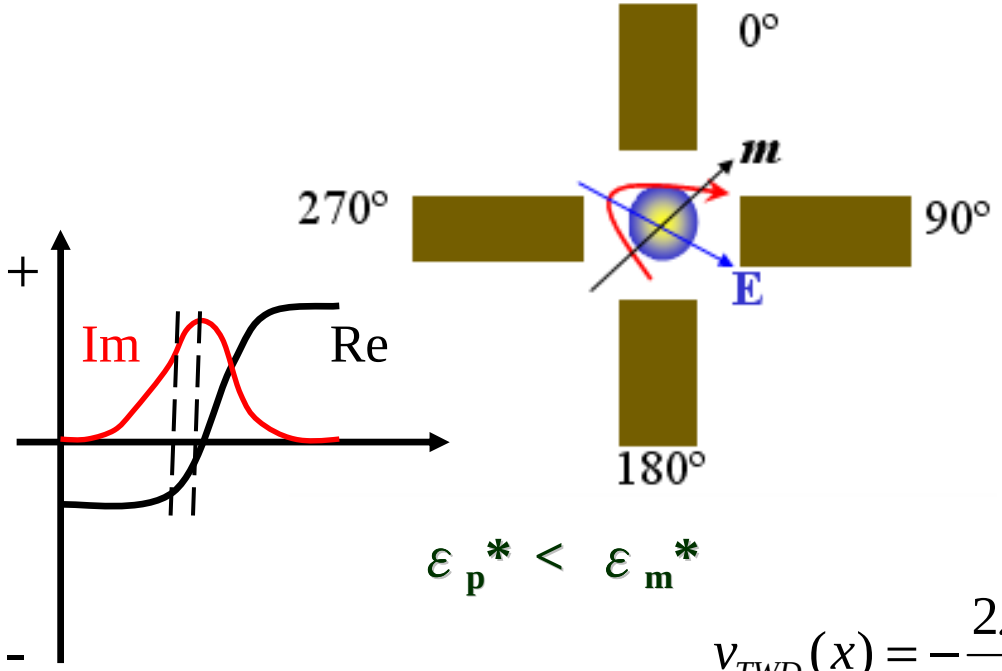
3D DEP focusing **3D twDEP force**



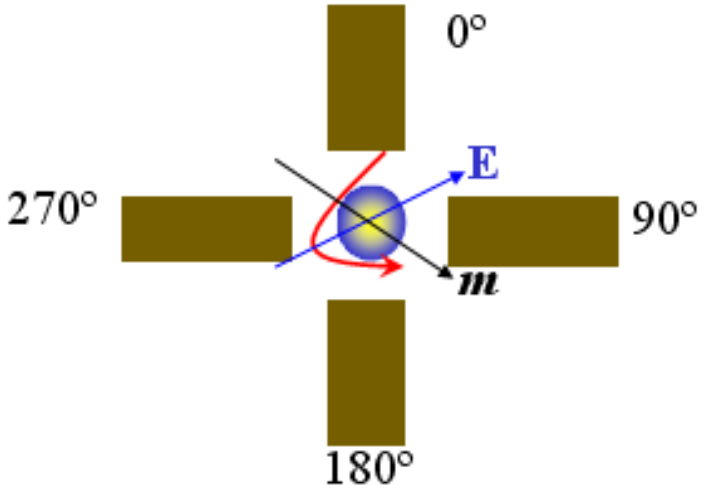


I-F Cheng et al., Lab on a Chip, 9, 3193(2009).

The Theory of Traveling Wave DEP Induced

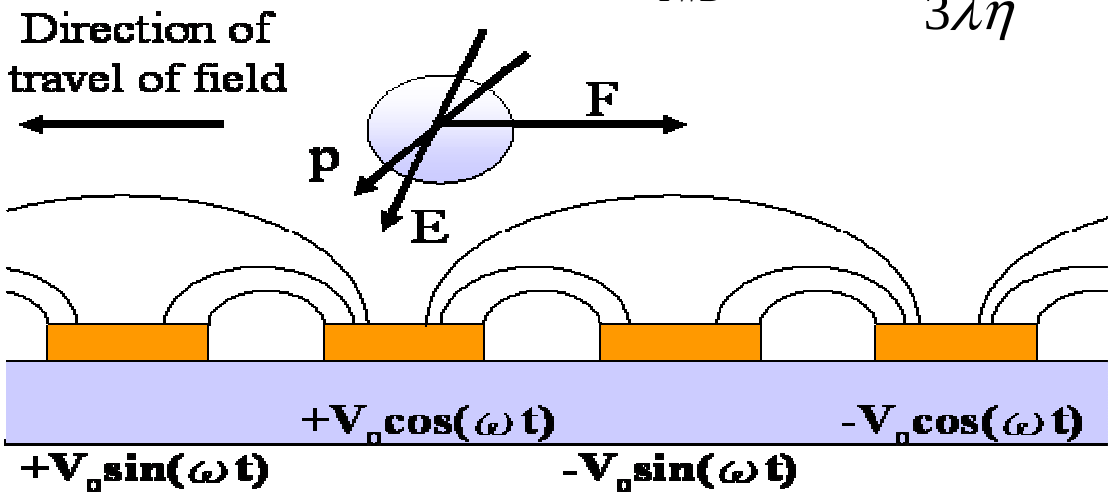


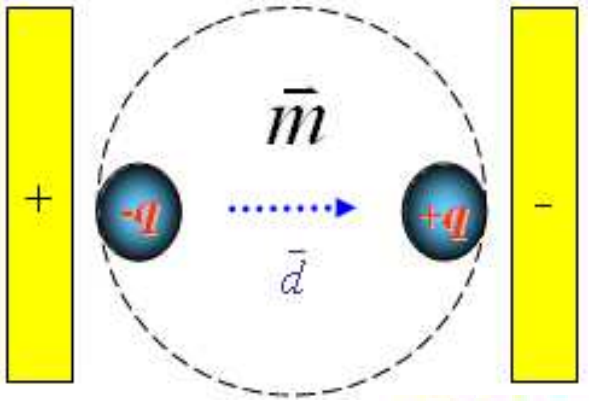
$\varepsilon_p^* < \varepsilon_m^*$



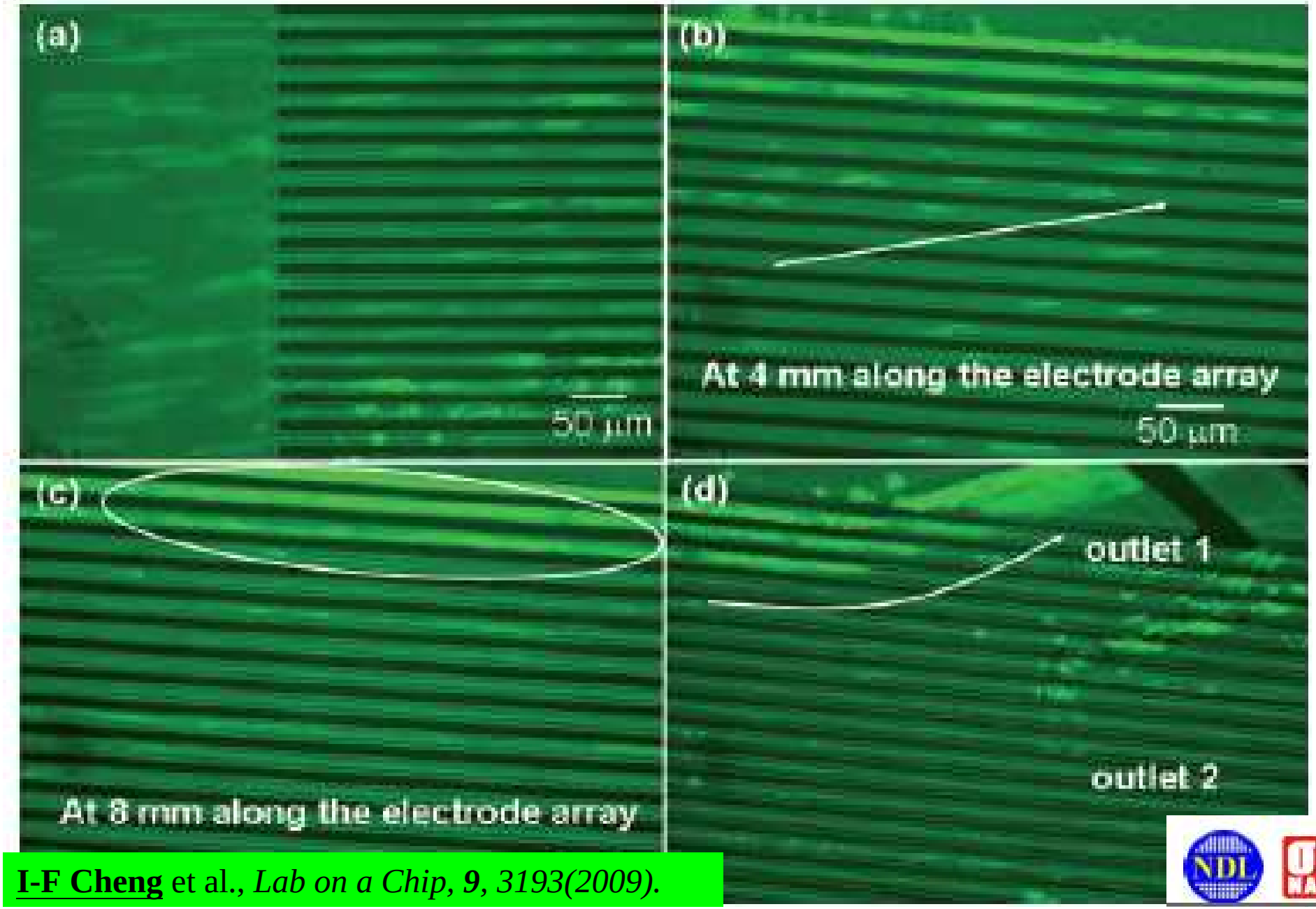
$\varepsilon_p^* > \varepsilon_m^*$

$$v_{TWD}(x) = -\frac{2\pi\varepsilon_m r^2}{3\lambda\eta}\,\mathrm{Im}[f_{CM}(\omega)]E^2$$



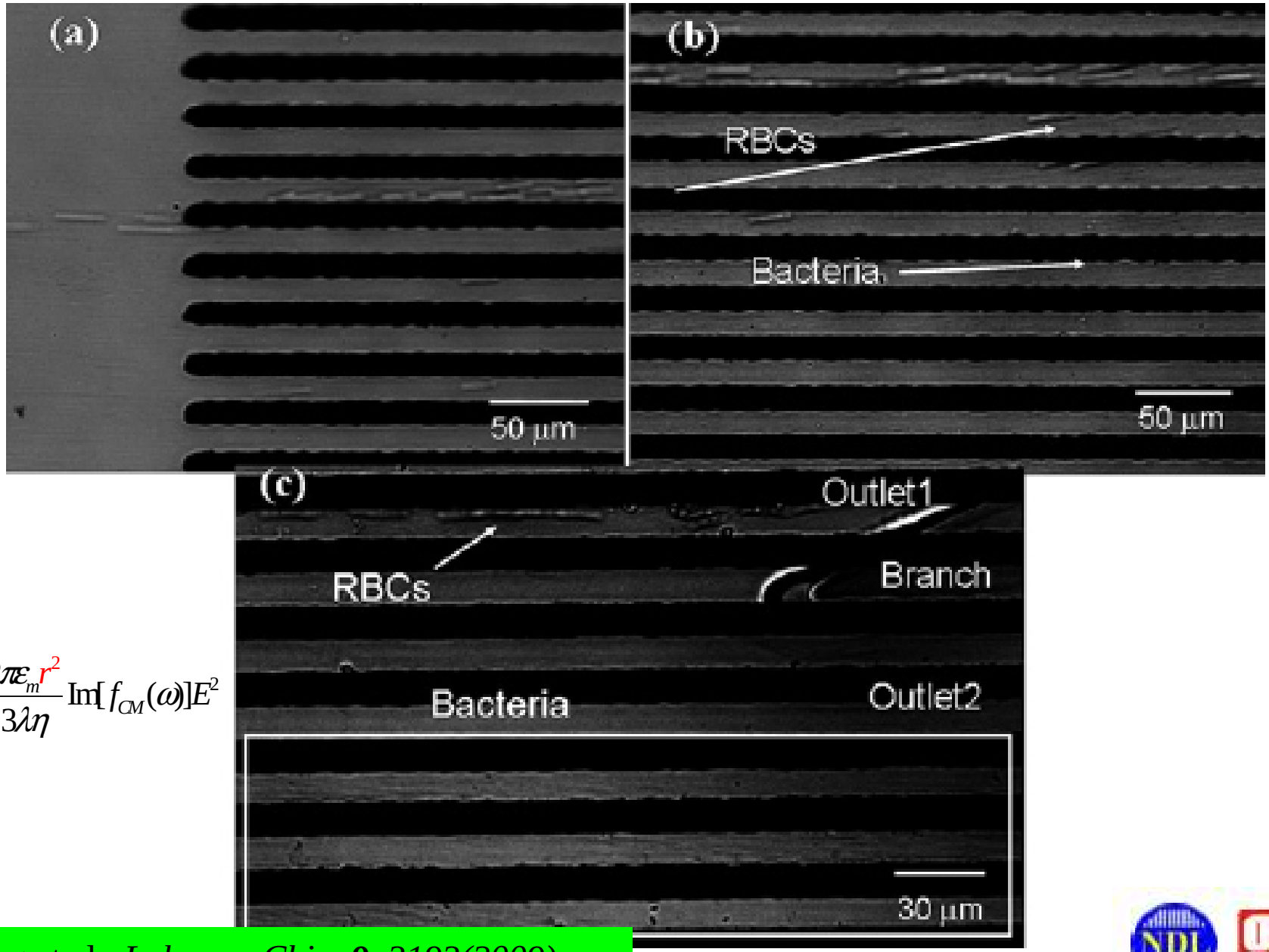


High Speed Manipulation of RBC



I-F Cheng et al., *Lab on a Chip*, ***9***, *3193(2009)*.

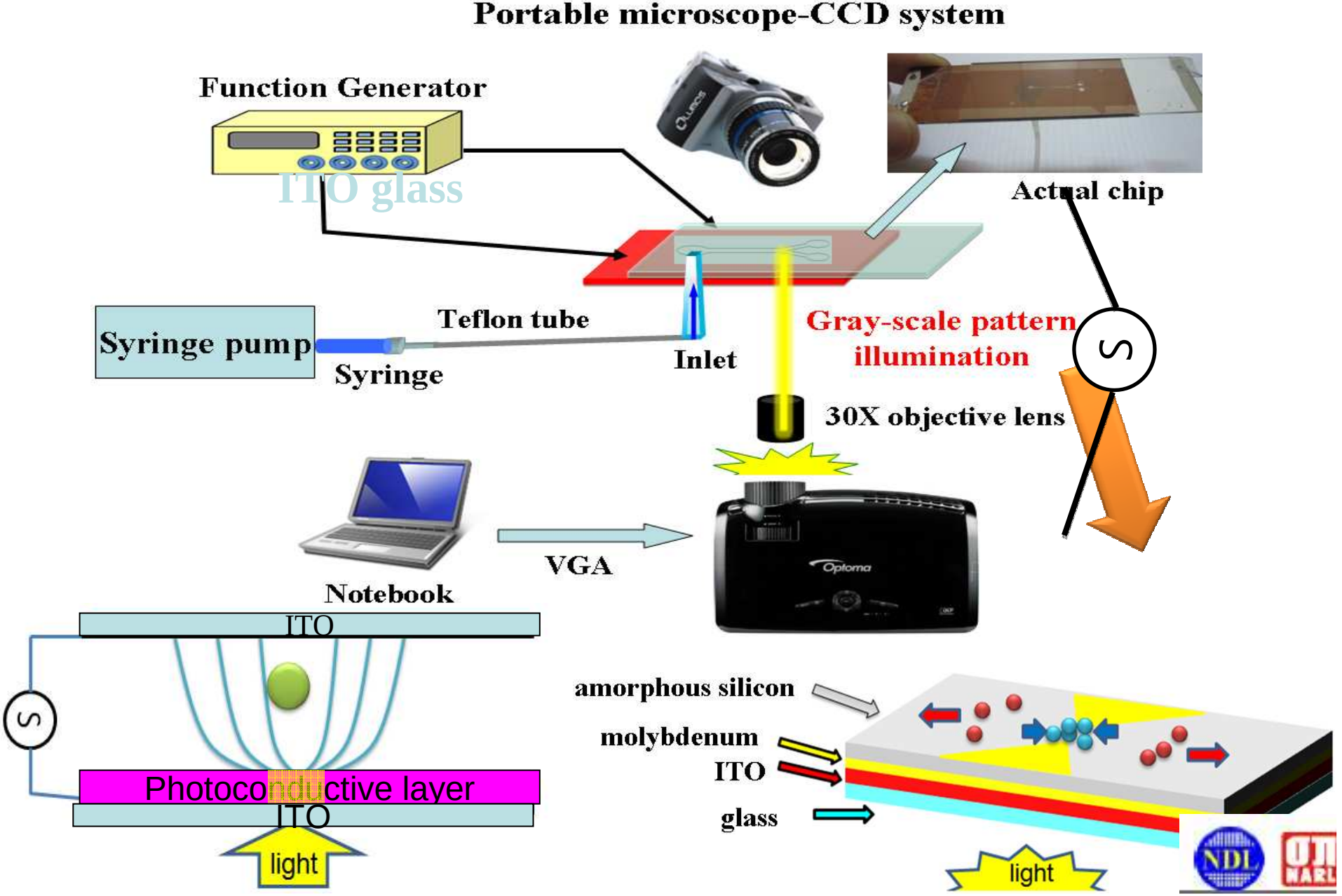
RBC and Bacteria Sorting



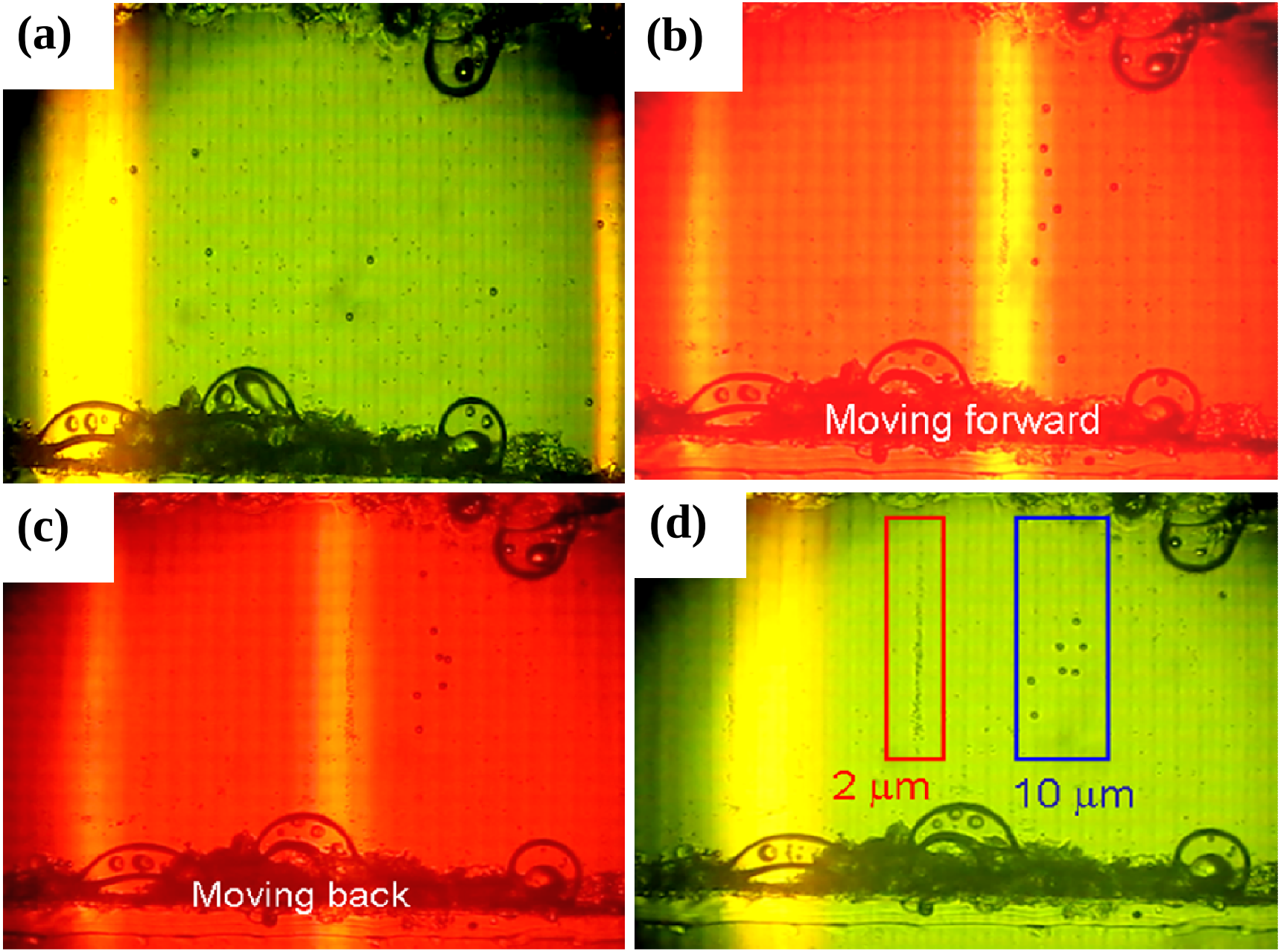
$$v_{TWD}(x) = -\frac{2\pi\varepsilon_m r^2}{3\lambda\eta}\,\mathrm{Im}[f_{CM}(\omega)]E^2$$

I-F Cheng et al., *Lab on a Chip*, ***9***, *3193(2009).*

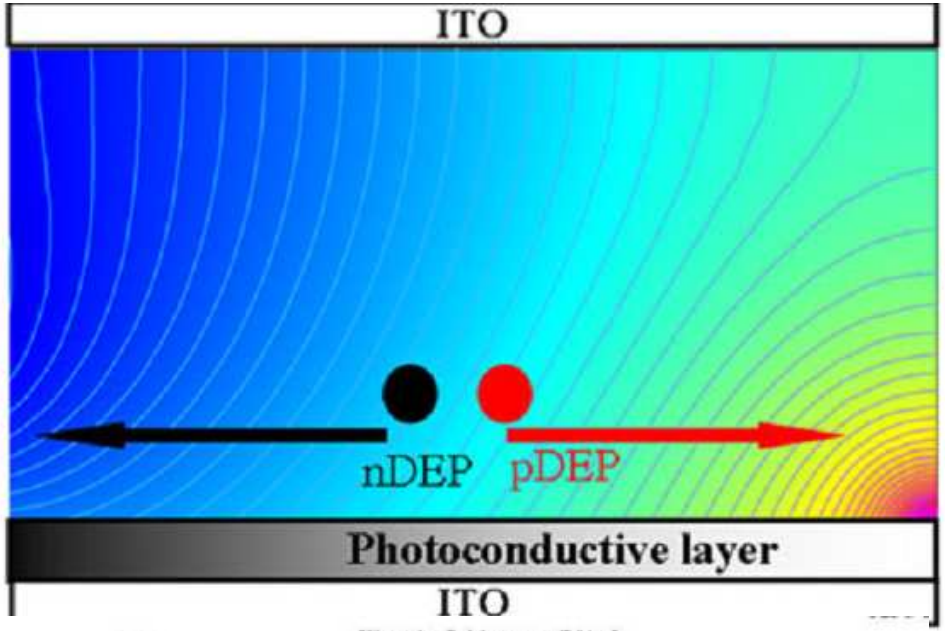
Light-induced Dielectrophoresis for Passive and continuous Separation of Microparticles

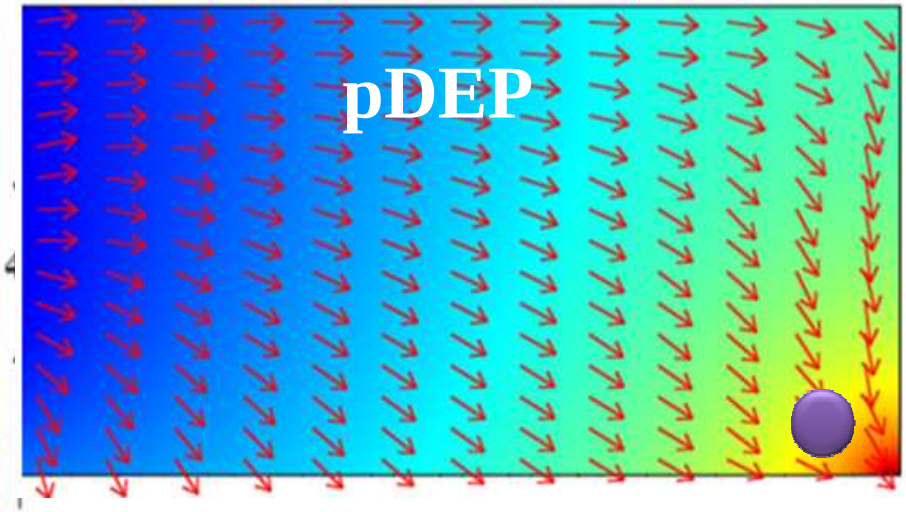


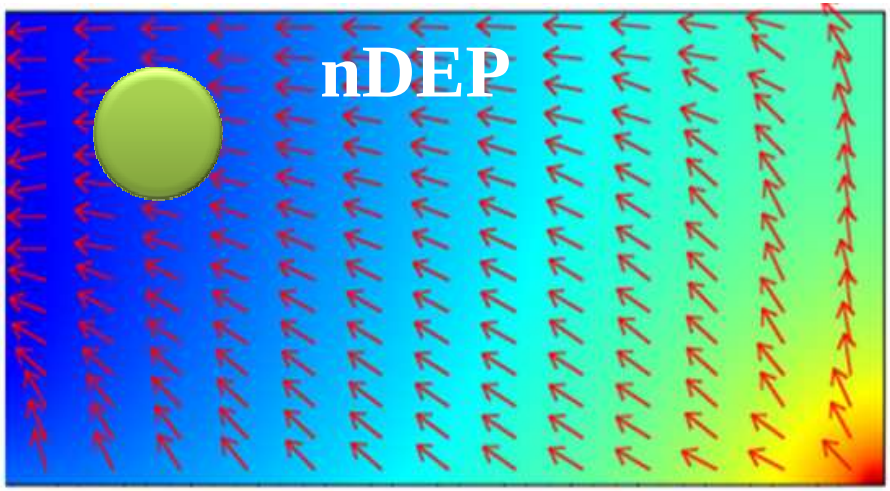
Dynamic Separation

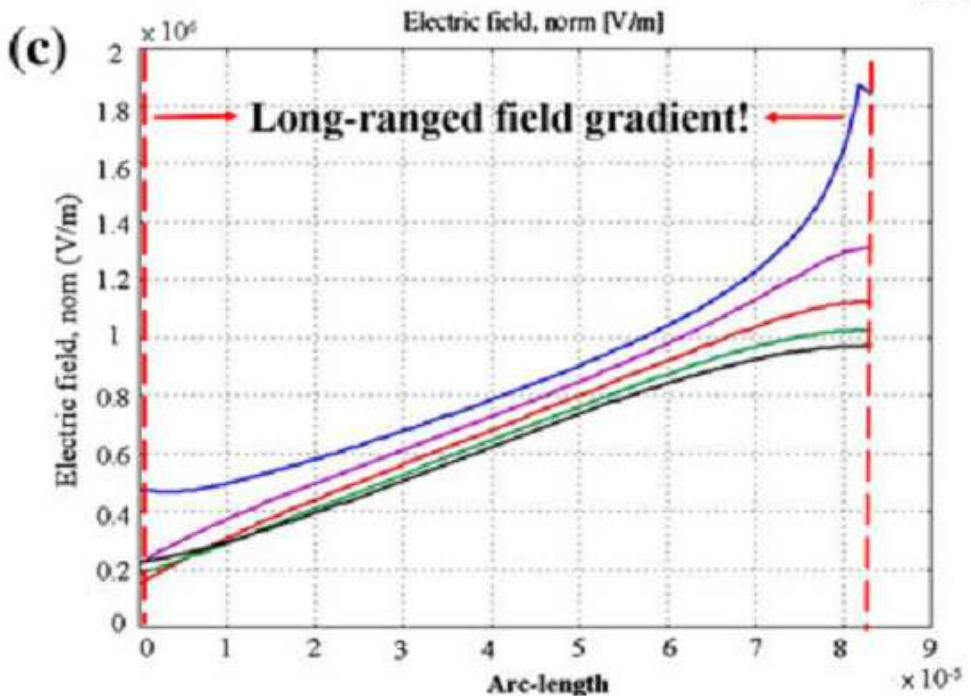


Motivation and Gray-Scale Pattern Design

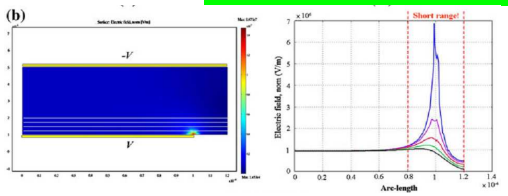






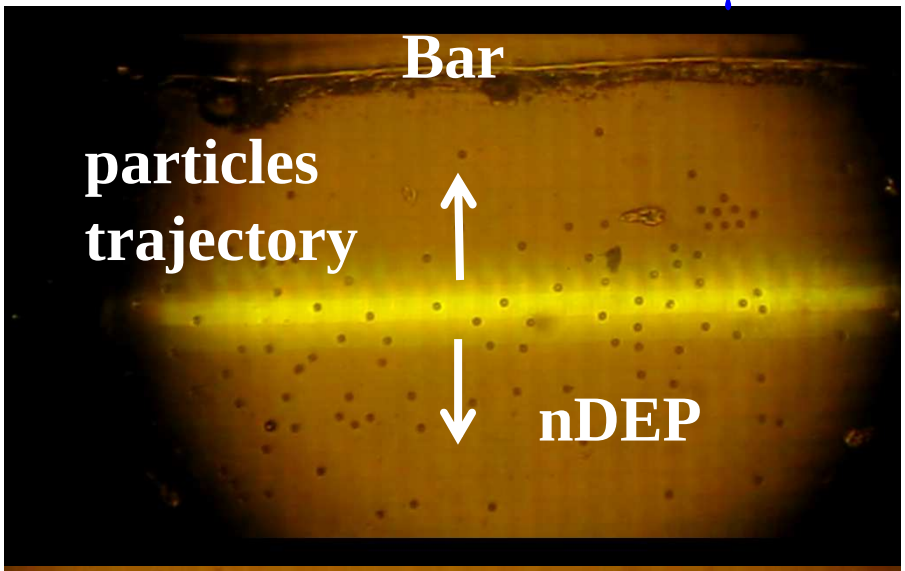


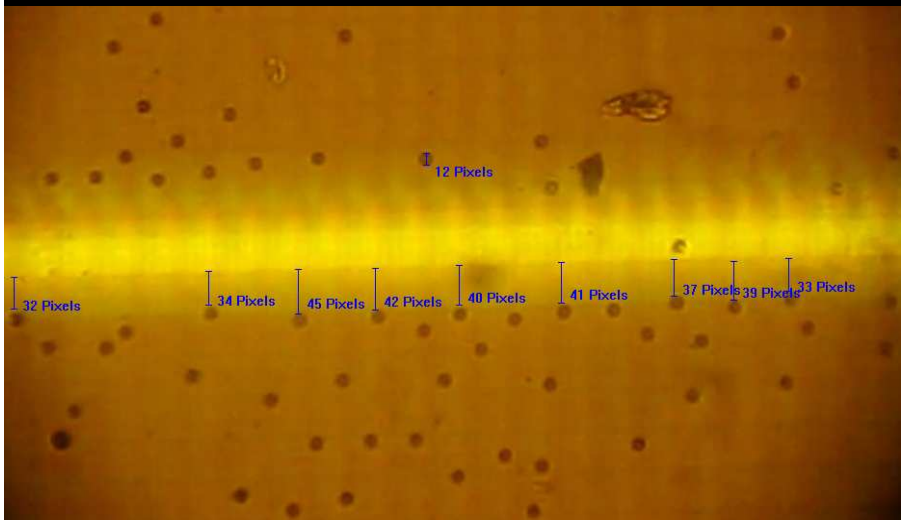
I-F Cheng et al., *Microfluid Nanofluid*, (2012) **12**, 95

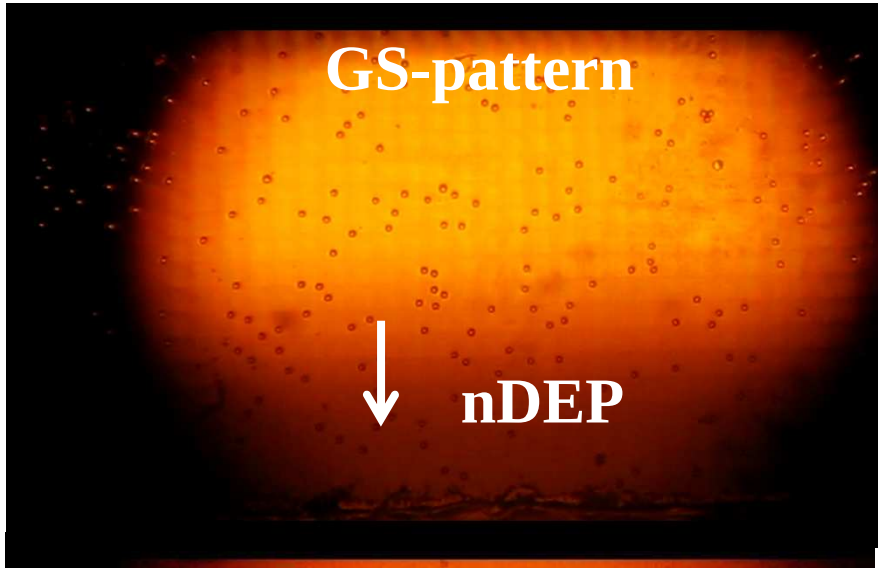


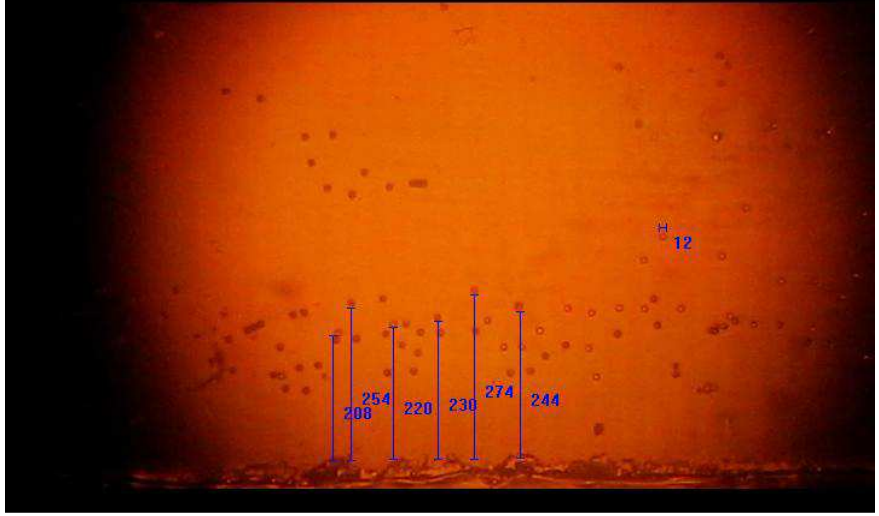
Investigation of the Working Ranges

10 μm latex in DI water









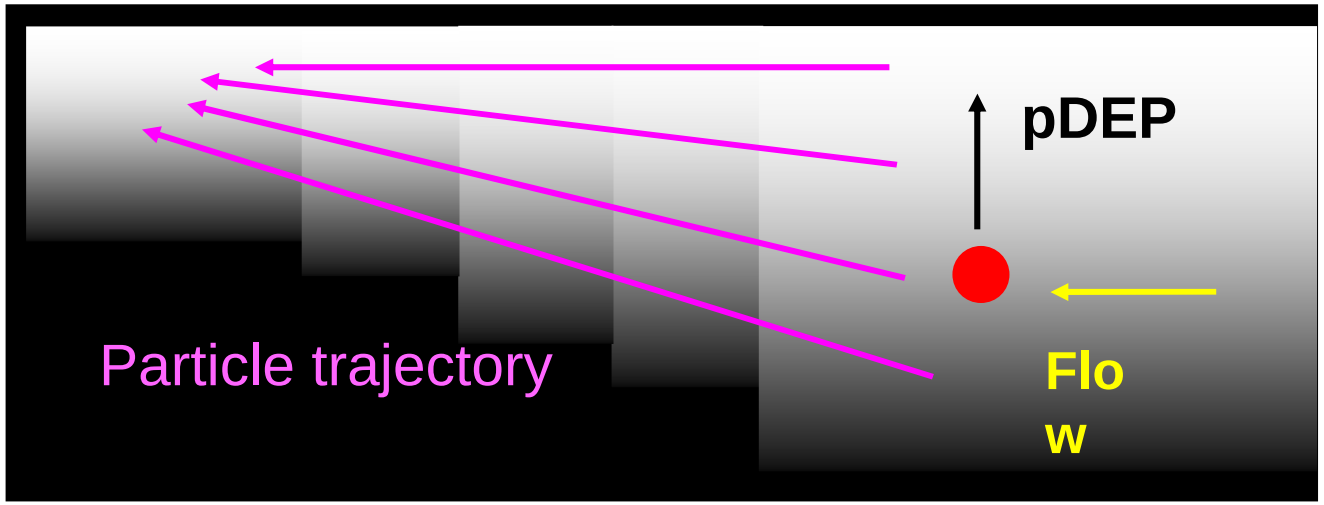
Average=38.11 μm

Average=361.67 μm

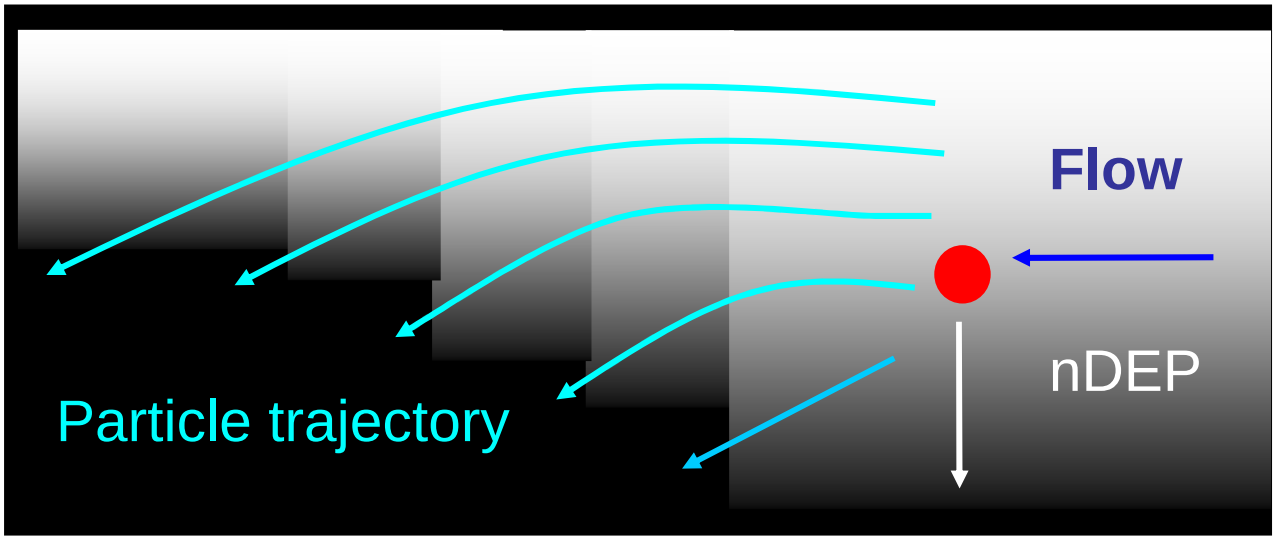
I-F Cheng et al., *Microfluid Nanofluid*, (2012) **12**, 95

Stepwise Gray-Scale Pattern Design

(a)

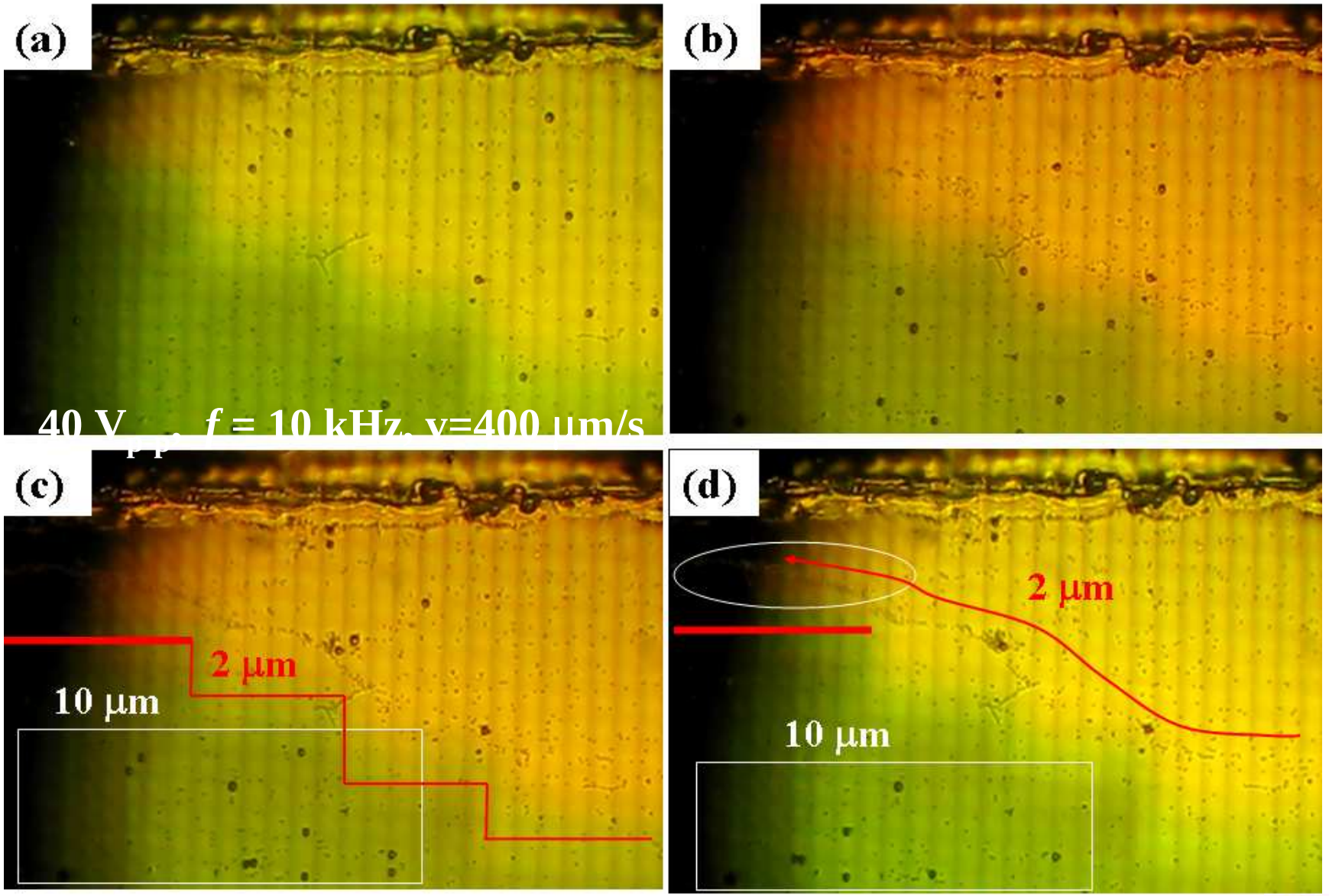


(b)



I-F Cheng et al., *Microfluid Nanofluid*, (2012) **12**, 95

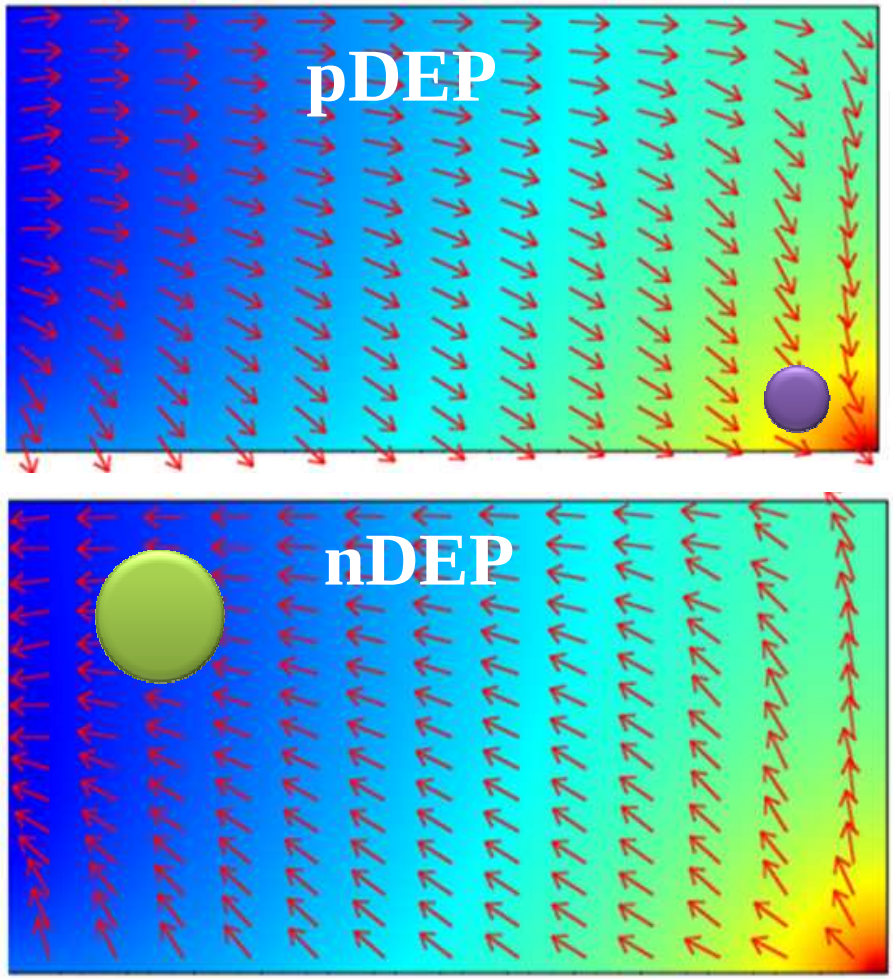
Continuous Separation of Latex Particles (10 μm & 2 μm)

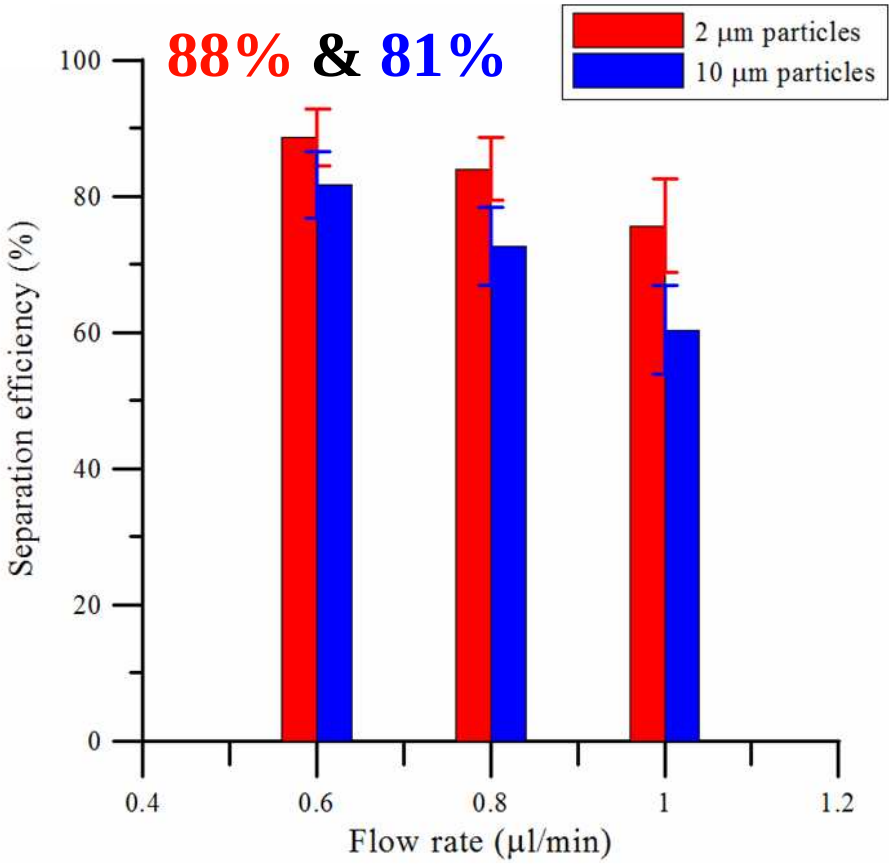


I-F Cheng et al., *Microfluid Nanofluid*, (2012) **12**, 95

Separation Efficiency

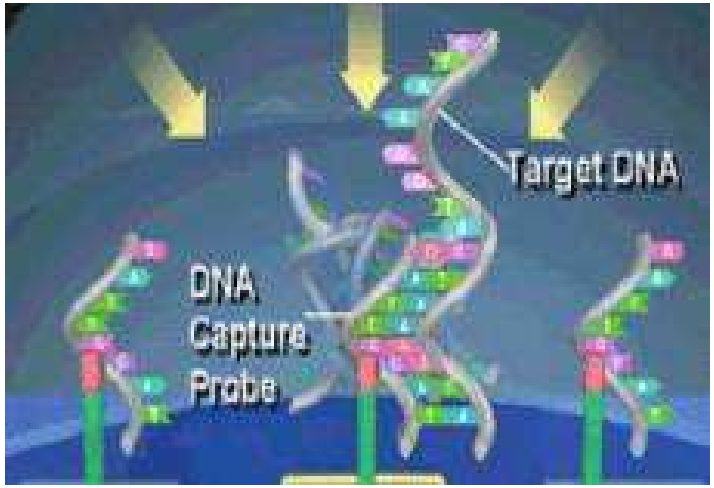
$$F_{DEP} = 2\pi r^3 \varepsilon_m \, \mathrm{Re}[\, f_{CM}\,] \nabla E^2$$

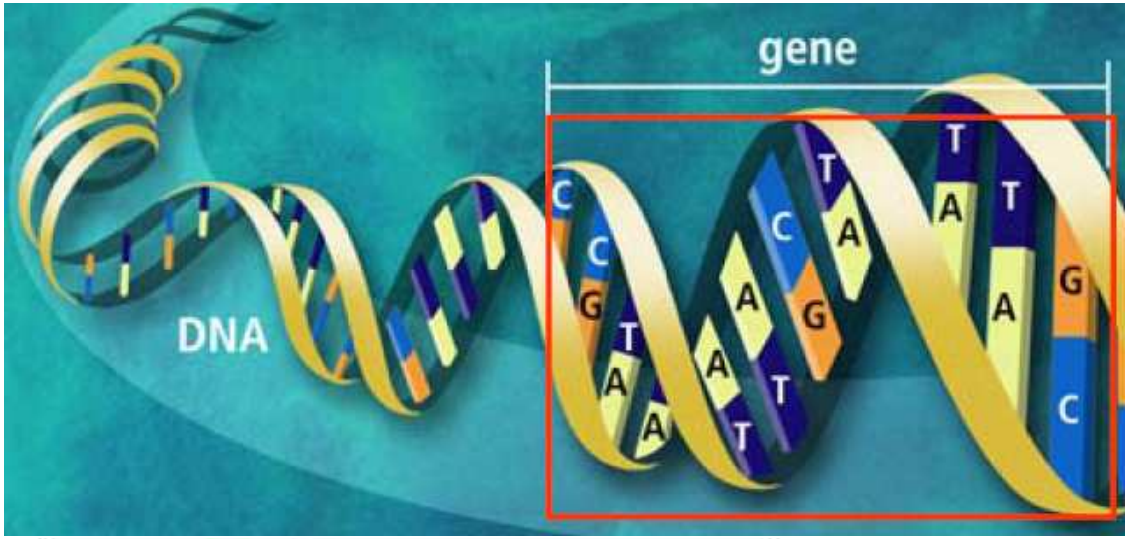


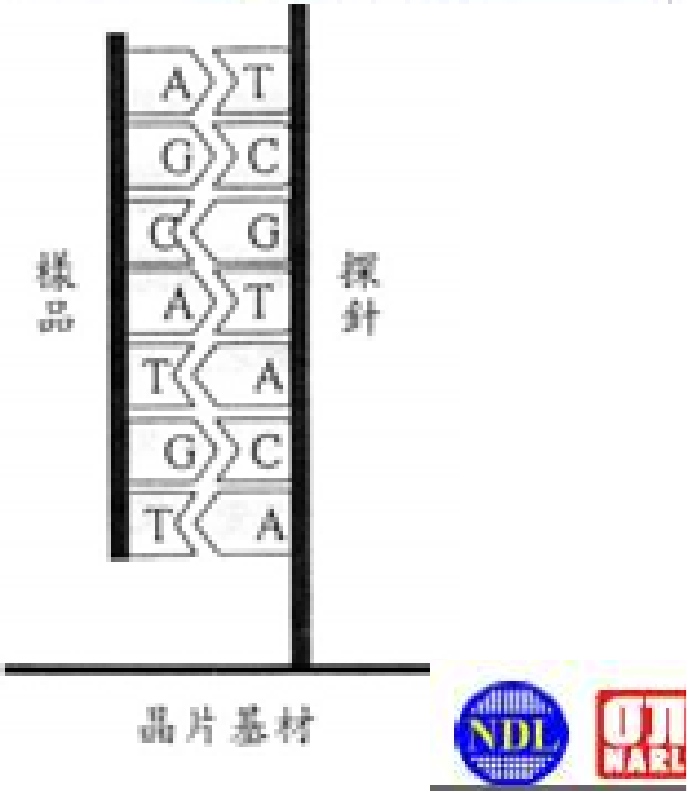


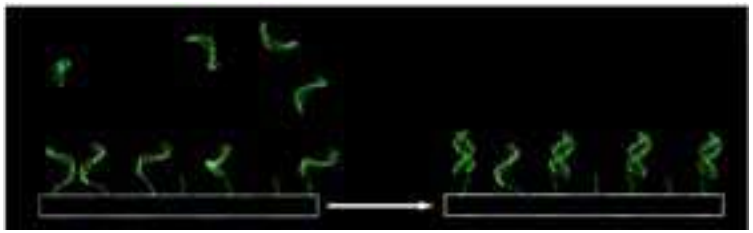
Efficiency: 2 μm > 10 μm

Genetic Detection





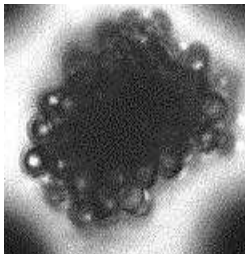


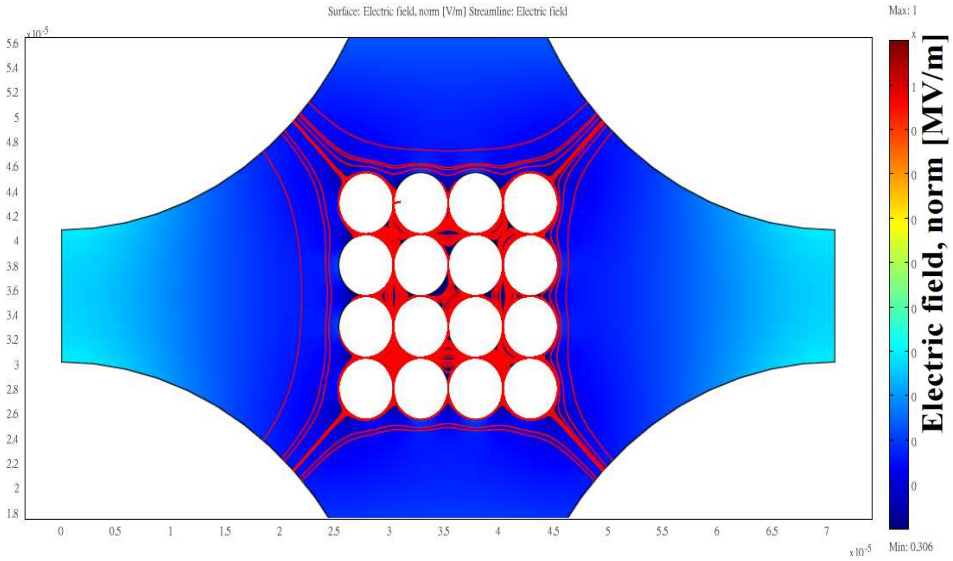


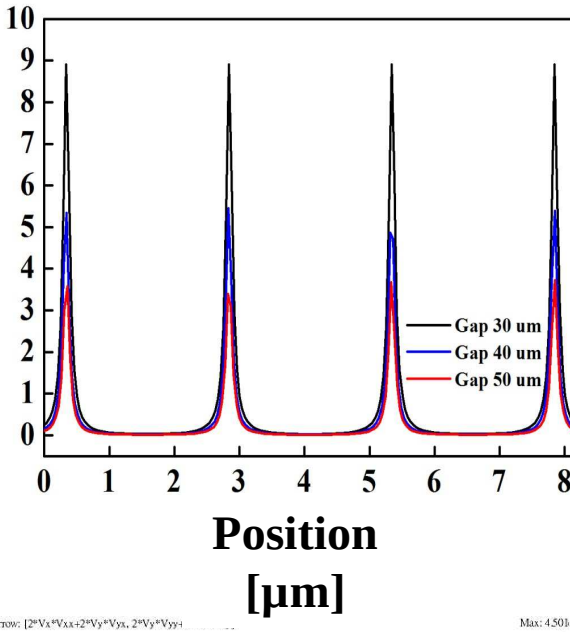
http://neurophilosophy.wordpress.com/2006/08/21/reseachers-will-use-dna-microarrays-to-probe-for-autism-genes/

Simulation of the Local Field Distribution for the Assembled Particles

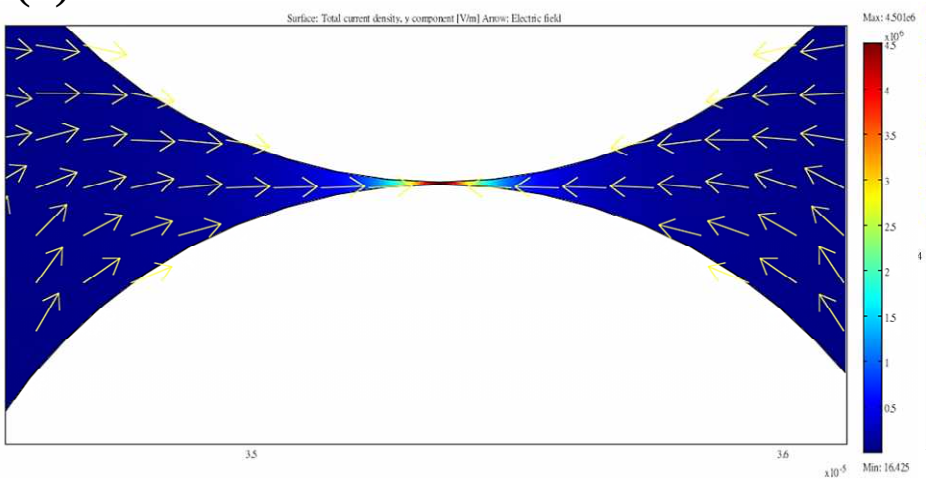
(a)

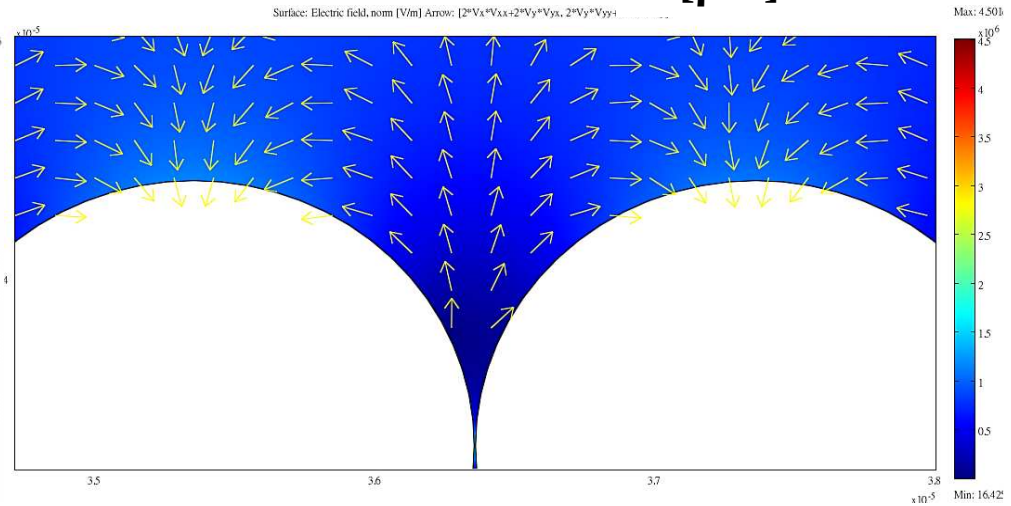




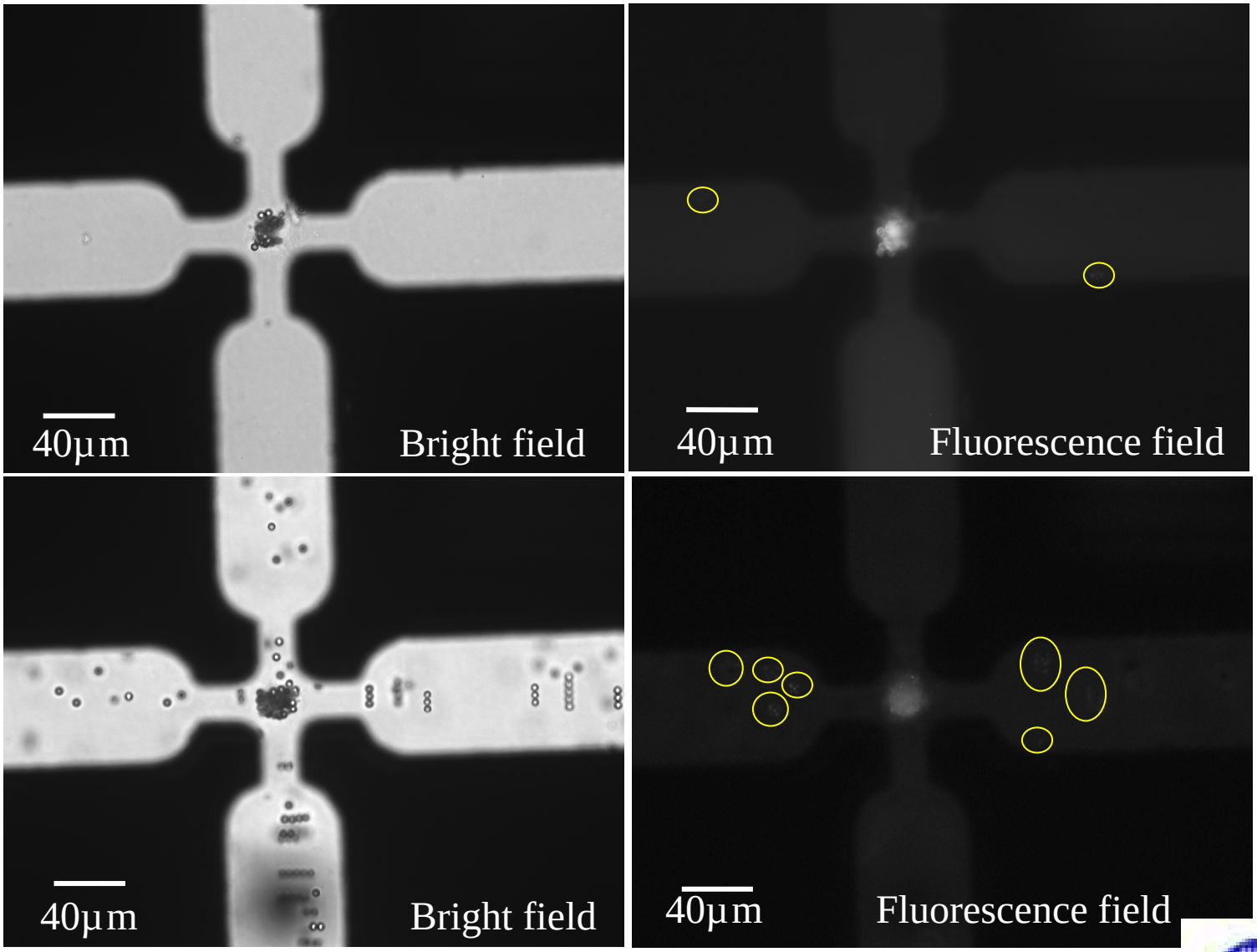


(b)

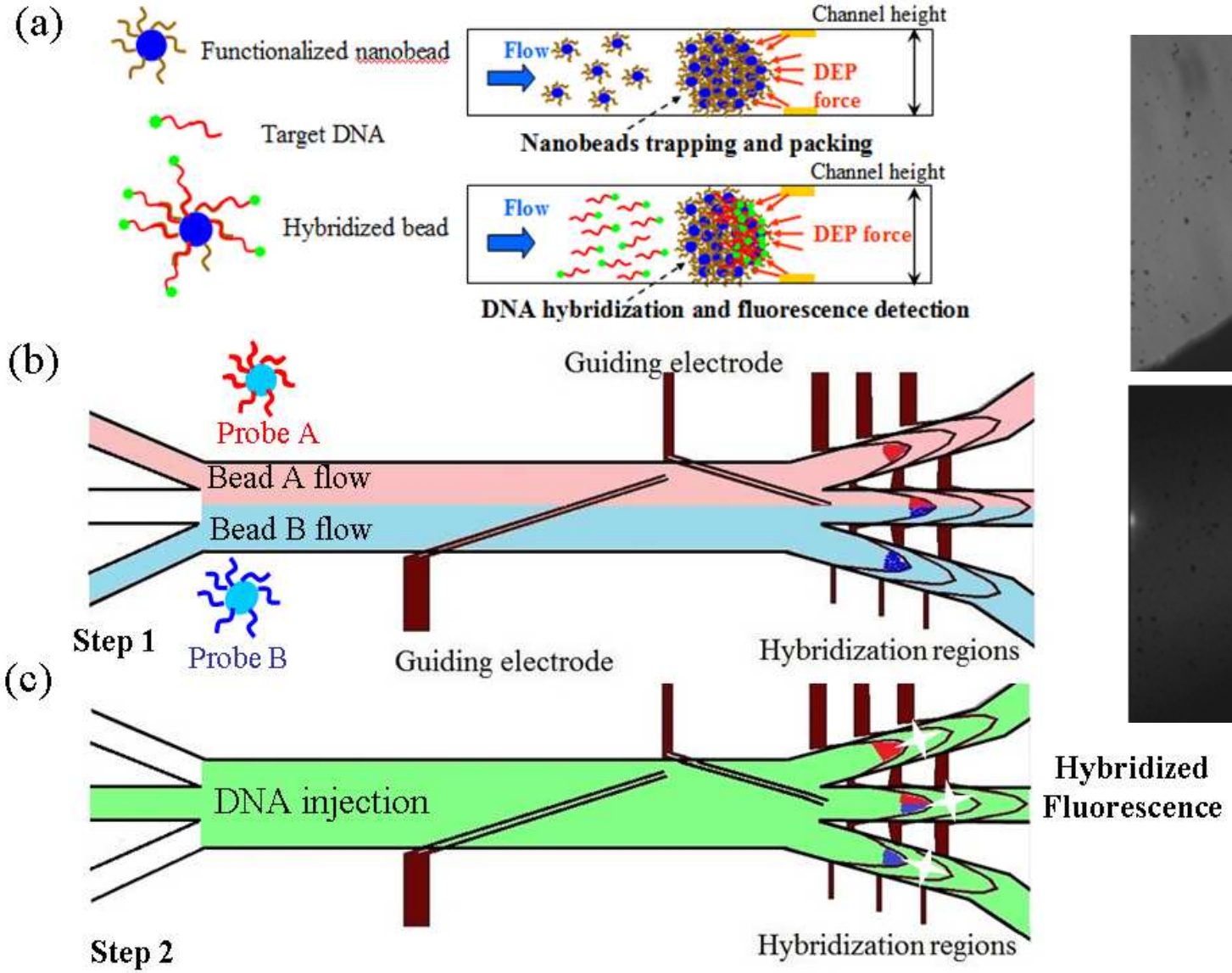


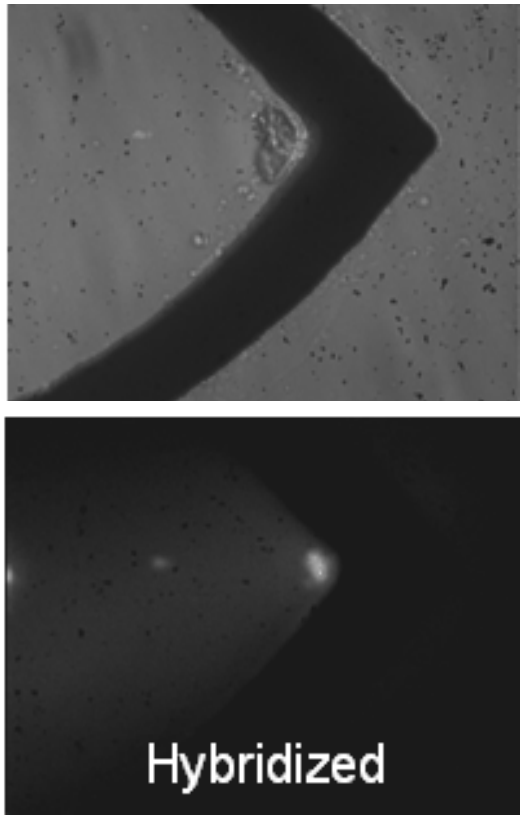


Nanobeads Trapping through the Amplified Electric Field



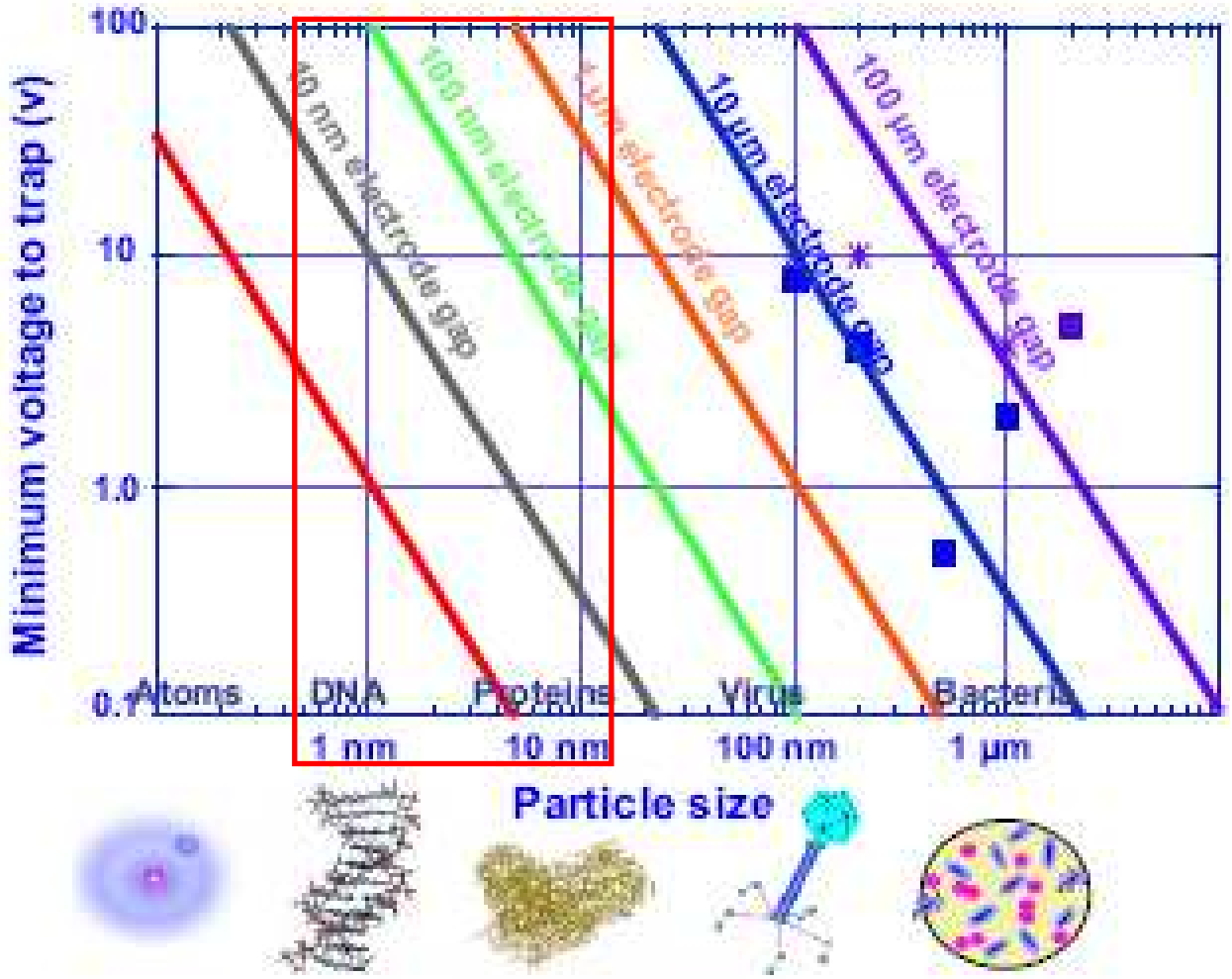
Electrokinetics and Shear Enhanced Sensitivity and Selectivity for DNA Hybridization/Immunoassay





Hybridized Fluorescence

Scaling Law for Dielectrophoretic Manipulation

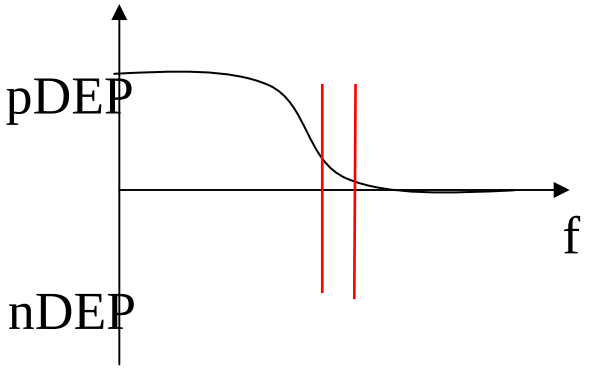


L. F. Zheng, et al., *Proceedings of the 3rd IEEE Conference on Nanotechnology*, 2003

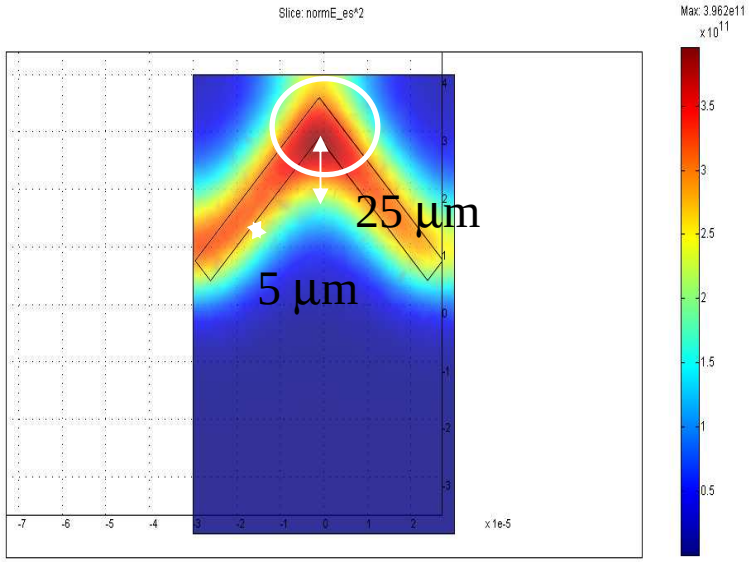
$$F_{DEP} = 2\pi r^3 \varepsilon_m \, \mathrm{Re}[\, f_{CM}(\omega)] \, \nabla E^2$$

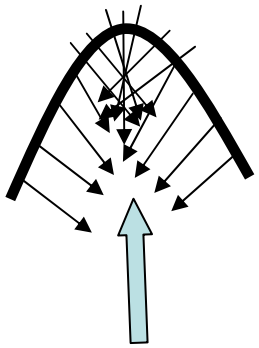
For DNA manipulation ~10^8 V/m

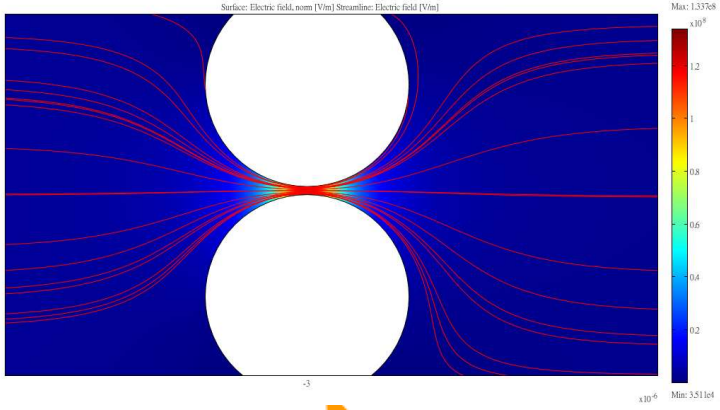
Theory and Mechanism

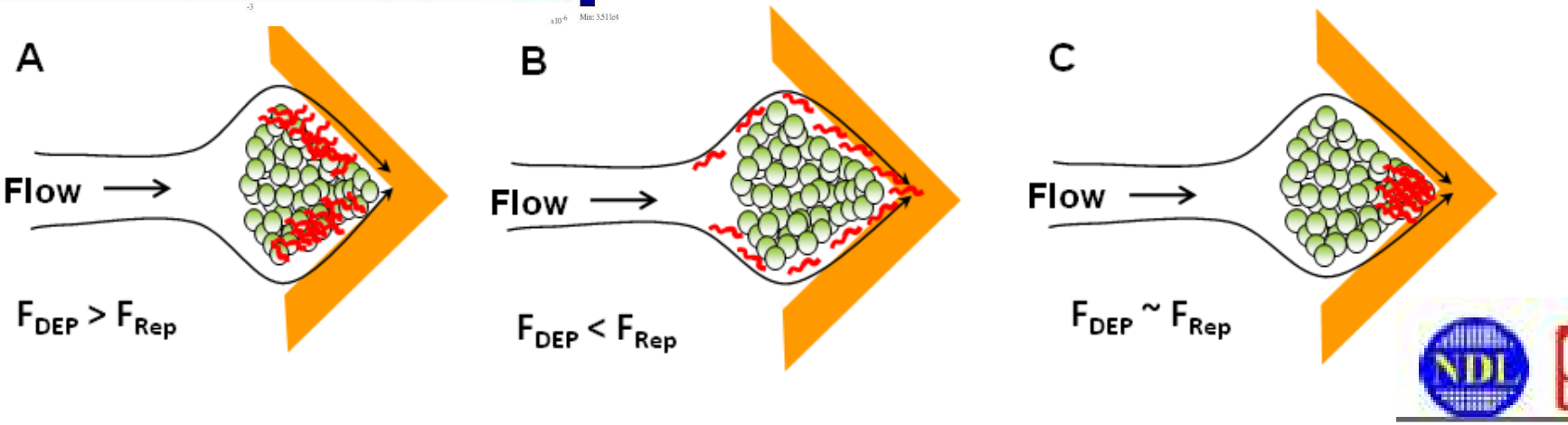


$f_{optimal} \sim D/\lambda^2$

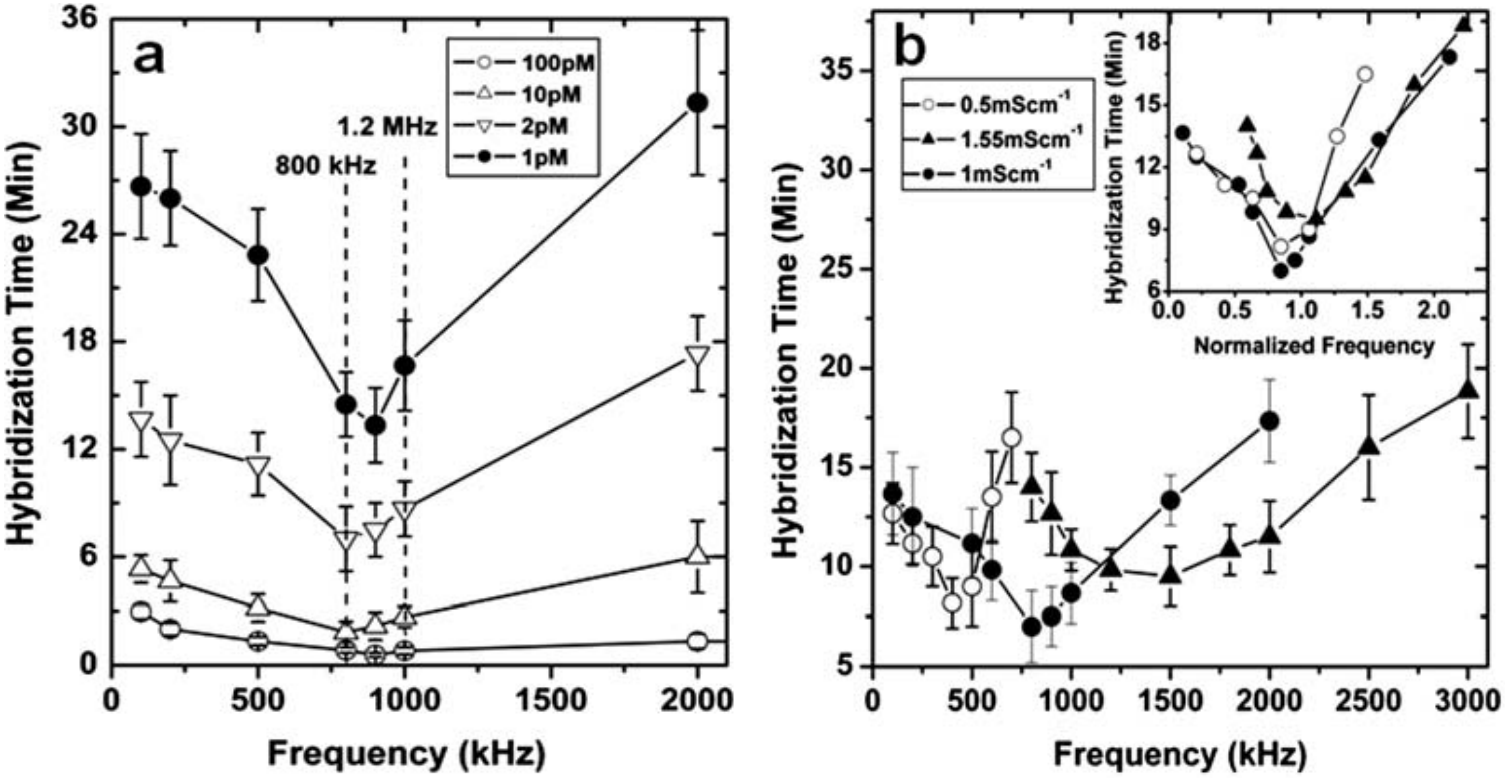


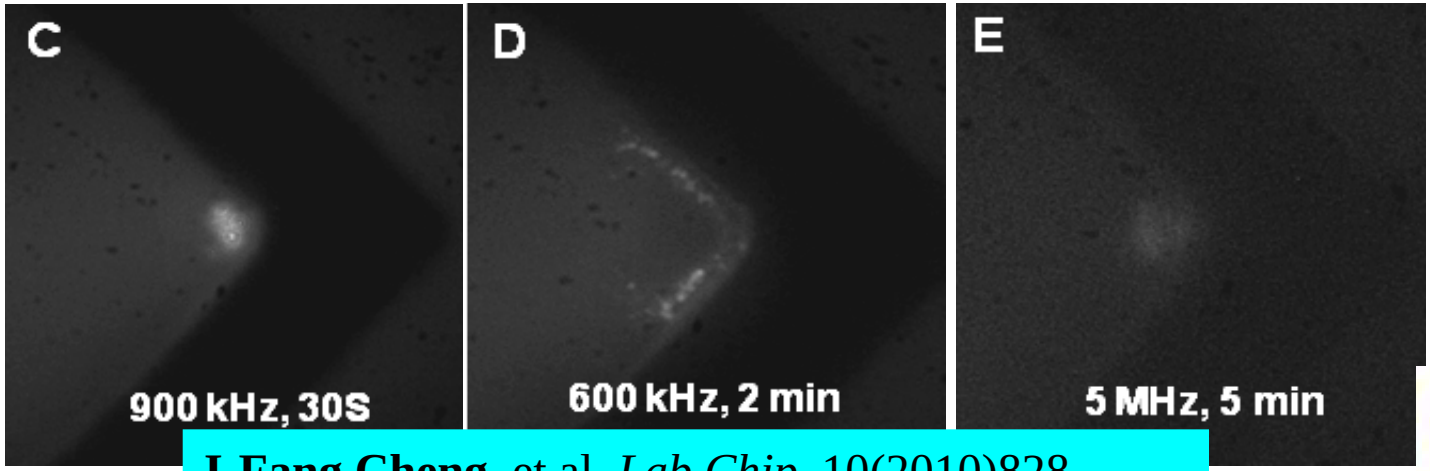






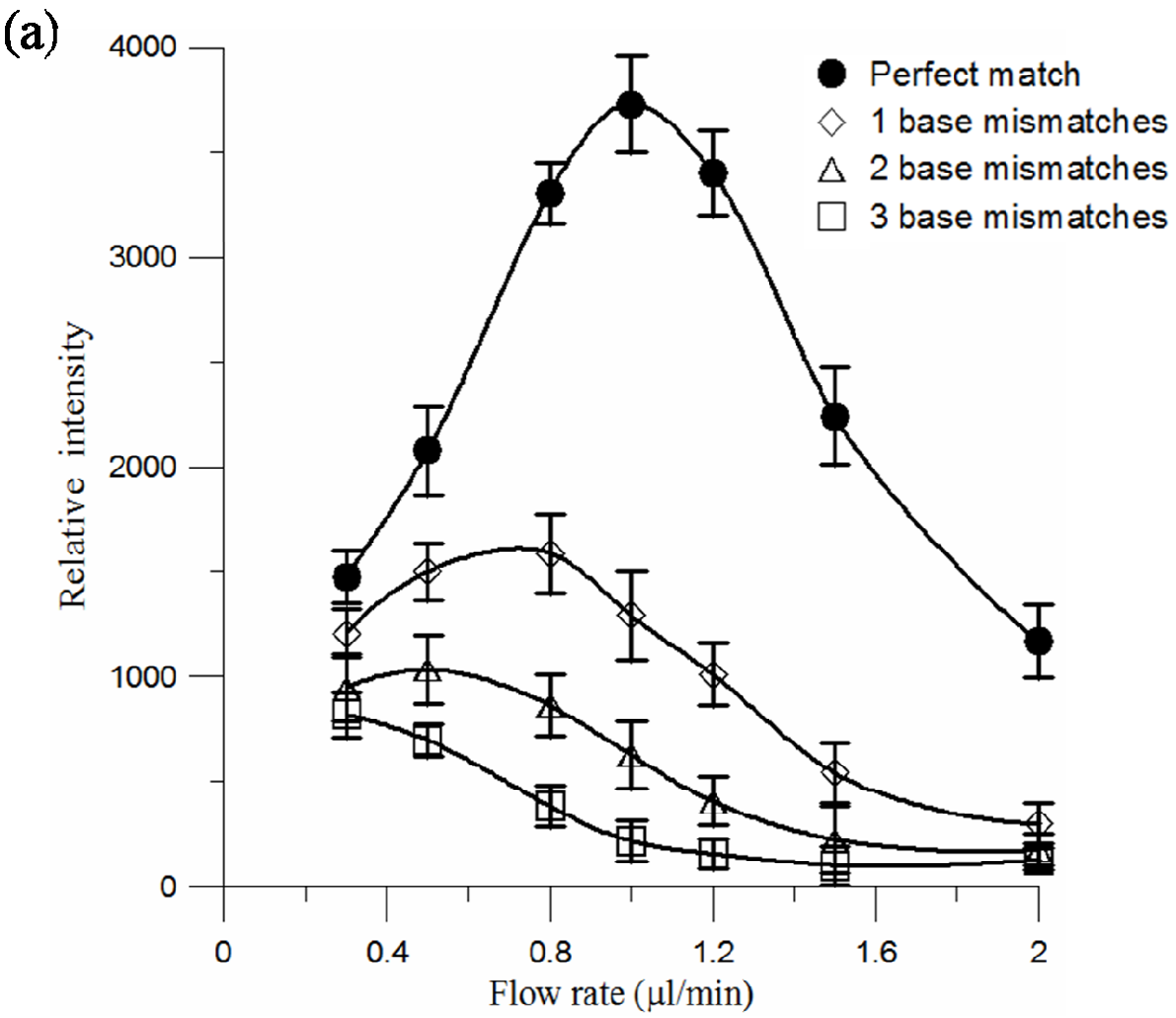
Frequency Dependence Hybridization

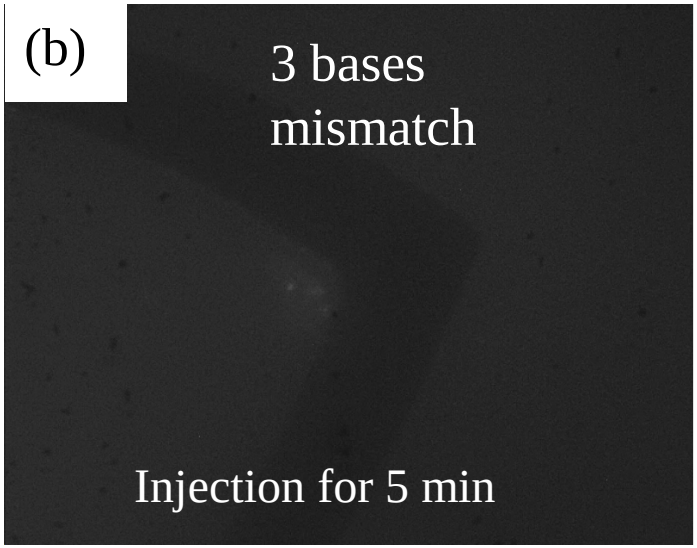


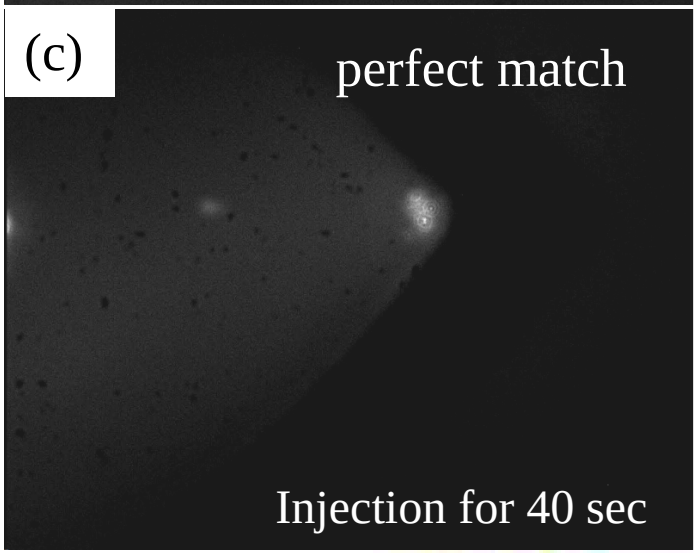


I-Fang Cheng, et al, *Lab Chip*, 10(2010)828.

Shear Force Enhanced Specificity

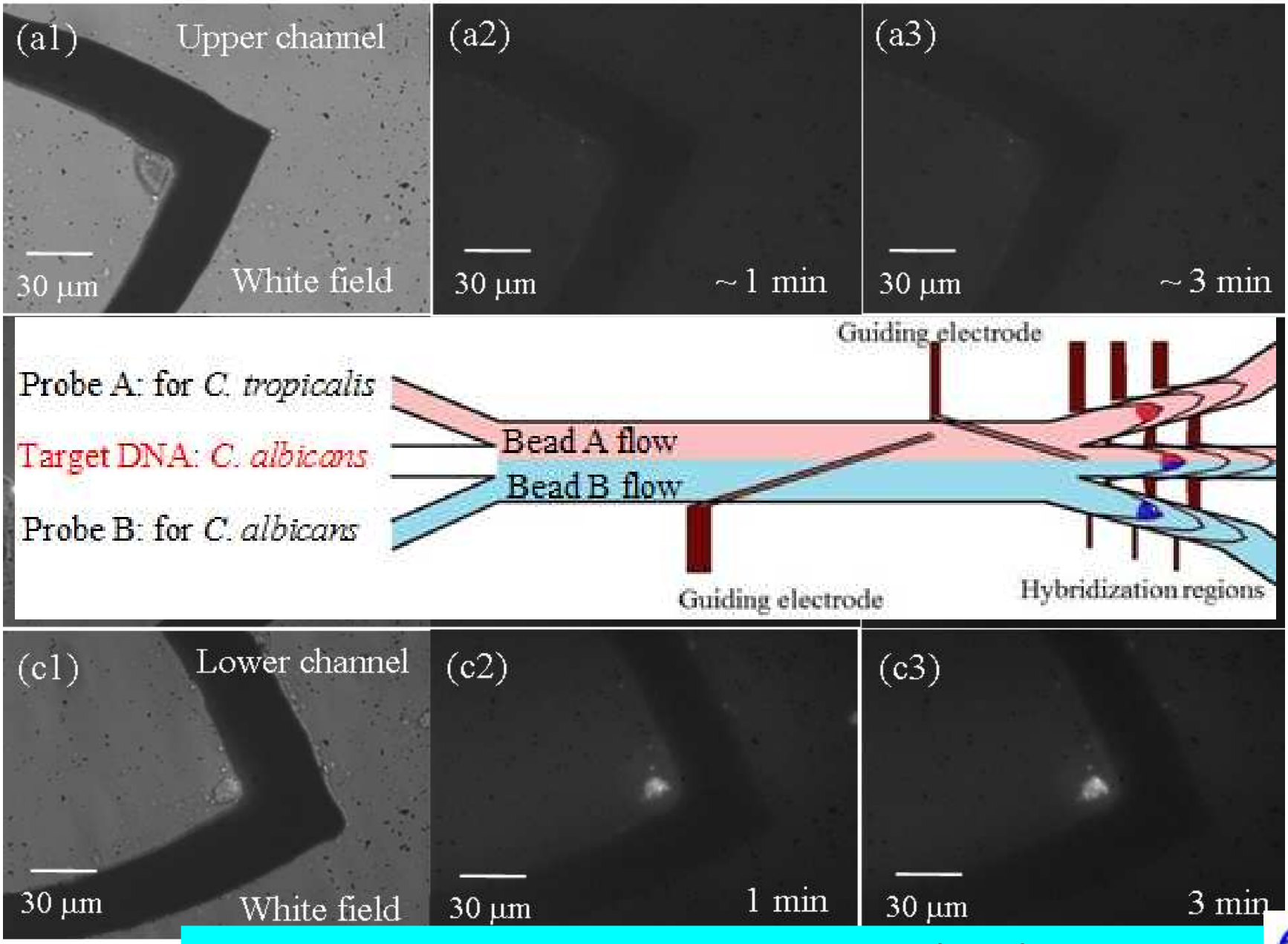






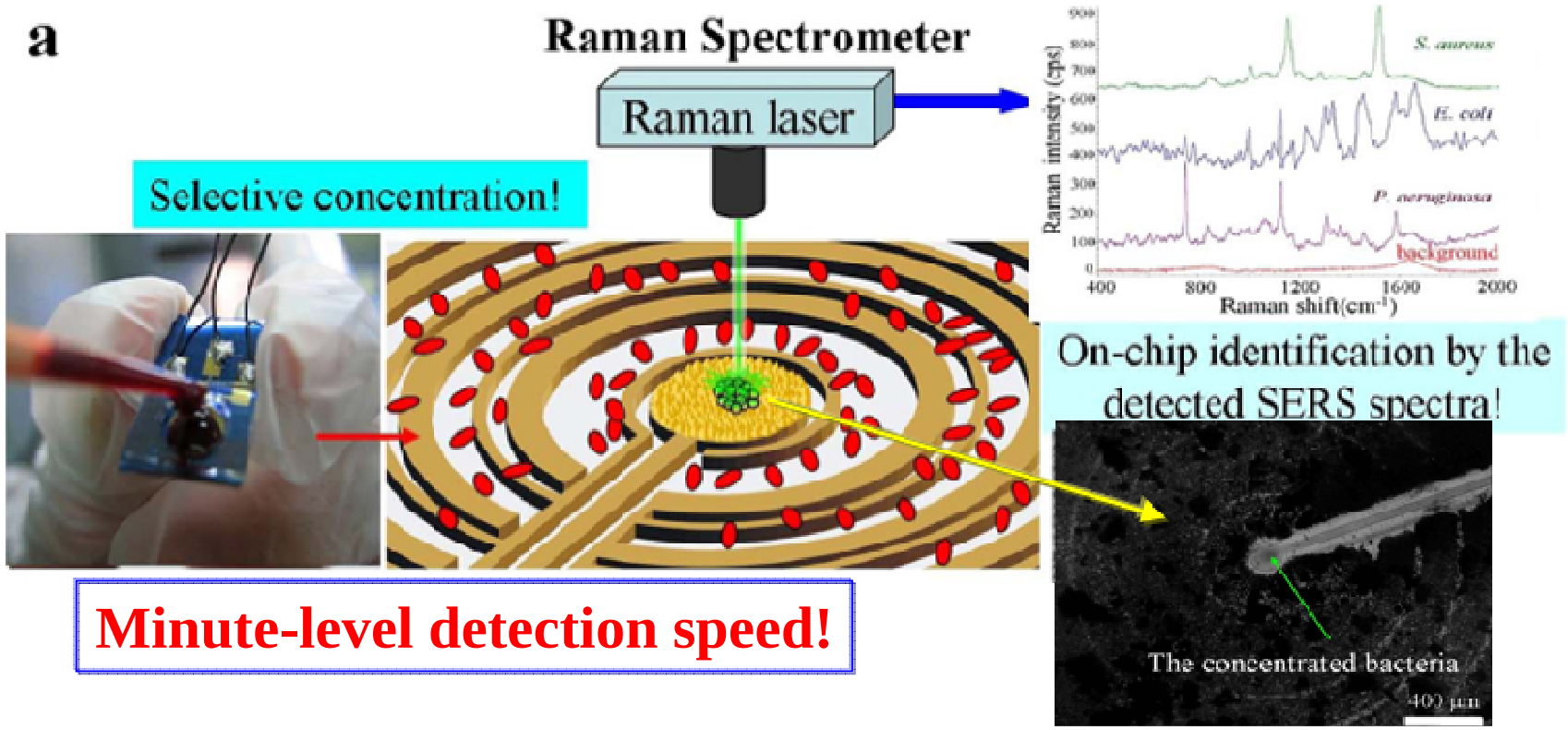
I-Fang Cheng, et al, *Biosensors & Bioelectronics*, (2012) **33**, 36-43.

Multi-target Discrimination of *Candida* Species



I-Fang Cheng, et al, *Biosensors & Bioelectronics*, (2012) **33**, 36-43.

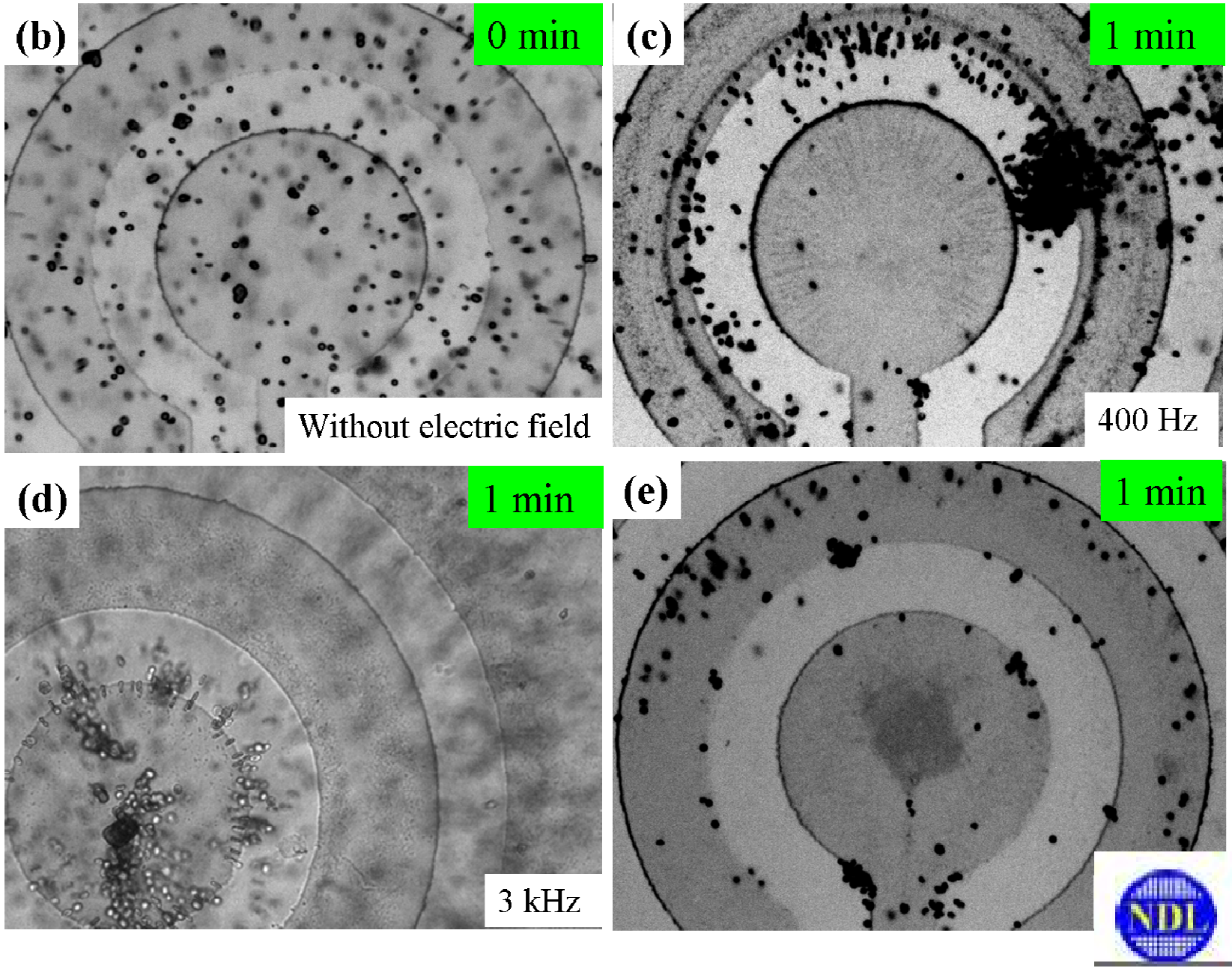
速测速决– 血液中稀少致病菌的快速鑑定技術(<5 min)



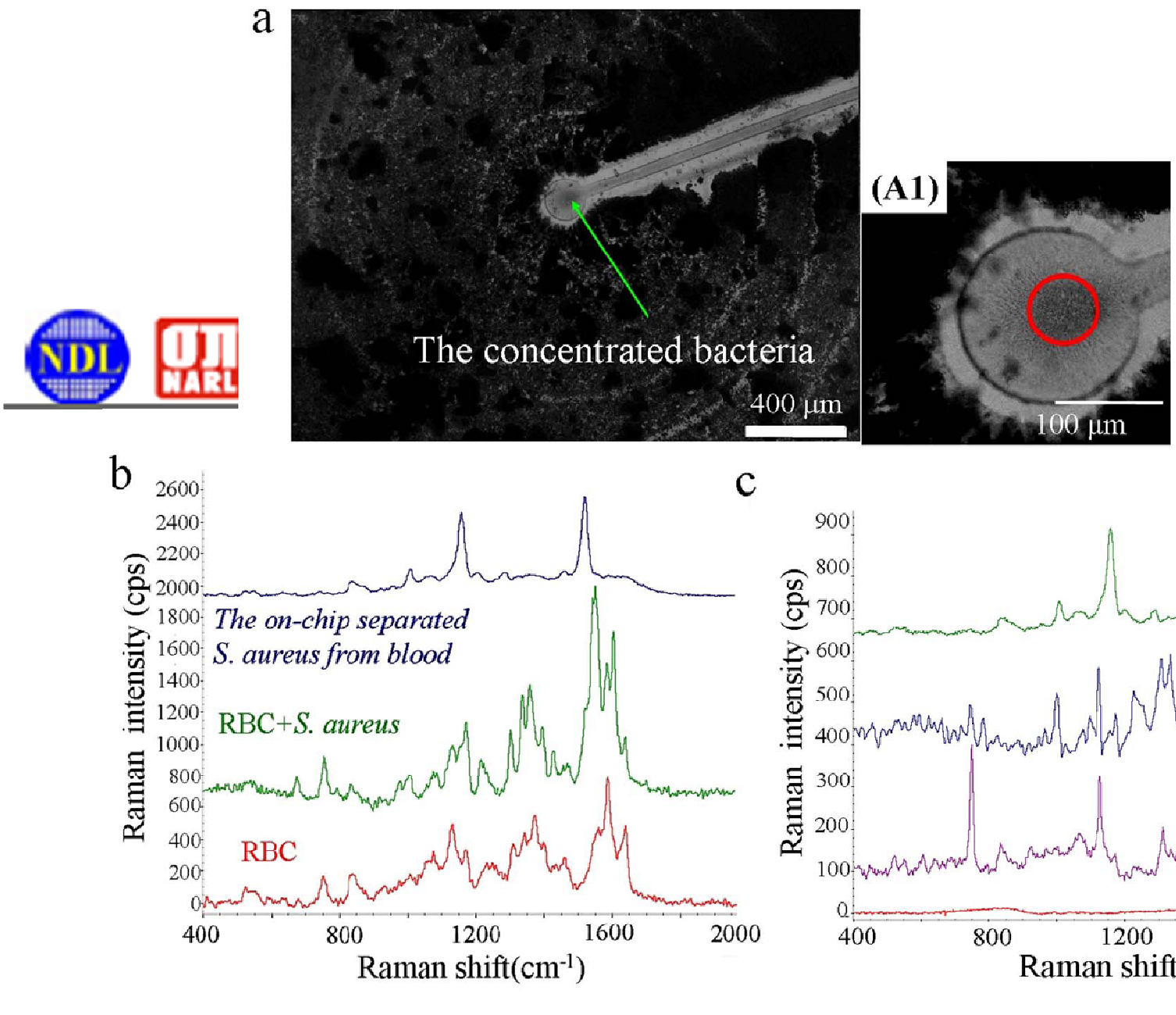
Minute-level detection speed!

I-F Cheng* et al., ***Sci. Rep.***,3, 2365 (2013)

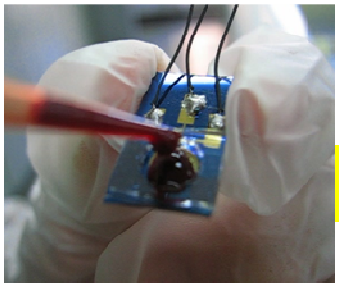
Selective Concentration of Bacteria



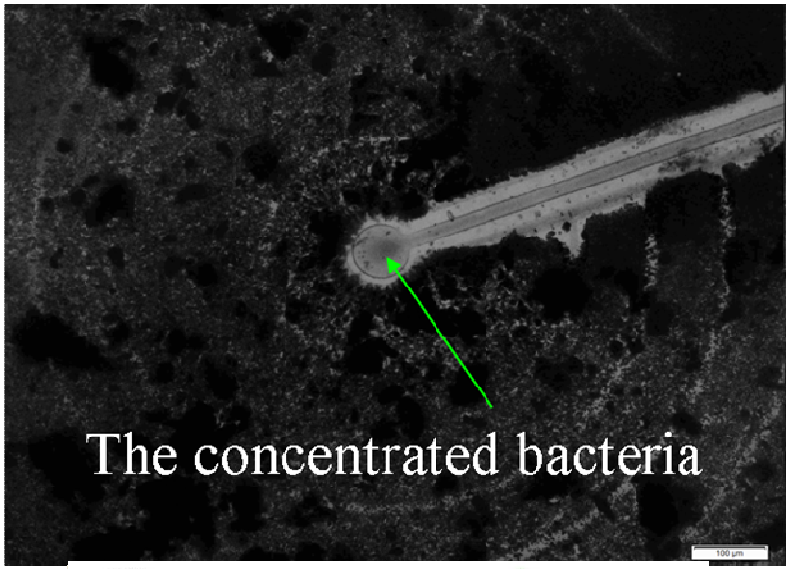
On-Chip SESR Identification of Bacteria

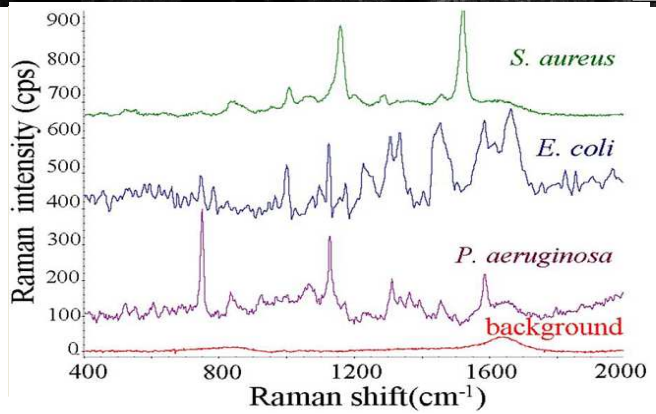


A Label-Free Method for the Rapid Identification of Rare-Pathogen from Human Blood



Hand-held chip!





- Without any surface immobilizations, antibody-antigen reactions, and complicated DNA processes.
- Ultrafast detection time: **~5 min** **(shorten detection time by a factor of 100)**
- Low detection limit: **3 ×10^3 CFU/ml** (match to early stage detection)
- Low cost for a chip **(<0.5 US.$)**

→ **Selective concentration of pathogen (~ 3 min)**

→ **Identification by their detected signatures (~2 min)**

- Three types of bacteria for the **most commonly isolated infection in Bacteremia** can be detected and identified via their detected signatures.

EK-SERS晶片 與現今技術的相關競爭性

檢測方法 / 技術特徵	EK-SERS Chip	PCR	DNA 微陣列	ELISA
檢測極限	3x10³ CFU/ml	100 nm-1 μM ~ 10³ CFU/ml	~100 pM ~ 10³ CFU/ml	10 ng/ml
檢測目標	全細胞檢測	DNA	DNA	全細胞或蛋白質檢測
樣本量	~50 μl	~50 μl	~100 μl	~200 μl
前處理與修飾	不需要	DNA抽取與放大	DNA放大與雜交	表面修飾與結合反應
重複清洗步驟	不需要	需要	需要	需要
辨識度	可 (細菌光譜指紋)	可 (DNA 引子)	可 (DNA 探針)	可 (抗體)
晶片與試劑成本	低 (元)	中 (百元)	中 (百元)	高(千-萬元)
總檢測時間	約 5 分鐘	約 4 小時	約8小時	8-12小時

Acknowledgement

We greatly thank the National Science Council (NSC) of Taiwan for supporting the research funding.
NSC 101-2218-E-492 -002 (新進人員研究計畫)
NSC 102-2221-E-492 -001 -MY2 (優秀年輕學者研究計畫)

We thanks for our collaborators:
Dr. Wu-Chou Su, Medical School of Cancer Center, NCKU
Prof. Hsien-Chang Chang, Department of Biomedical Engineering, NCKU
Prof. Chien-Wei Liu, Department of Mechanical Engineering, Yuntech. University
Prof. Hung-Wei Wu, Department of Computer science Engineering, KUST
Dr. Wei-Lung Huang, Department of Internal Medicine, NCKU

Thanks for your attention!

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