NEMS and Nano fabrication for bio-applications

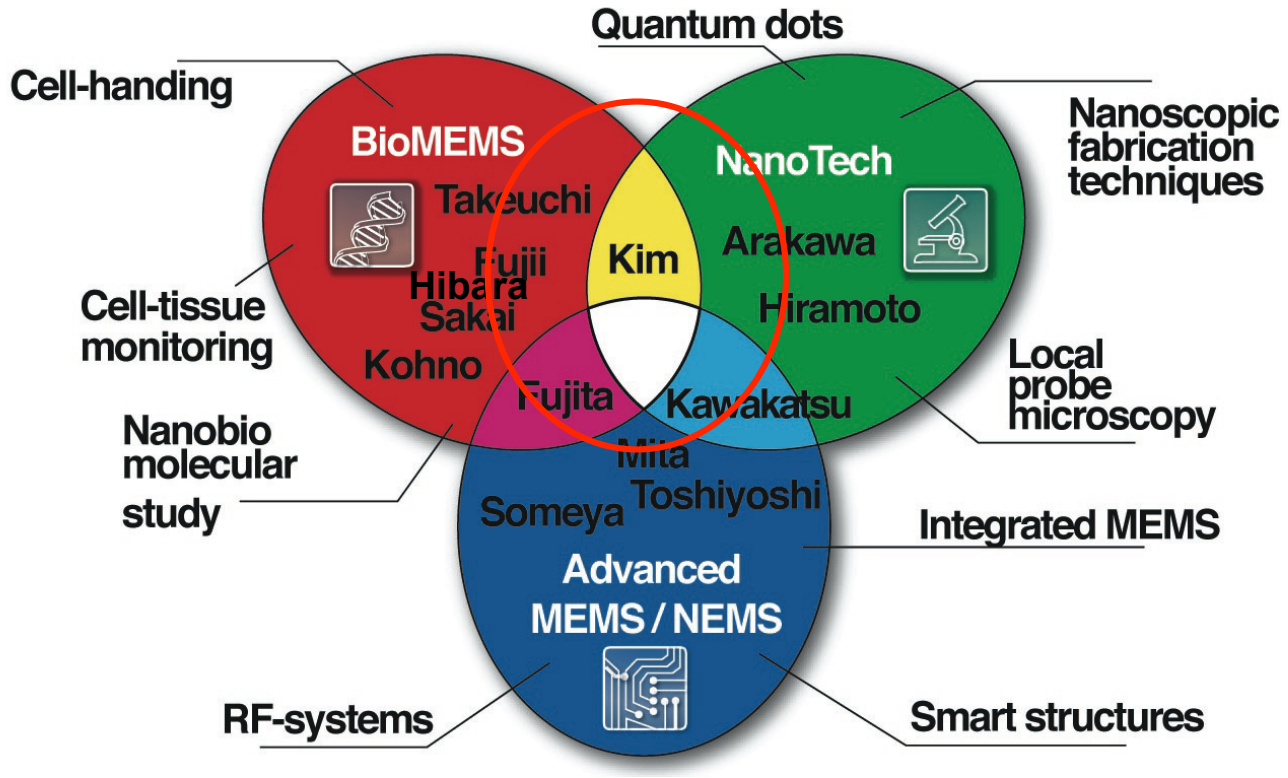
Beomjoon KIM, Associate Professor

Center for International Research on Micro Mechatronics (CIRMM)
Institute of Industrial Science
The University of Tokyo

LIMMS Research Coverage

Since its creation (1995) : MICRO & NANOTECHNOLOGY

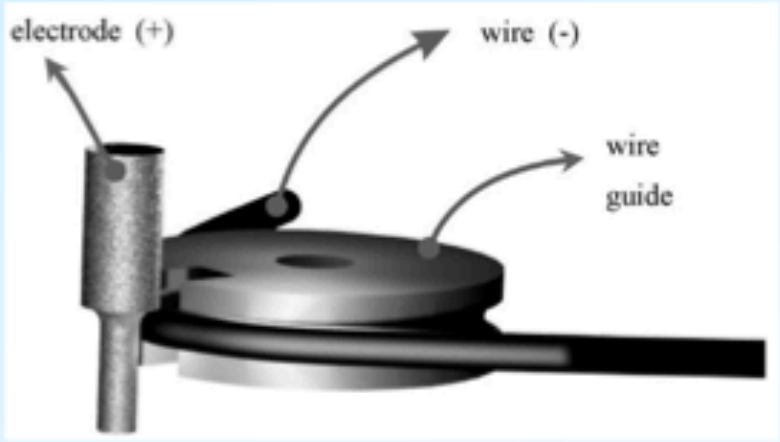
NOWADAYS : 3 research axes

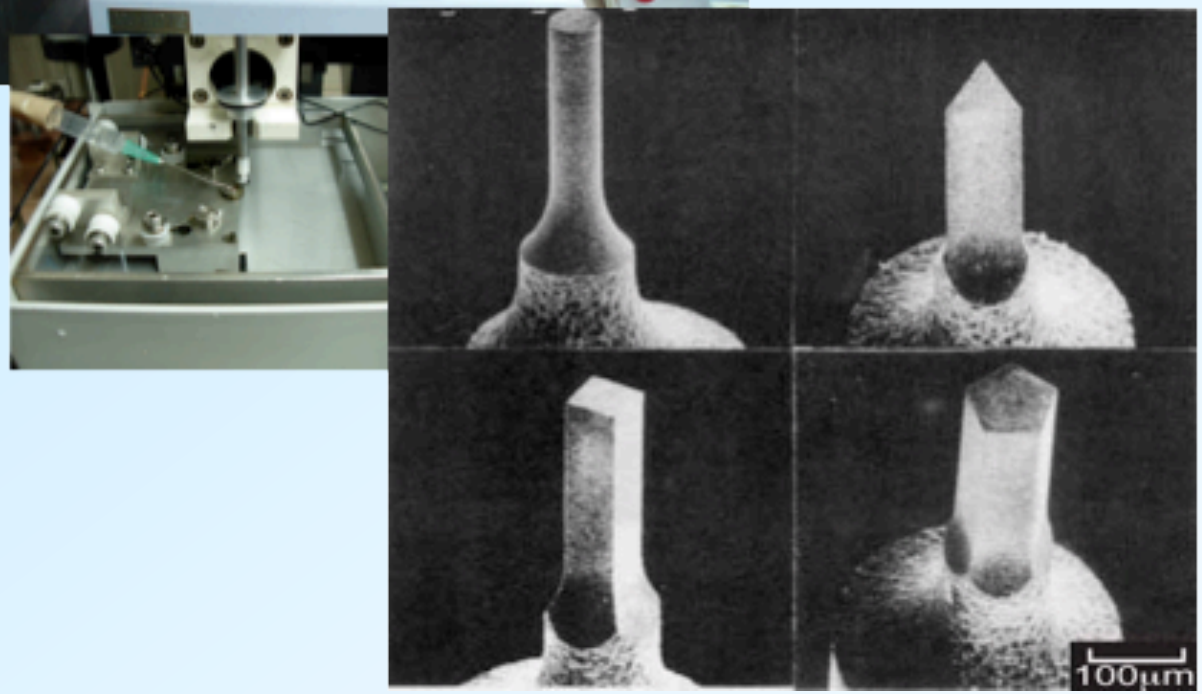


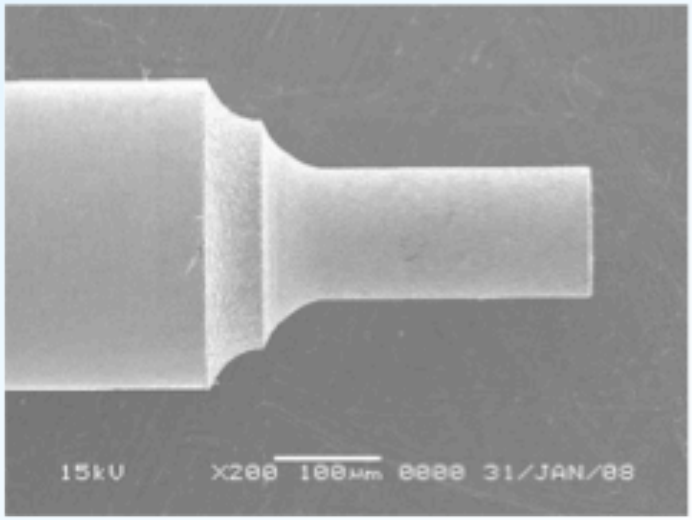
- New NANOTECHNOLOGIES (process and characterization)
- ADVANCED INTEGRATION of MEMS & NEMS functions
- Micro and nanotech applied to the BIOLOGY

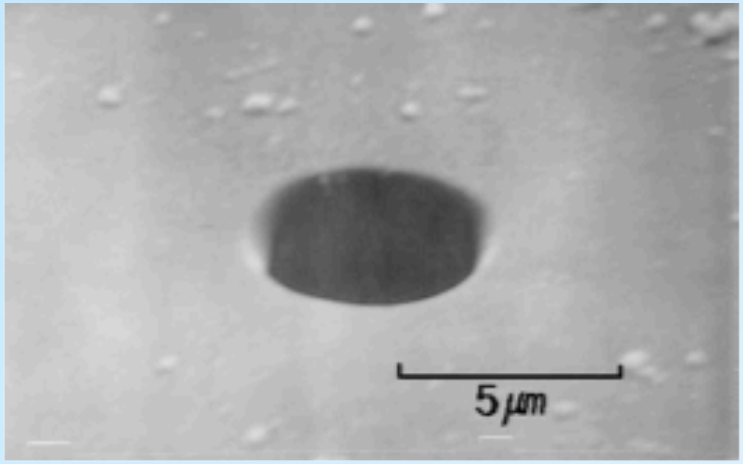
1993-1998 東京大学精密機械工学専攻、生産技術研究所　増沢研　修士/博士

マイクロ放電加工　　WEDG: Wire Electro Discharge Grinding





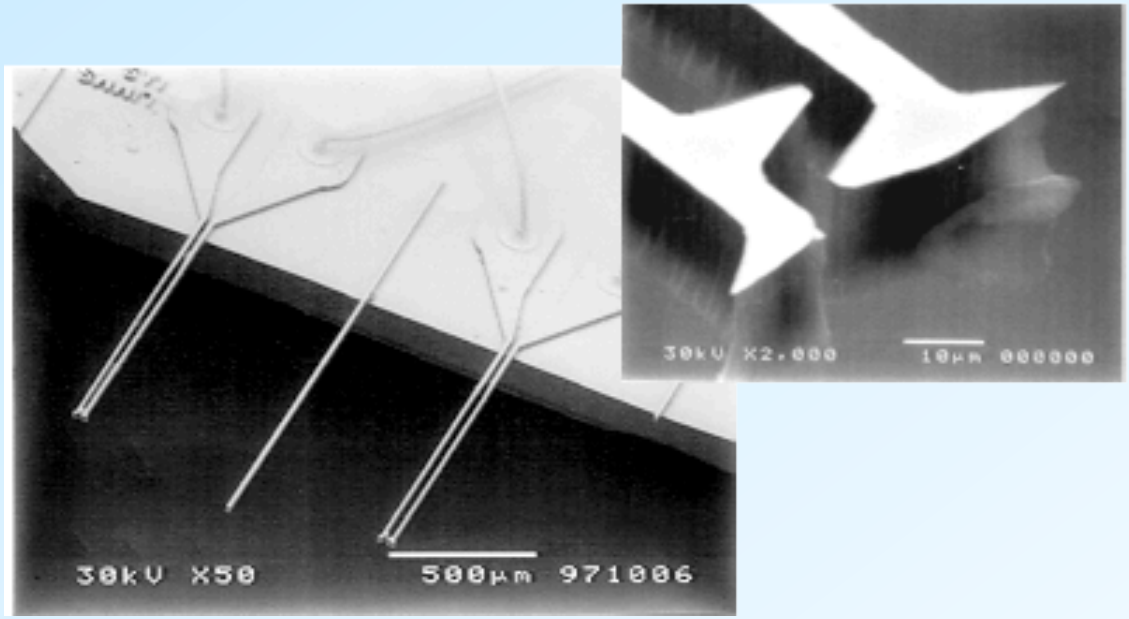


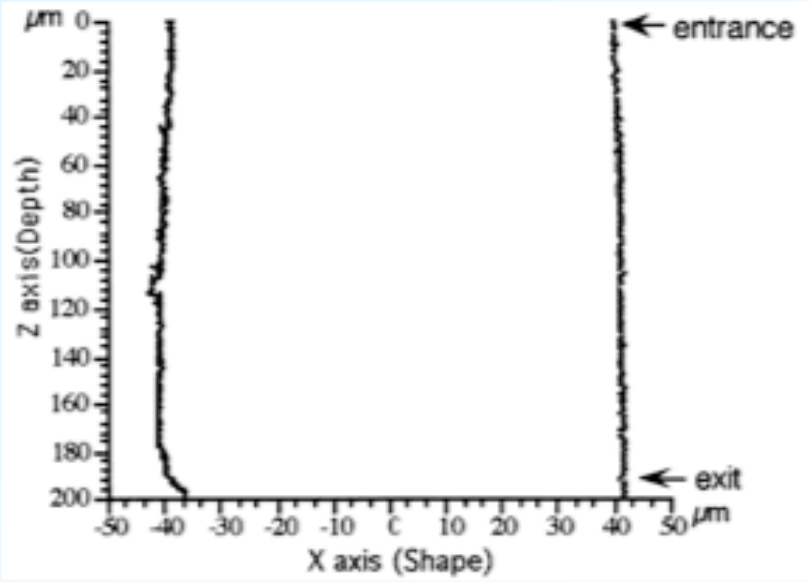


A microhole in quarts glass machined by USM (ultrasonic machining)

細穴の内部形状の測定

AFM/STM Like ?





GOAL: To achieve Low-cost, high performances
(high sensitivity, integrated functions, etc.) Bio-sensors

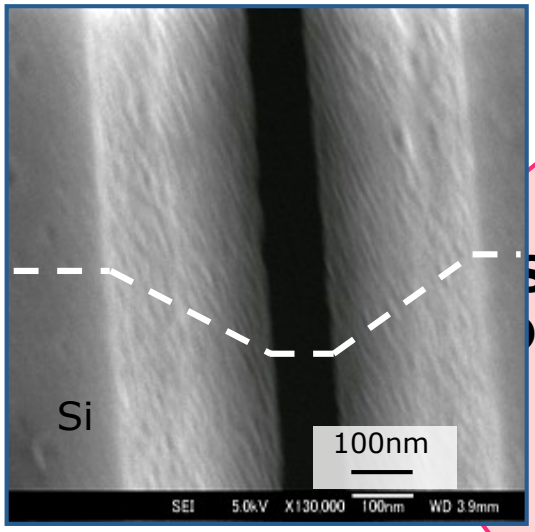
Top down:
* Shadow mask patterning
* Electro-spray deposition
* Electroplating with AAO nano porous membranes

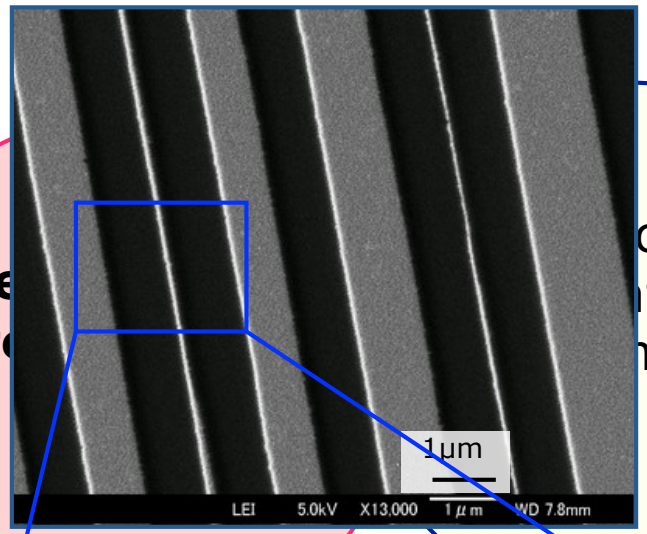
Bottom up:
* Micro/nano contact printing with SAM
* liquid μCP and R2R micro CP
* Optical soft-lithography for 3D micro pattern

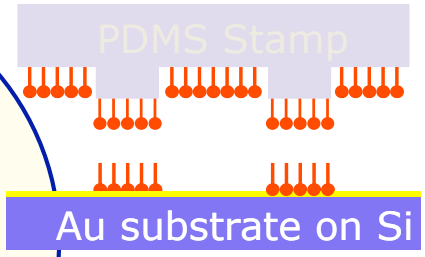
Nano fabrication technology:
To develop unconventional Nano lithography & nano fabrications with low-cost, larger area even in 3D curved surfaces

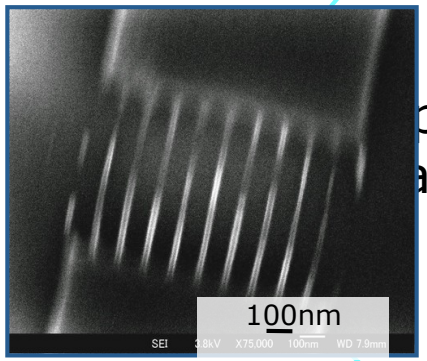
Unconventional Nano fabrication

Mix and Match Unconventional Nano patterning technology

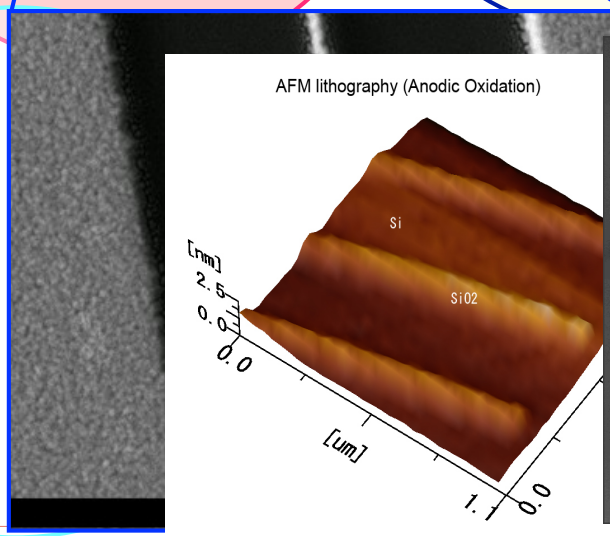


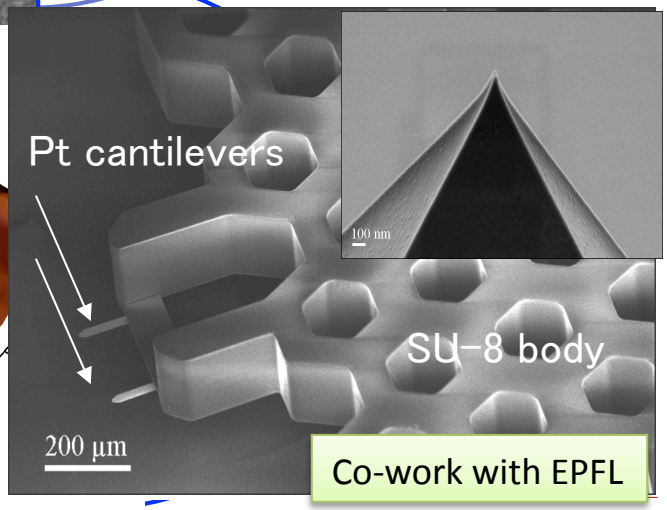






Array of 30nm wide nanowire



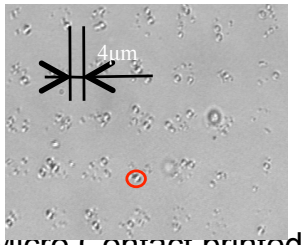


Co-work with EPFL

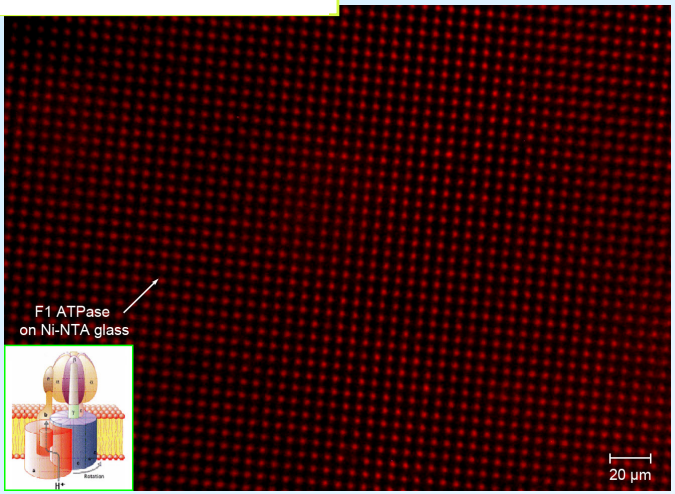
- Development of (1) **unconventional micro/nano patterning**
  of (2) **novel micro/ nano probes**
  for bio-MEMS device/Single cell/singular molecule sensing device

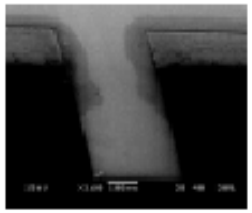
（1）広面積、新規ナノパターニング技術の開発(ソフトリソグラフィー、プローブリソ、シャドウパターン）
（2）バイオ物質（細胞、たんぱく質、DNAなど）の計測デバイスの開発

Biology application

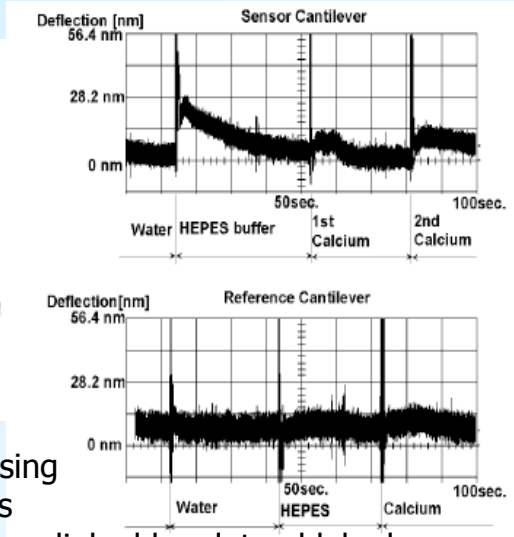


μCPを用いたF1-ATPaseの Micro Contact printed F1-ATPase protein

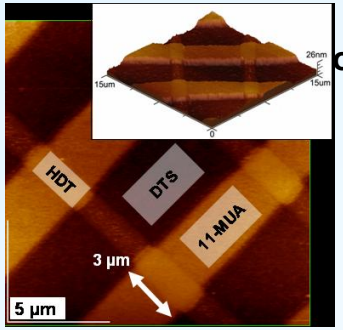


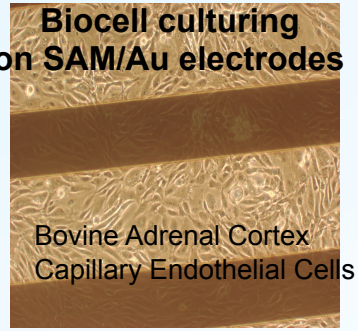


SEM of protein deposited protein film and cantilever



Polymer cantilever biosensor using electrospray deposition of proteins
(α-lactalbumin IgG patterned, cross-linked by glutaraldehyde vapor, co-work@RIKEN)

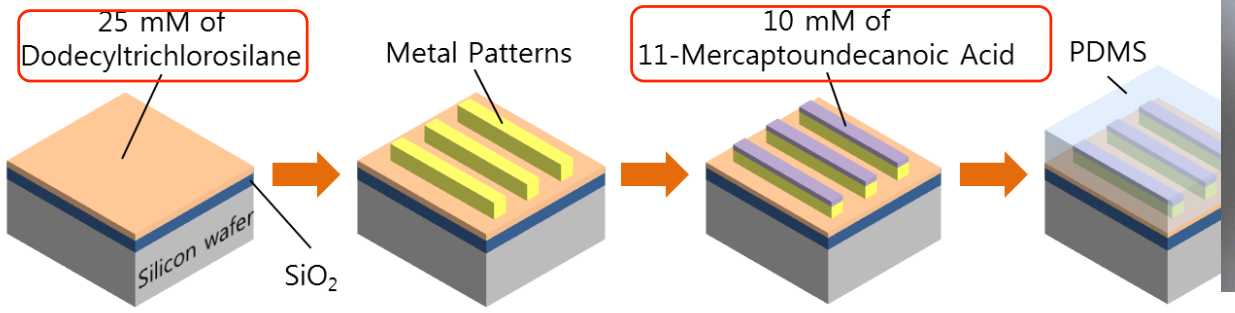


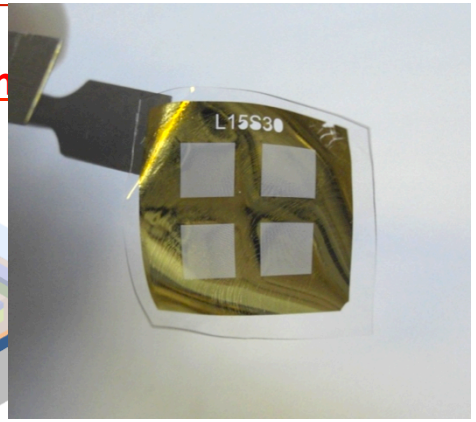


SAM表面処理法を用いた生体細胞のパターニング

Fabrication of Micro Structures on Convex/ Concave Substrates

Fabrication Process of PDMS Photomask and Optical Softlithograph





Cross Section A-A'

(a) SAM (DTS) Treatment on Oxide Substrate

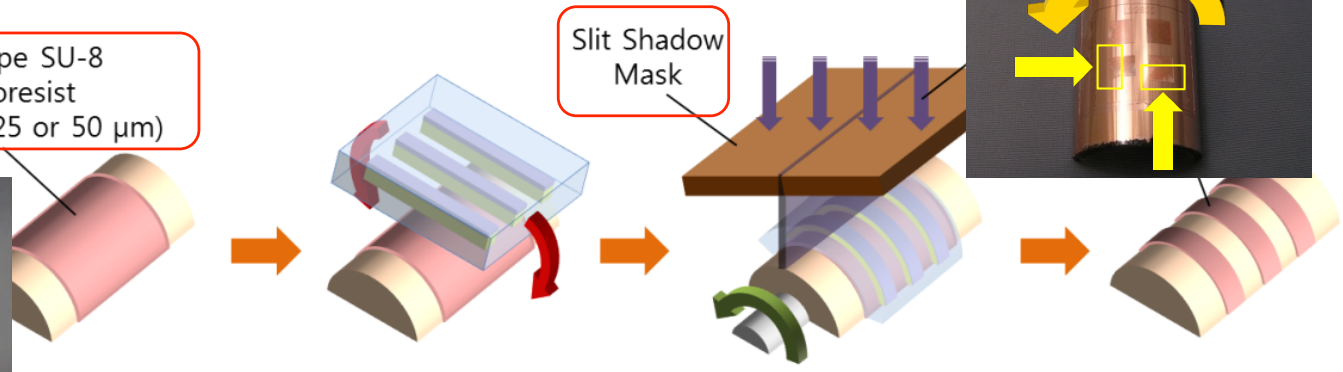
(b) Metal (Cr/Au) Patterning

(c) SAM (11-MUA) Treatment On Metal Patterns

(d) PDMS Spincoated and Cured

(e) PDMS Flexible Photomask

Fabrication process for PDMS flexible photomask



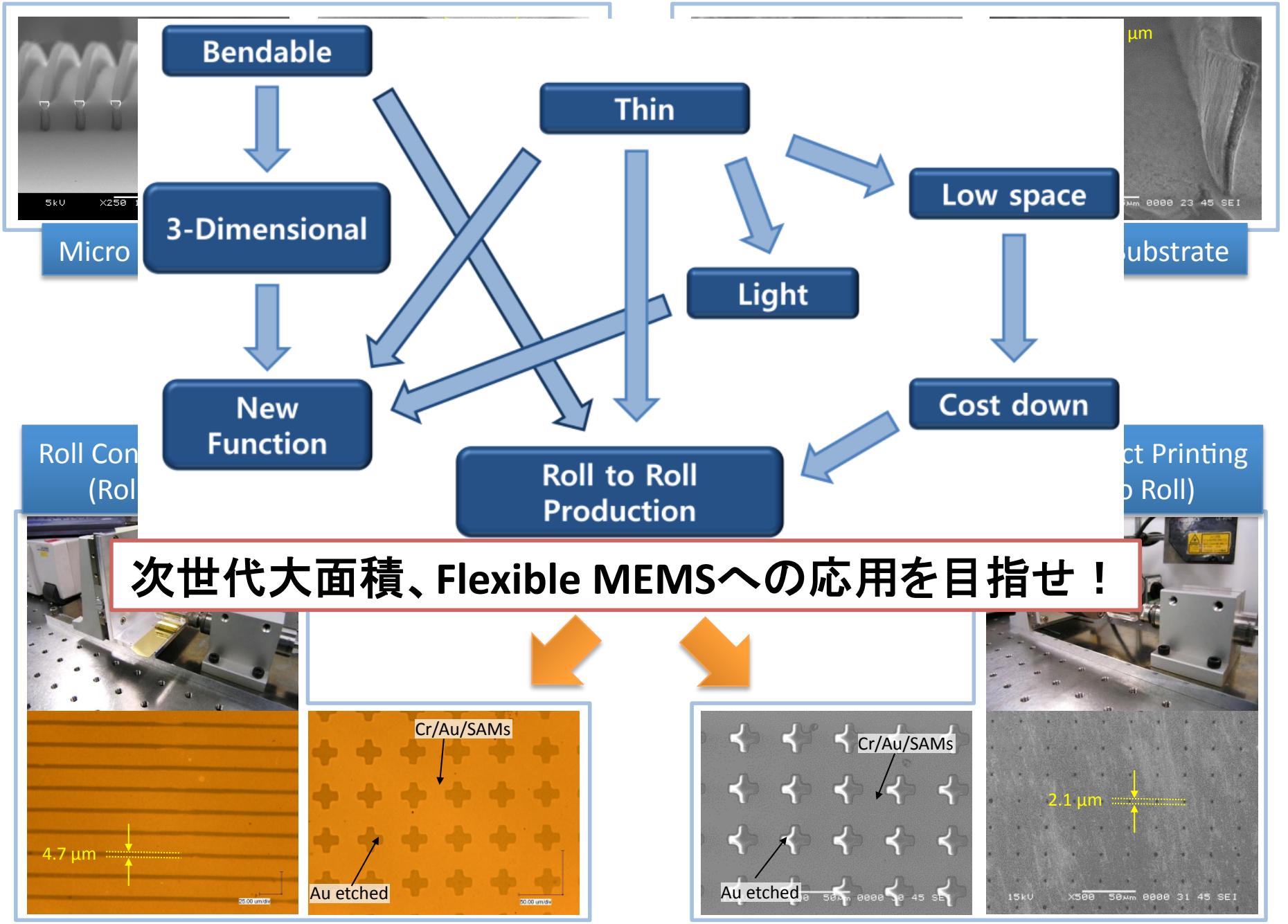
nicoat™ Coating
Film Attachment

(c) Flexible Photomask Wrapped on Substrate

(d) UV Exposure with Rotation & PR Development

(e) Micro Structures on Curved Substrate

Fabrication process for SU-8 structures on convex substrates


Bendable
Thin
3-Dimensional
Low space
Micro
Light
Substrate
New Function
Cost down
Roll Con
(Rol
Roll to Roll Production
ct Printing
o Roll)
次世代大面積、Flexible MEMSへの応用を目指せ！
4.7 µm
Cr/Au/SAMs
Au etched
Cr/Au/SAMs
Au etched
2.1 µm

GOAL: To achieve Low-cost, high performances
(high sensitivity, integrated functions, etc.) Bio-sensors

Nano wires :

1> Nanowire heater fast,local temperature control (bio-thermal appl.)

2> CMOS-compatible Si FET nanowire sensor (for biosensing)

3> Surface phonon polaritons heat transfer

Top down:

* Shadow mask patterning
n
D nano porous membranes

ottom up:

Micro/nano contact printing with SAM
liquid μCP and R2R micro CP
Optical soft-lithography for 3D micro pattern

2011 Journal list
J.Micromech. Microeng.
Lap on a Chip

Nano fabrication technology:
To develop unconventional Nano lithography & nano fabrications with low-cost, larger area even in 3D curved surfaces

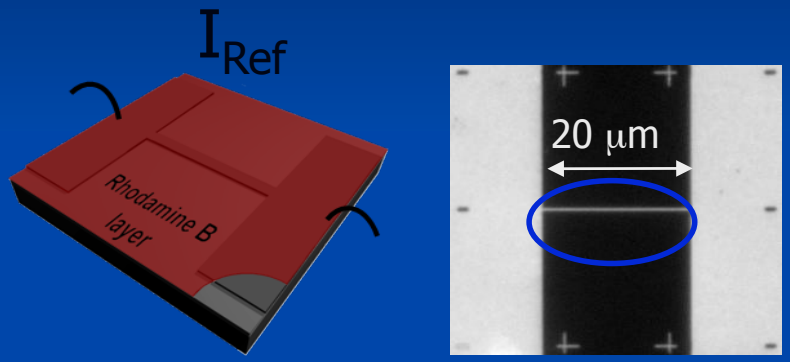
Peter Löw et al, ***Small*** (2008)

Previous work:

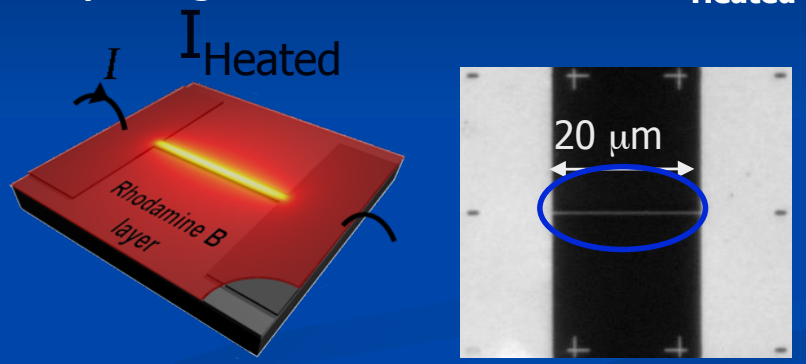
Temperature mapping with Ni nanowire & Rhodamine B

1. Capture fluorescent images:

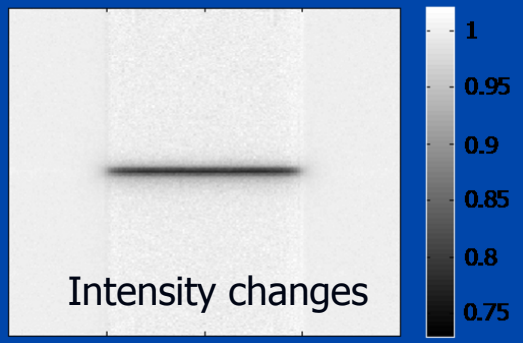
a) Reference image - $\mathbf{I_{Ref}}$

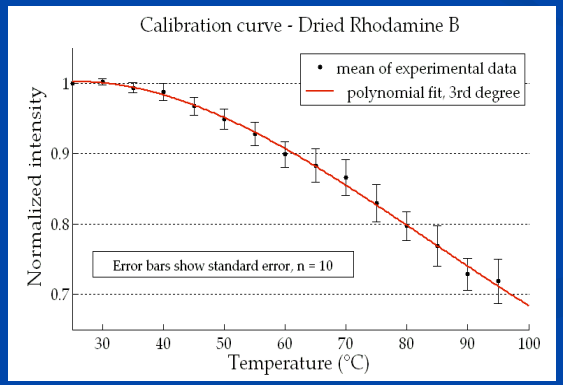


b) Image of heated structure - $\mathbf{I_{Heated}}$



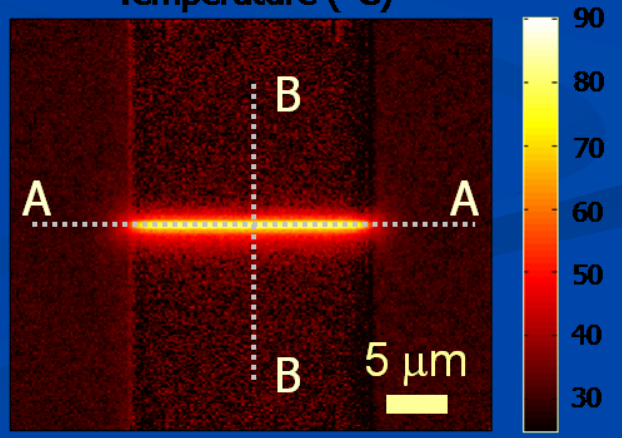
2. Normalization of intensity changes: $\mathbf{I_{Heated}/I_{Ref}}$





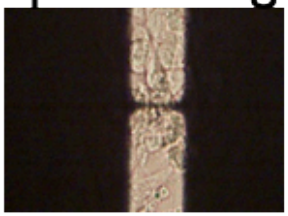
T (Intensity)

3. Conversion to temperature

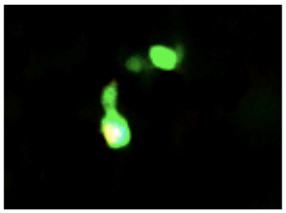


Cell heating and HSP-expression result

Optical image

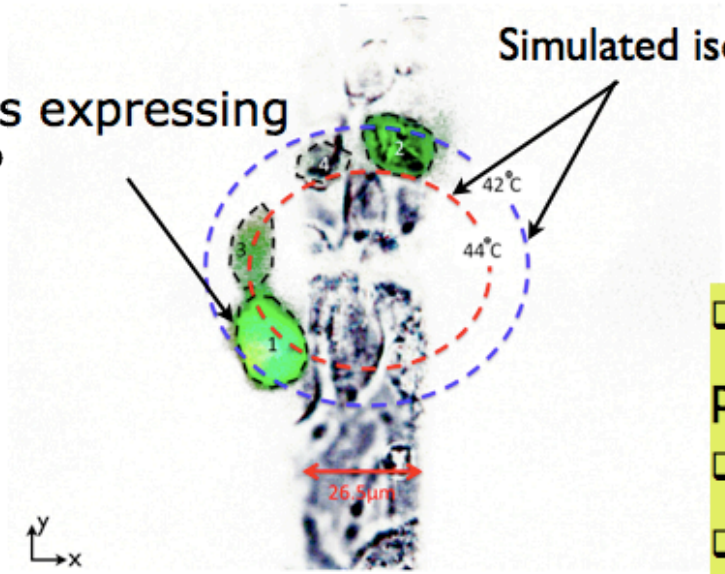


Fluorescence image

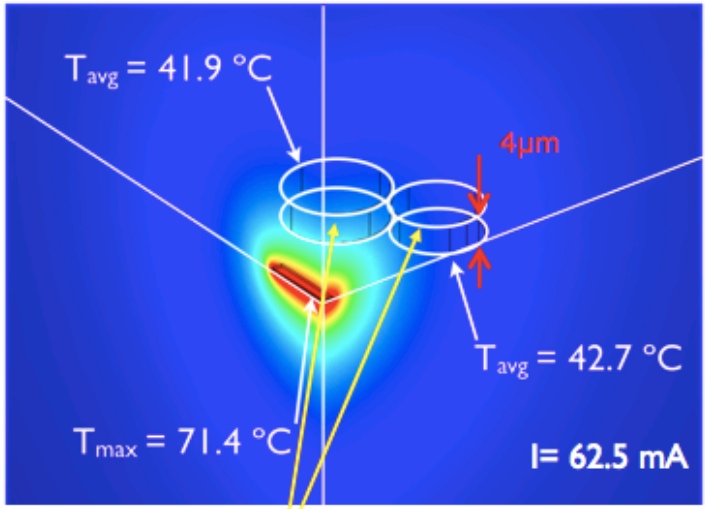


Cells expressing GFP

Simulated isotherms



Patrick et al. Lab Chip (2011)



Cell models at the same position as cells expressing GFP

- Heat-shock happened in a range **42-44°C** predictable from current literature
- Accuracy of our method : **±1°C**
- **High confinement** of heat-shock possible

Non-conventional fabrication of field-effect transistor silicon nanowire based label-free biosensors

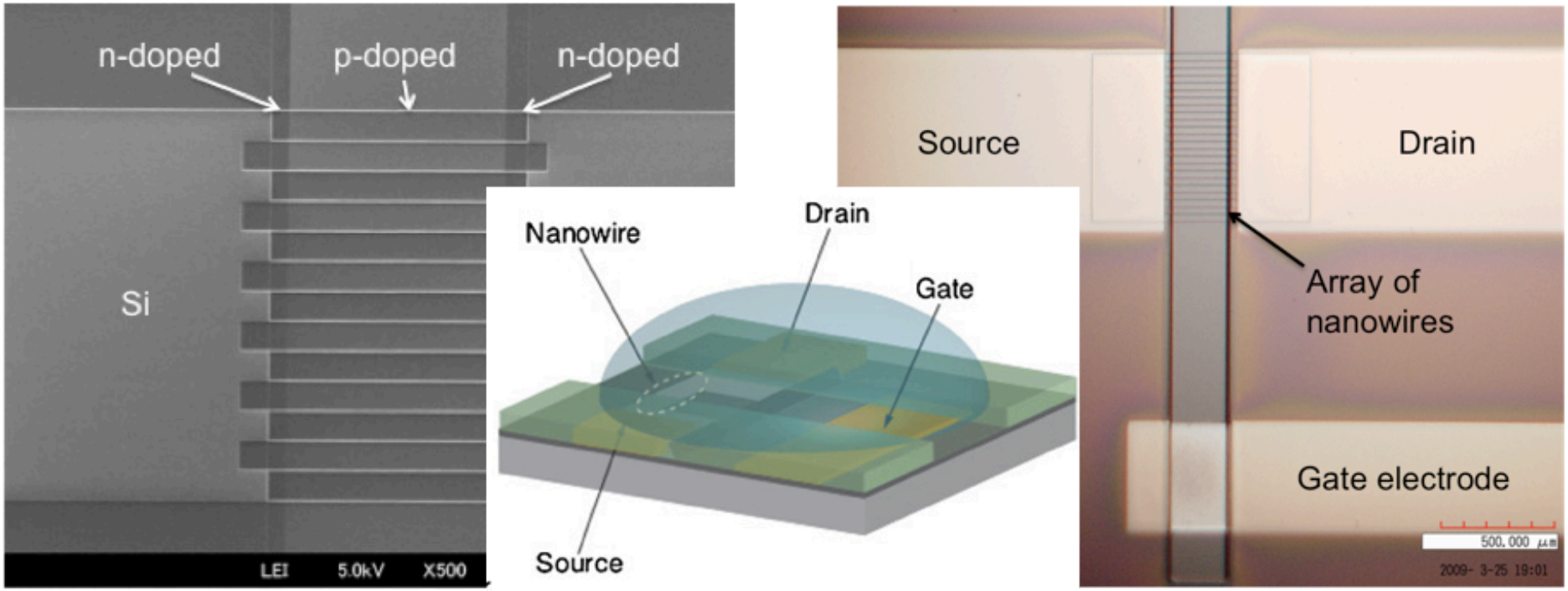
P. Ginet, S. Akiyama, H. Fujita and B.J. Kim
Institute of Industrial Science, The University of Tokyo

LIMMS
Laboratory for Integrated Micro-Mechatronic Systems
LIMMS/CNRS-IIS UMI 2820

INSTITUTE OF INDUSTRIAL SCIENCE · UNIVERSITY OF TOKYO ·

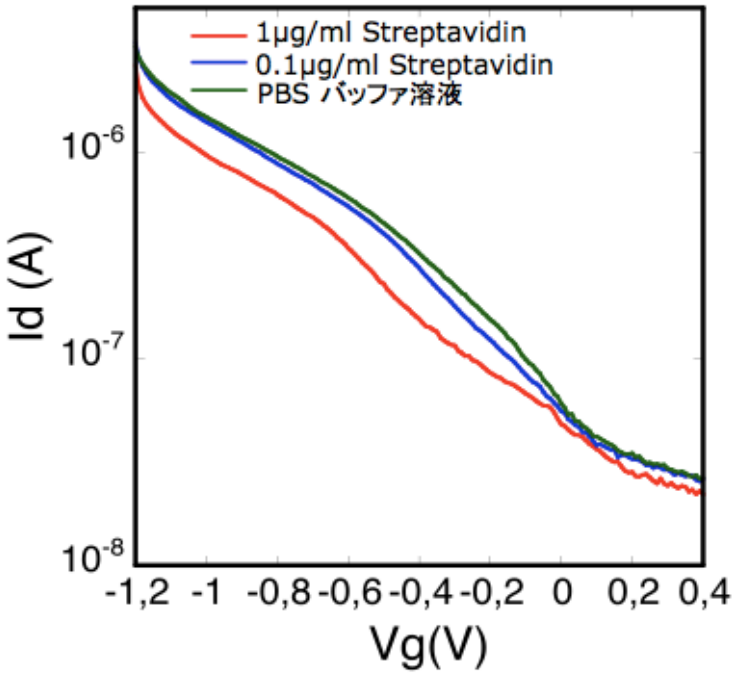
KIM Lab.

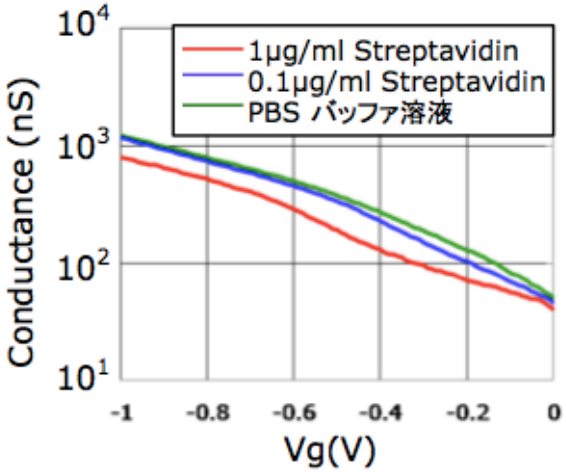
Silicon nanowires : FET functionalization



- A top-gate gold electrode is used to adress individually each NW array and to avoid the high voltages required for backside type gate electrodes

タンパク質のセンシング





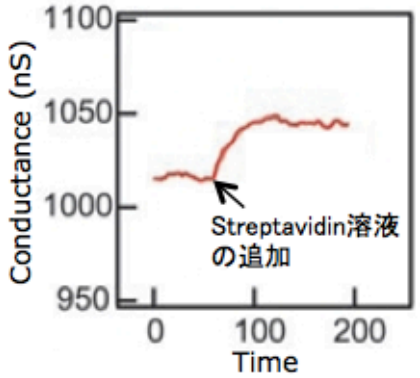
ゲート電圧－0.3V
⊿S/S=20%

ゲート電圧－1Vから0Vの範囲内
でタンパク質の検出が可能

- $pI_{streptavidin} > pH_{BHF\ 0.01x}$
- clear detection of streptavidin at 1μg/mL
- weak but reproducible detection at 0.1 μg/mL

他の研究例との比較

0.3ng/mL Streptavidinのセンシング

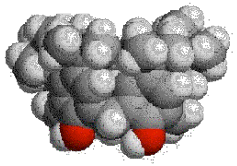


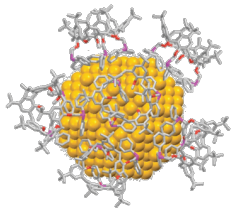
⊿S/S=3%

G. Zheng et al., *Nature biotechnology*, 2005

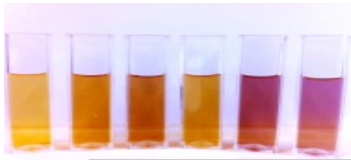
Real Hot Topics at this moment

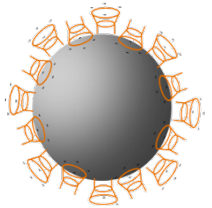
- Micro heaters chamber device→**Supramolecular interaction between biomolecules and calixerenes capped Silver nanoparticles**. Study of the mechanism of aggregation and the effect on the plasmonic resonance, nucleotides





Bulky calixarene ligands prevent gold nanoparticles from agglomerating yet leave much of the particles' metal surface accessible for small-molecule catalysis.



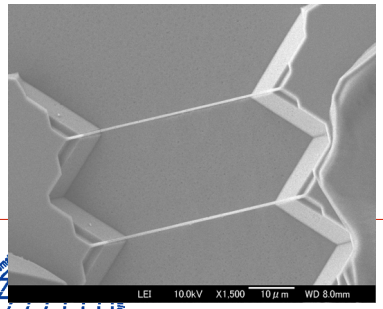


2011, ***Chemical Science,***
IEEE ***NEMS*** submitted

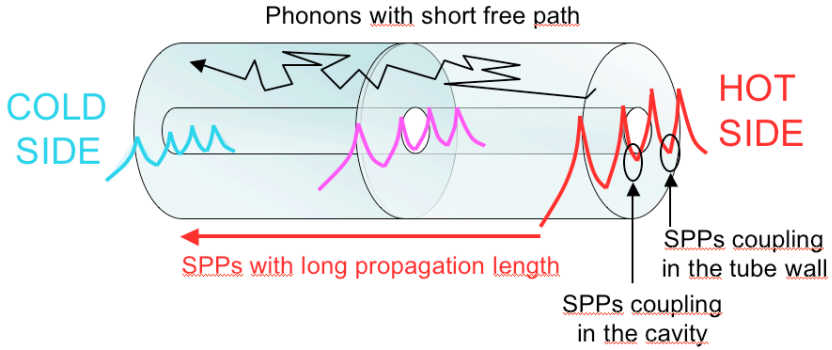
- New investigation of thermal conductance in nanostructures→

Surface phonon polaritons Heat transfer enhancement ?

abnormal heat conduction phenomena related to ballistic regimes of transport. Design by modeling a micro/nano structure that allows for strongly enhancing the coupling between SPPs. Experimental works to prove their contribution to heat conduction.



2010-2012, ***科研基盤B***



CIRMM/Institute of Industrial Science,

GOAL: To achieve Low-cost, high performances
(high sensitivity, integrated functions, etc.) Bio-sensors

Nano channel/fluidics :
1> Single DNA molecule's mobility investigation
2> Long DNA separation in nano fluidic devices

Nano wires :
1> Nanowire heater fast,local te
2> CMOS-compatible Si FET nanowir sensor (for biosensi
3> Surface phonon polaritons heat tra sfer

Top down:
* Shadow mask patterning
* Electro-spray deposition
* Electroplating with AAO nano porous membranes

ottom up:
Micro/nano contact printing with SAM
liquid μCP and R2R micro CP
Optical soft-lithography for 3D micro pattern

Nano fabrication technology:
To develop unconventional Nano lithography & nano fabrications with low-cost, larger area even in 3D curved surfaces

NOT Published YET

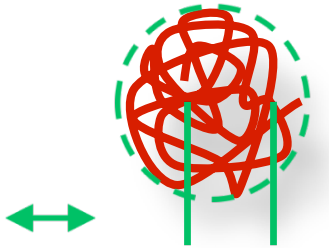
The 2nd stage ;

DNA electrophoresis under pressure gradient in nanoslit device

LONG DNA separation success!
- Length dependant mobility

'Shadow evaporation' to achieve the device scale to deform DNA.

Conventional UV lithography ***cannot easily fabricate the relevant scale*** for DNA confinement.



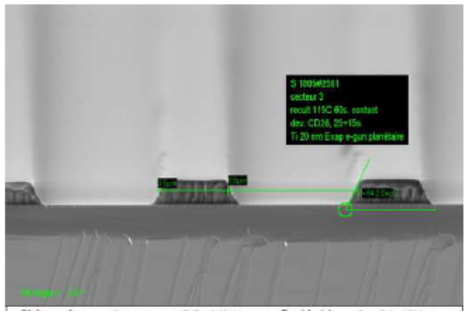
R_g

Radius of gyration

λ-DNA ; 0.69 ± 0.05 μm

T4-DNA ; 1.46 ± 0.2 μm

Sub-micrometer scale required



5 μm with UV lithography

metal evaporation with tilted angle ; θ

S1805 series ; ~ 500 nm high with trapezoidal profile

h; PR thickness

~ nanometer scale

; Silicon nitride

; Silicon

; Photoresist

; Metal

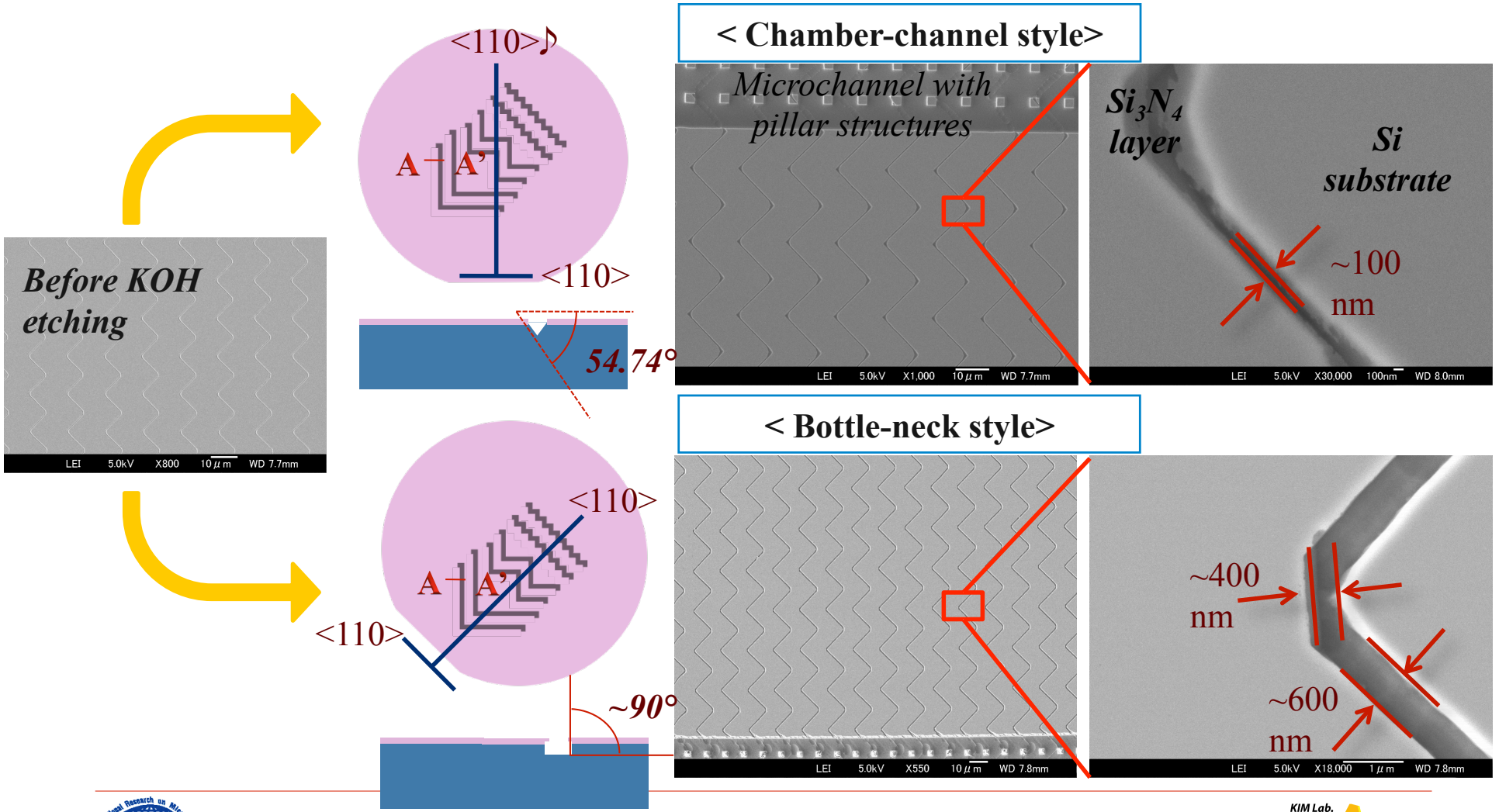
$g \sim h \cdot \tan\theta$

~ nanometer scale

From vertical nano to lateral nano

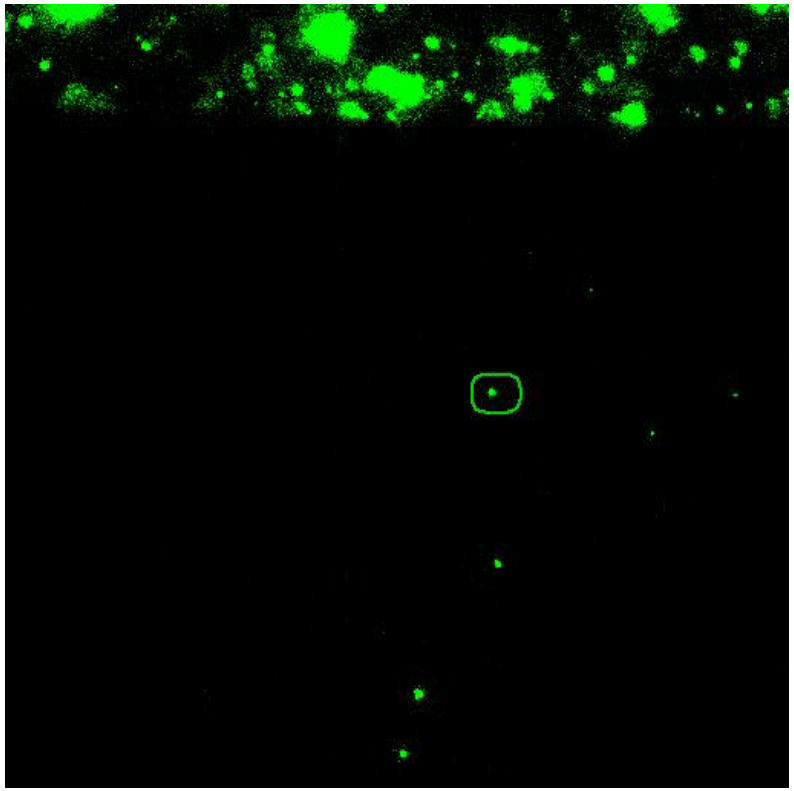
'Anisotropic etching' of zigzag pattern to achieve the repetitive deformation of DNA.

The alternating structure of wide and narrow parts can be fabricated by parallel at ONE TIME process.



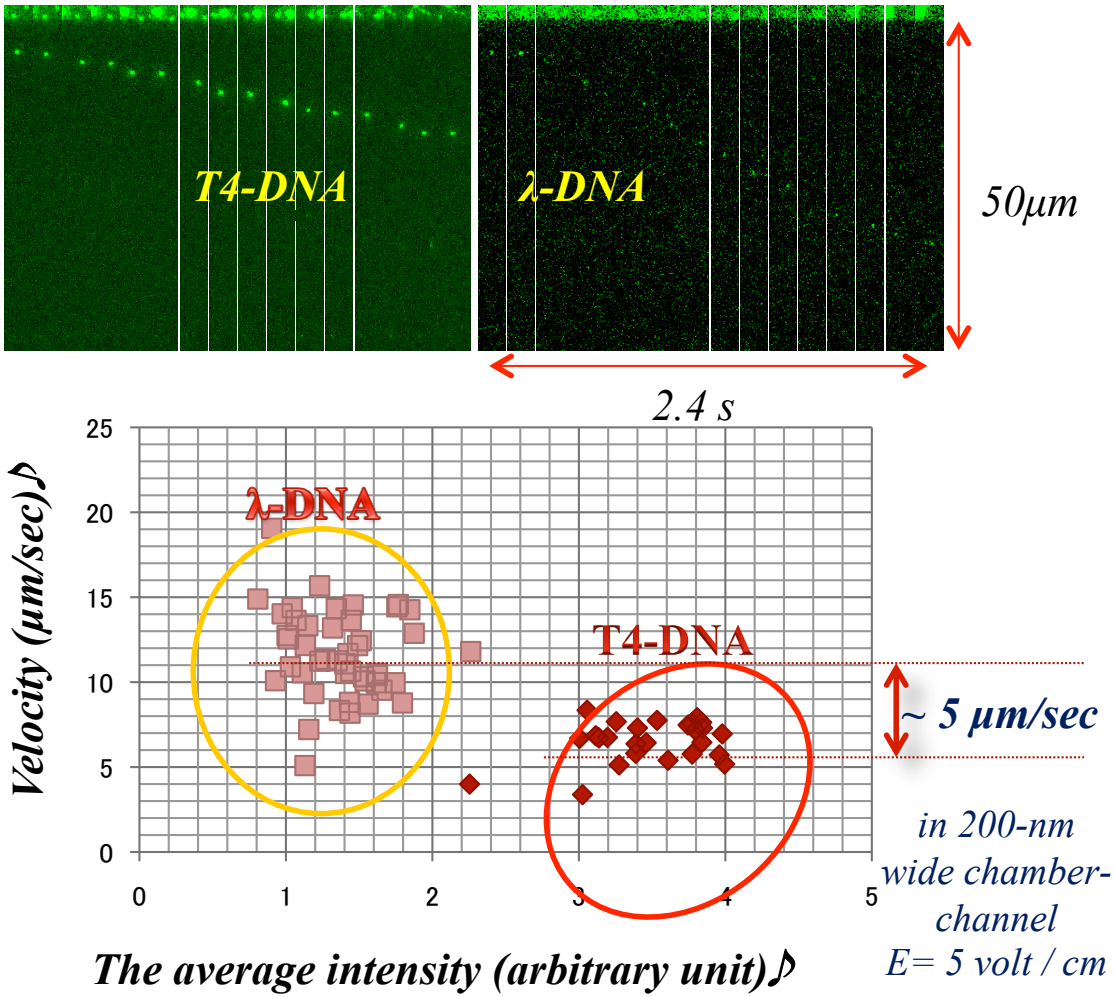
The length dependent mobility in chamber-channel type device

The large T4-DNA is slower than the small λ-DNA.



in 200-nm wide chamber-channel
E= 5 volt / cm

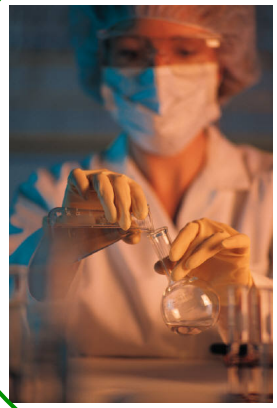
10 μm♪



in 200-nm wide chamber-channel
E= 5 volt / cm

B.J. Kim lab. (NEMS -> 将来のVision)

-Practical Point-of care & disposable bio-sensor chip (interface with electrical signals).
- “Chip in a Lab”-> Smart Portable “ Lap on a Chip”



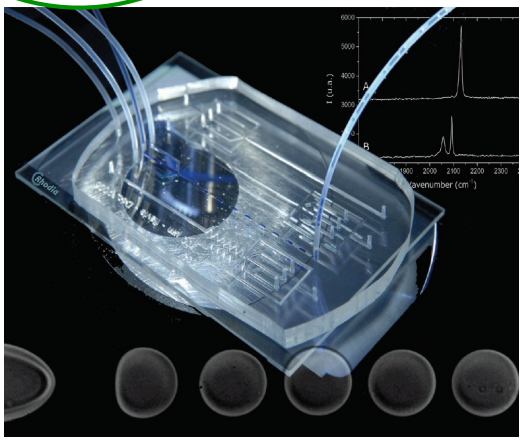
Lap

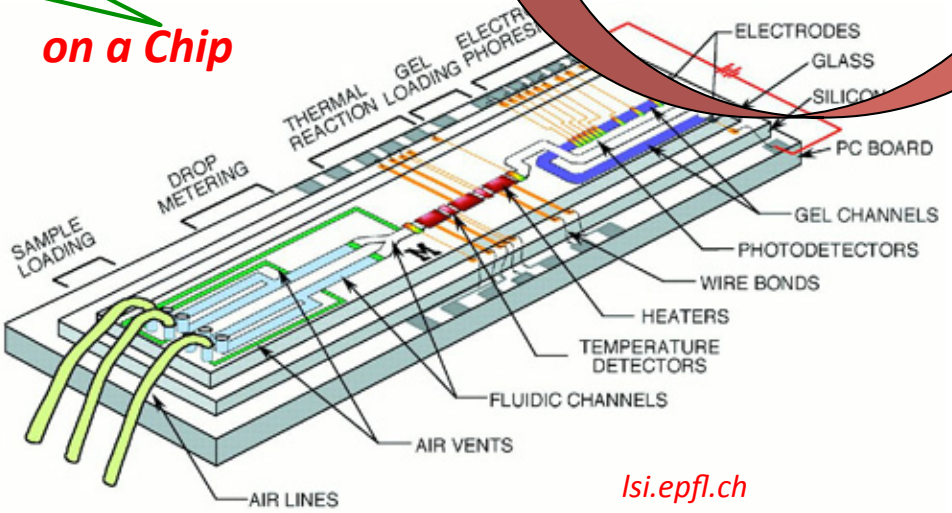
MEMS/NEMS for bio-applications?

Point of Care Portable Chip!

Chip in a Lab

on a Chip



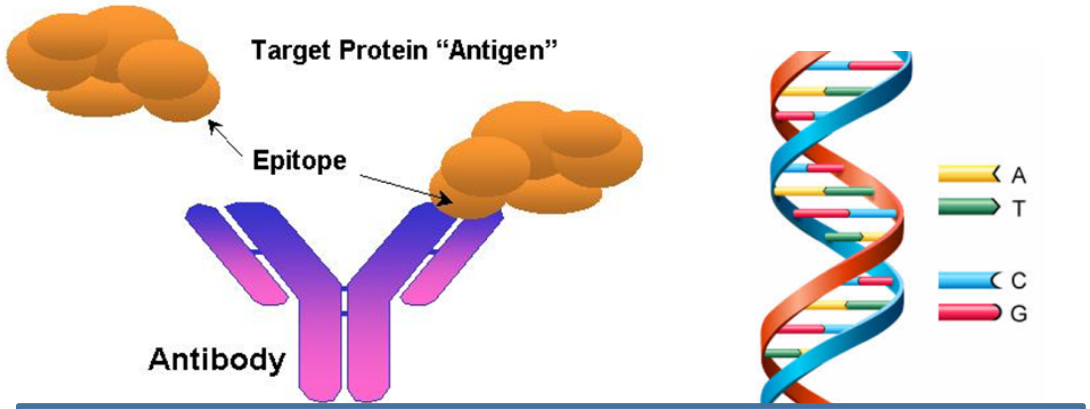


lsi.epfl.ch

Biosensors:

Needs: micro fludics
micro pump,
valves, etc.

Key: interface sensor



Enzyme, antibody, cell. DNA

Signal transducers
(electrical, optical, mechanical, etc.)

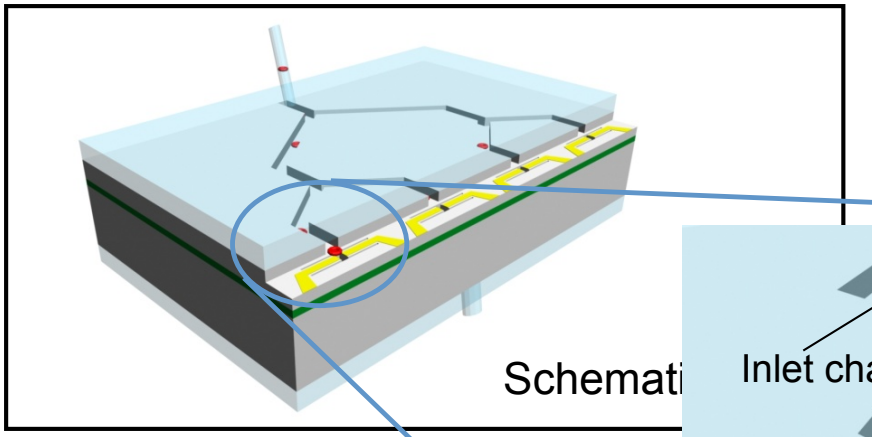
Electrical signal

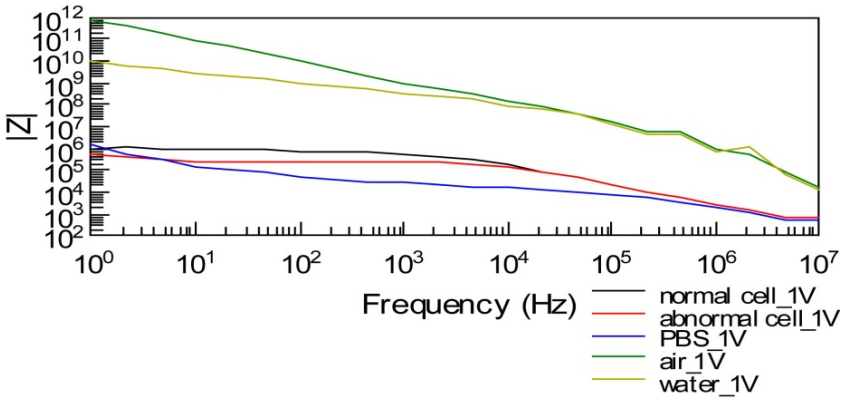
Label-free optical

1. Twin Microcantilever Type Sensor Arrays for electrical/physical characterization of single cell

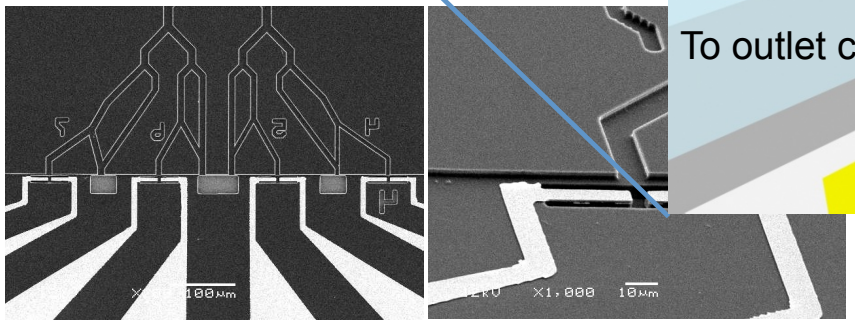
単一細胞（特に、赤血球）の電気・物理的特性を測るMEMSデバイスの開発

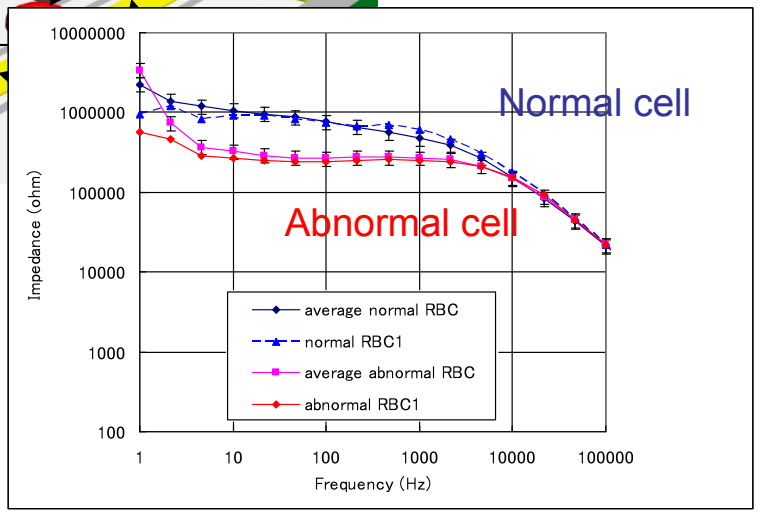
Y.H. Cho et al., ***J. of MEMS*** (2006)

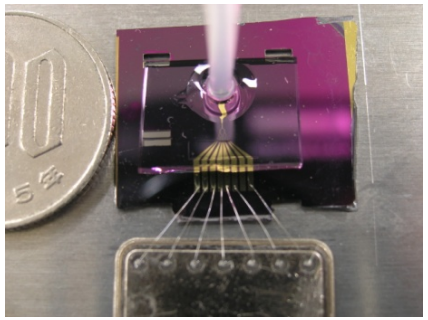




Impedance magnitudes of air, DI water, PBS, normal RBC, and abnormal RBC





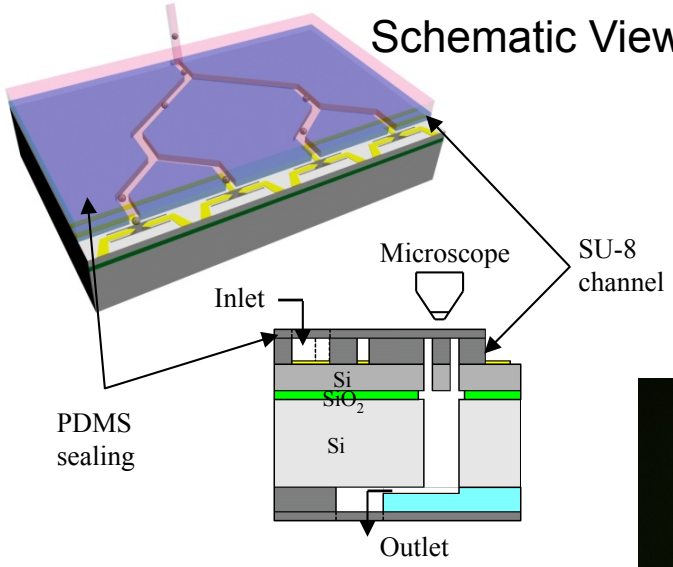


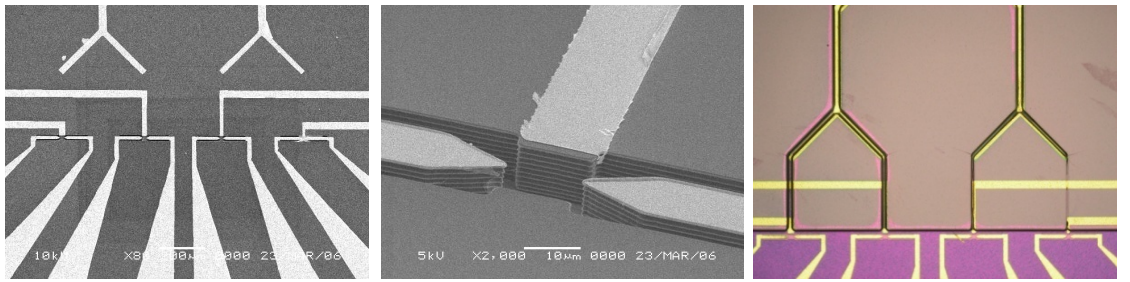
Fabrication Results

Average impedance value for normal and abnormal RBC through the same device (7 times/each cell)

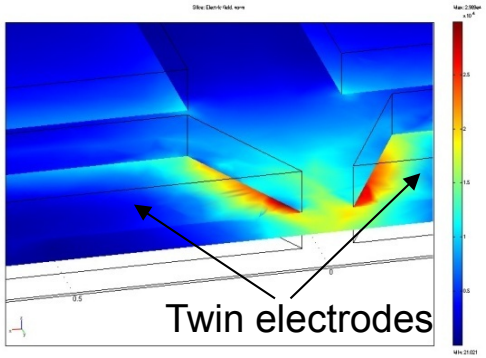
2. Single-cell Electroporation Microchip with Three Dimensional Si Microelectrodes for Gene Transfection

単一細胞のエレクトロポレーション用マイクロチップの開発と分析



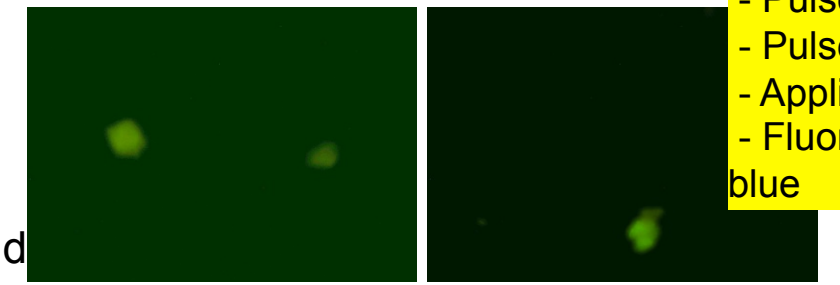


Fabrication Results



Simulation results of electric field around microcantilever electrodes
(Max≈ 3×10^4 V/m)

Expression of GFP after 24 hours



Expression of GFP after 44

◆ Experimental conditions
- Jurkat (T-lymphocyte) cells
- Waveform generator (Tabor Electronics Ltd.)
- Pulse duration: 100 ms
- Pulse period: 1 ms
- Pulse sequence: 10 times
- Applied voltage: 0.7
- Fluorescence: GFP, trypan blue

Y.H. Cho et al., ***Transducers '07 - Lyon***