
Advanced 10 Robotics Applications based on Micro-Nano fabrications

Prof. F. Arai

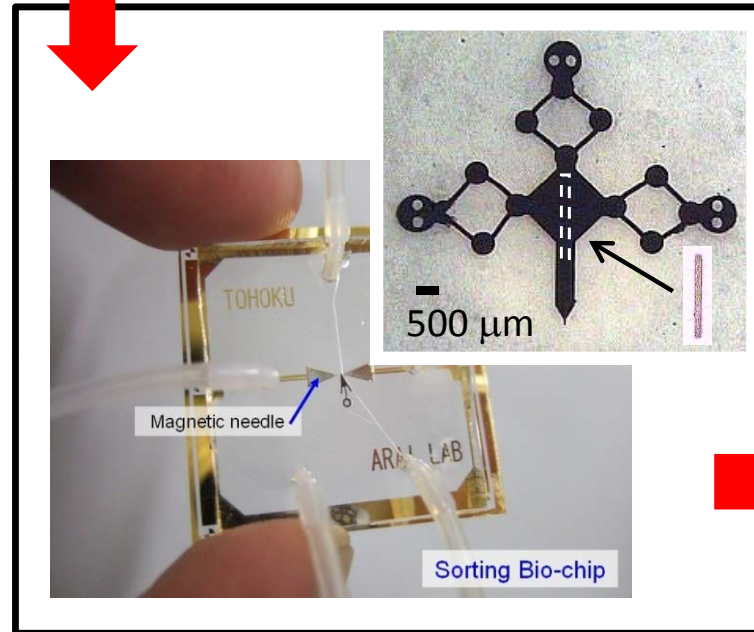
Dept. of Mechanical Engineering Science
Nagoya University



Role of On-chip Technology

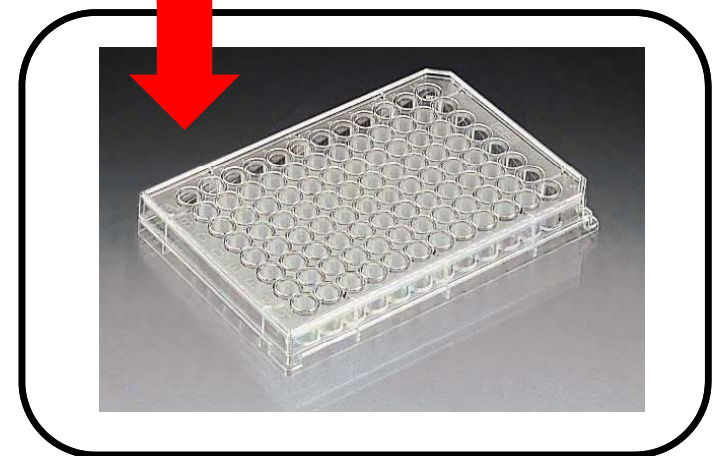


Sample



Robot-on-a-chip

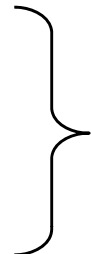
Clone sorting
Dispensing



Cell culture plate

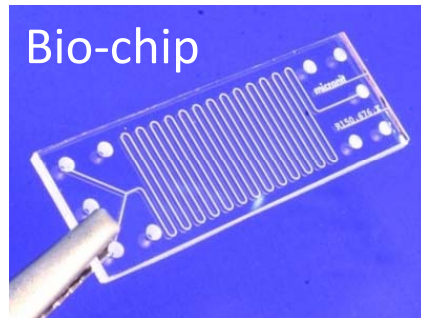
Physical/chemical interaction

- Inside cell
- Between cells
- Cell-environment



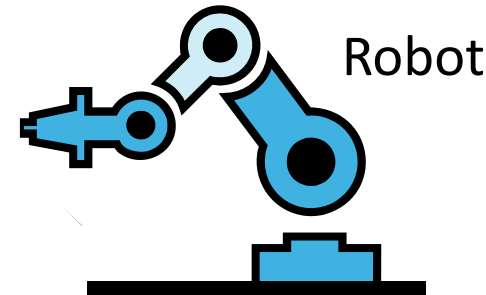
- Measure response
- Clarify functions
- Model dynamics

Robot-on-a-Chip (Robochip)



Bio-chip

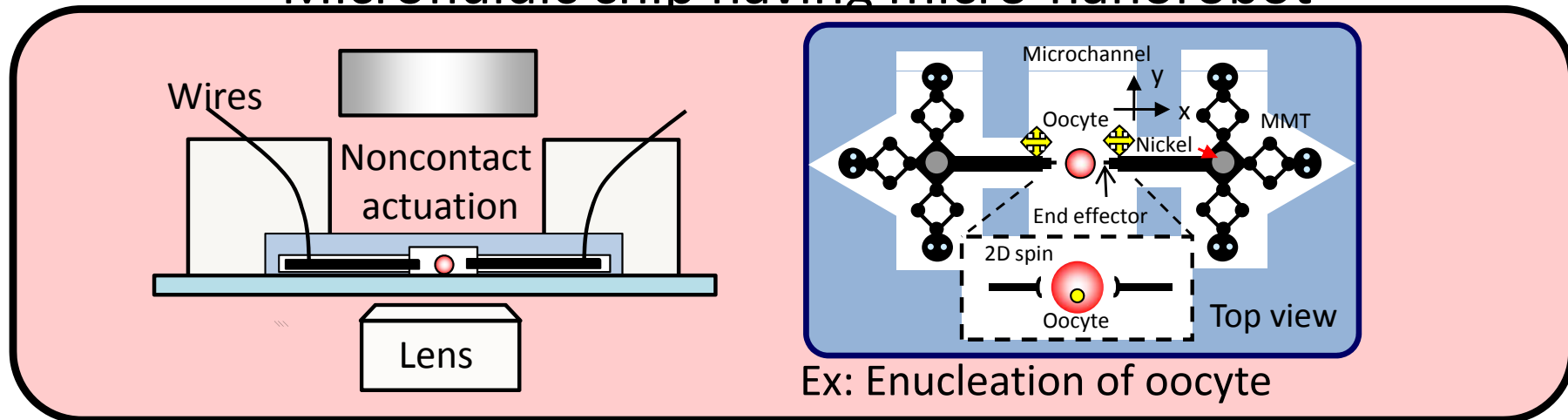
+



Robot

Environment
Microfluidic chip having micro-nanorobot

For mechanical interaction

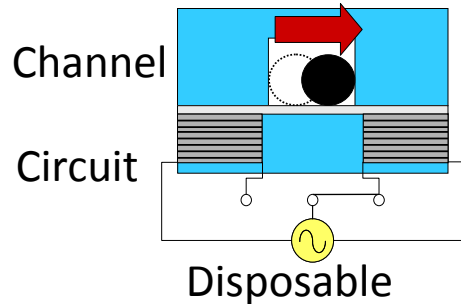


Target: single-cell based measurement, analysis, cloning and anatomical manipulation, etc.

Microrobot (Microtool) ⇒ Precise & Arbitrarily Shape

Transition of Micro-robot (Microtool)

Magnetic actuators



μN , mN order

2004



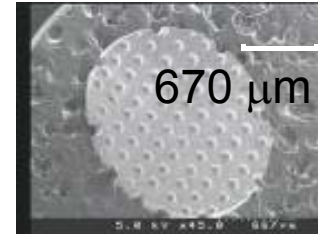
Wire

2006



Molding, photolitho. Low friction, flexibility

2007

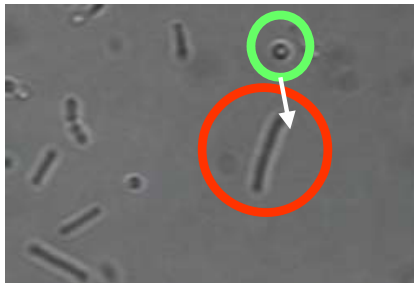


1. Multi-function
2. **Arbitrarily-shaped**
3. Multiple DOF

Optical tweezers

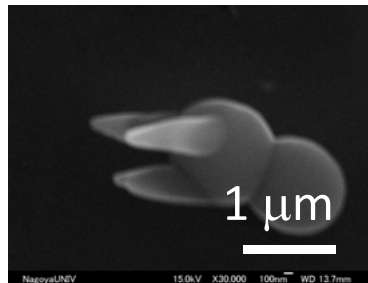
pN order

1999



Victims: bacillus
(rod-shaped bacteria)

2001



Microtool by
3D nanofabrication

2002



Trajectory control
SLM

2004



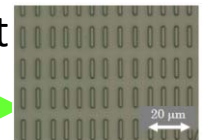
Photolithography

3D-6DOF

2006

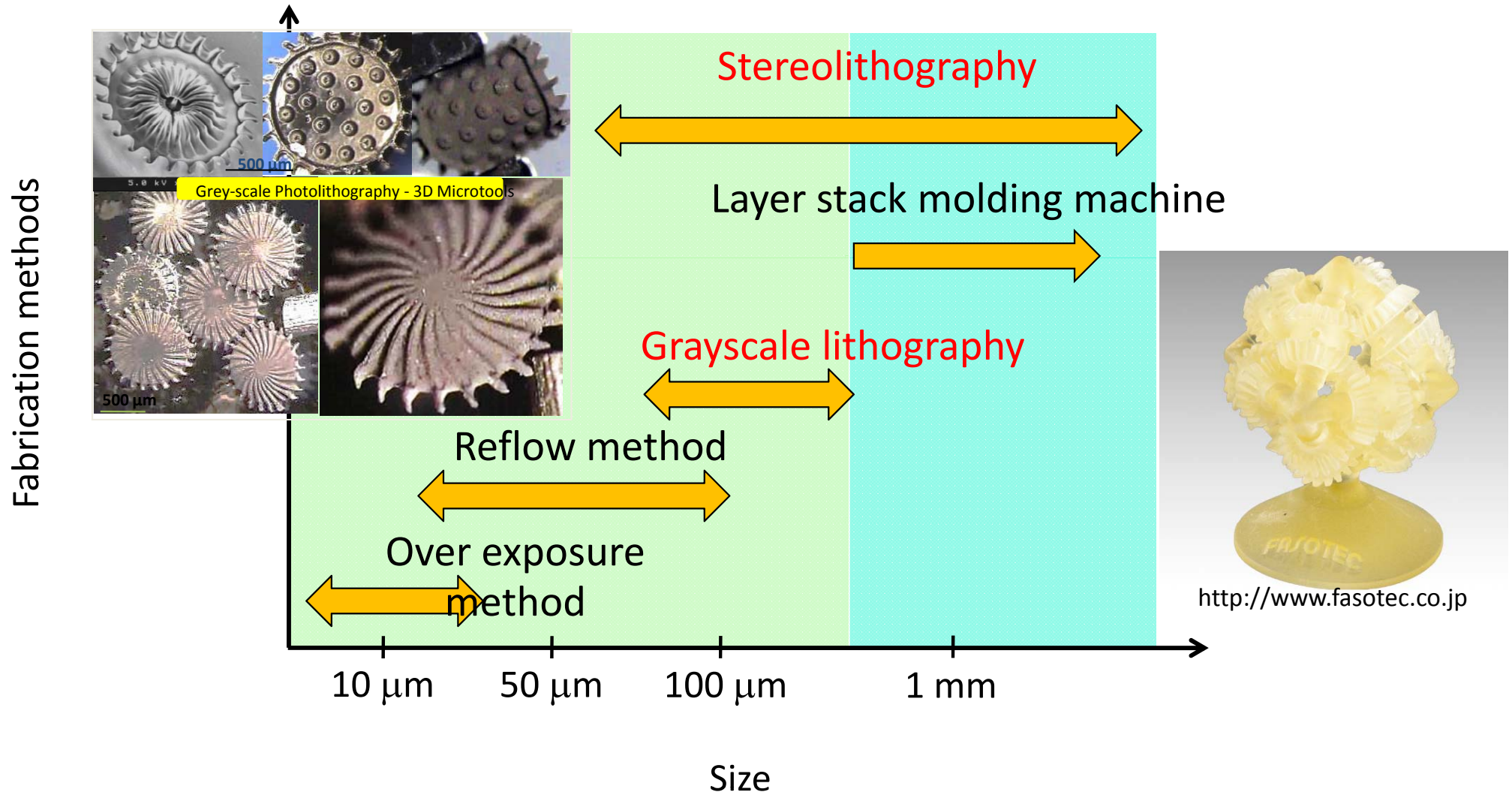


1. Multi-function
2. **Arbitrarily-shaped**
3. Multiple DOF



Classifications of Multi-scale Fabrications

Multi-scale Fabrication methods $\phi 10 - 500 \mu\text{m}$



Yamanishi et. al. JMEMS, Vol.19(2), p.350-357, (2010).



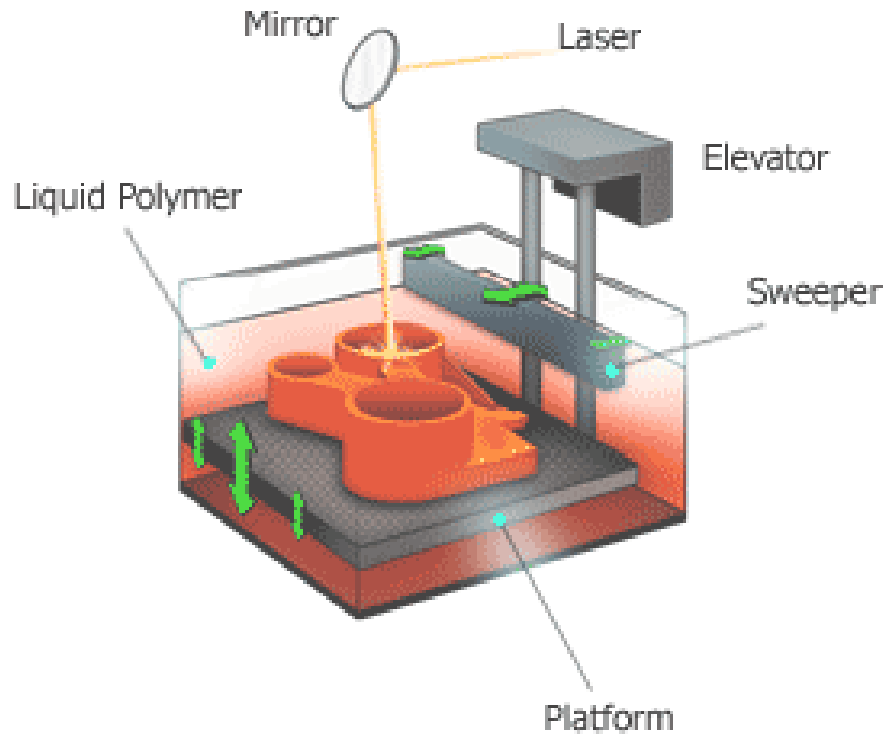
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StereoLithography



StereoLithography



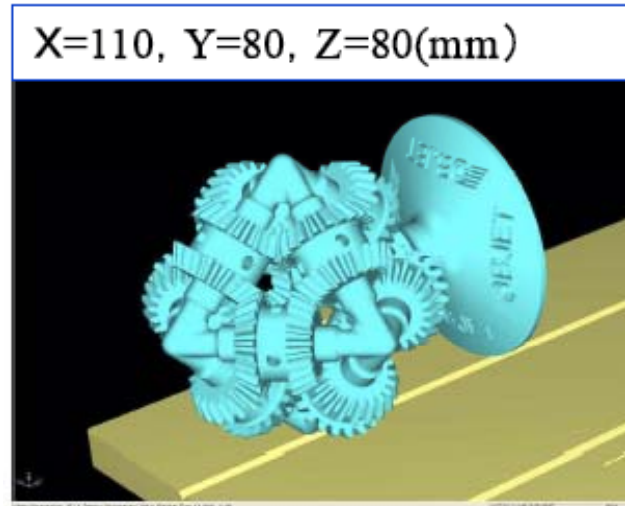
<http://stereolithography.com>

- 3D Systems, Valencia, CA
- patent 1986, beginning of RP
- photopolymerization using UV laser
- epoxies, acrylates (brittle)
- excellent accuracy $< 30 \mu\text{m}$
- relatively slow
- ¥2,000(cm^3)

StereoLithography



EDEN 250 (FASOTEC)



Model Material; 421 g
Support Material; 364 g
Forming Time; 12 h
Post-Processing Time
; 30min

3D Printing

- ZCorpSanders Prototype Inc., NH
- ink jet technology
- dual heads deposit part material (thermoplastic) and support material (wax)
- build layers as thin as 5 μm
- very fast and cheap process

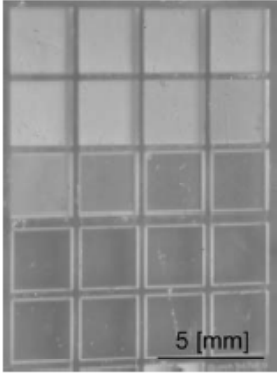
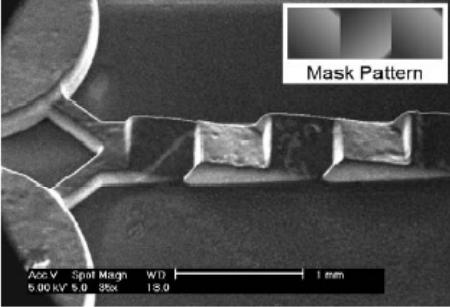
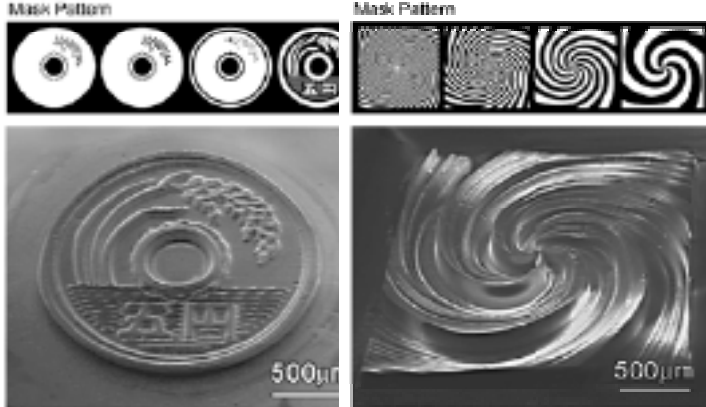


Gray-Scale Lithography

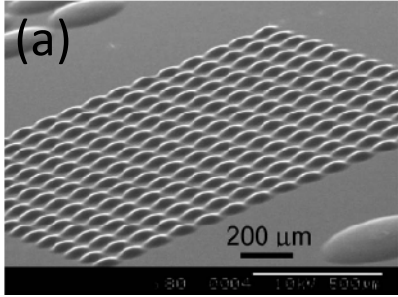
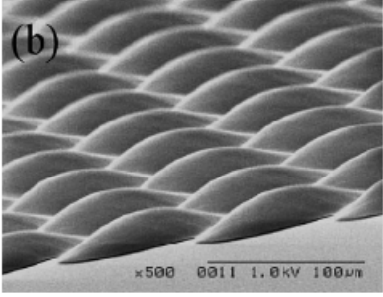
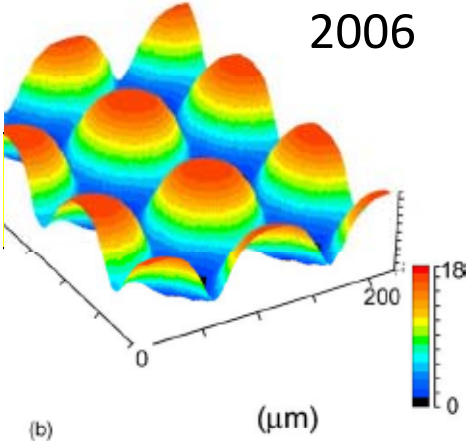


Background (Gray-scale Photolithography)

Prof. Matsumoto (Keio University): 1/20 Mask Reduction Method

2003	2004	2005
		
<p>HF Glass Etching <i>T.IEEE Japan, Vol.123(11), p.499-503, 2003</i></p>	<p>Sloped SU-8 +Back-side Exposure <i>T.IEEE Japan, Vol.124(10), p.359-363, 2004</i></p>	<p>Binary Optics <i>T.IEEE Japan, Vol.125(10), p.424-425, 2005</i></p>

Prof. Totsu (Esashi-Lab, Tohoku University): Maskless Exposure Method

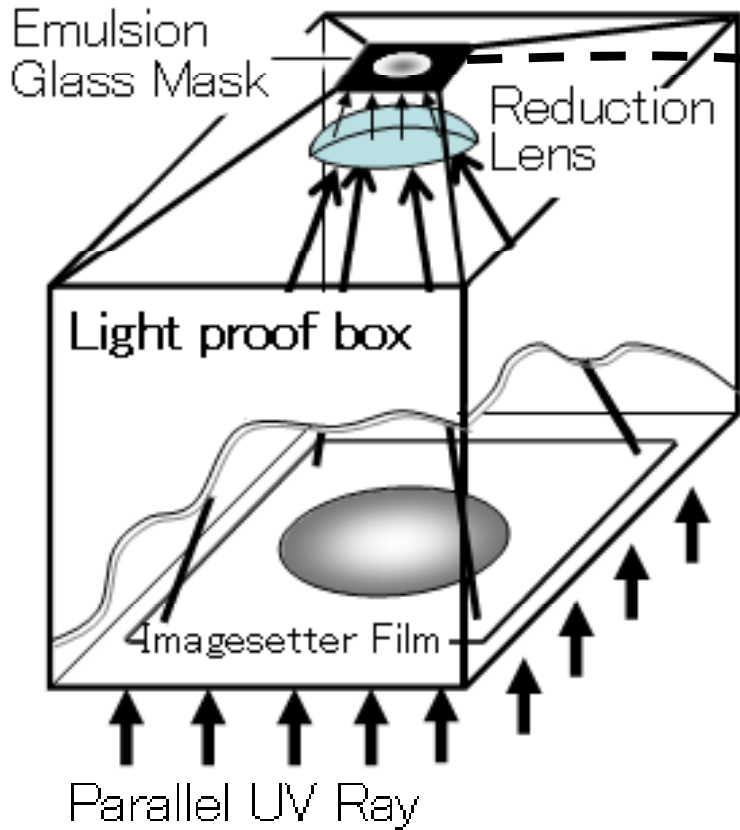
<p>1. Lens 2. Optics 3. Soft Lithography for Bio-analysis</p>	2005	2006
		
<p>Maskless Grey-scale <i>Sensors and Actuators A 130-131, p. 387-392, 2006</i></p>		

Gray-Scale Lithography (1/20 Mask Reduction Method)

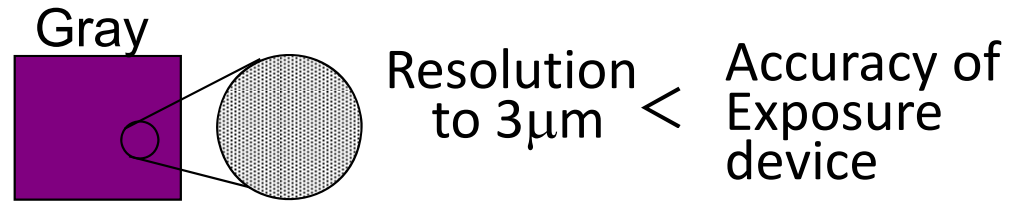


Background (1/20 Reduction Mask Method)

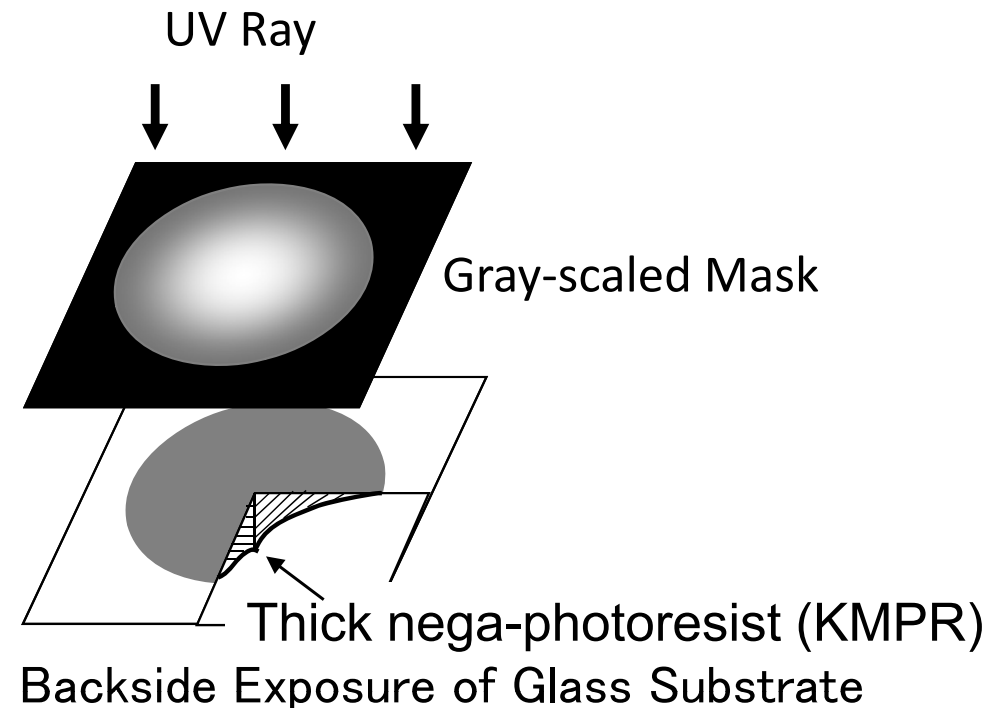
< Production of Gray-Glass Mask by 1/20 Reduction >



Gray(=Aggregate of black and white dots)



Exposure and Development



Produced Gray-emulsion gray mask

Theory of Gray Scale Photolithography

Theory of Lambert Beer

E_0 [mJ/cm²]: Energy of Radiation on the unit surface area of liquid resist

Exponentially Decreased

$$E(z) = E_0 \times \exp(-z/D)$$

Amount of Exposure at the Resist Depth Z

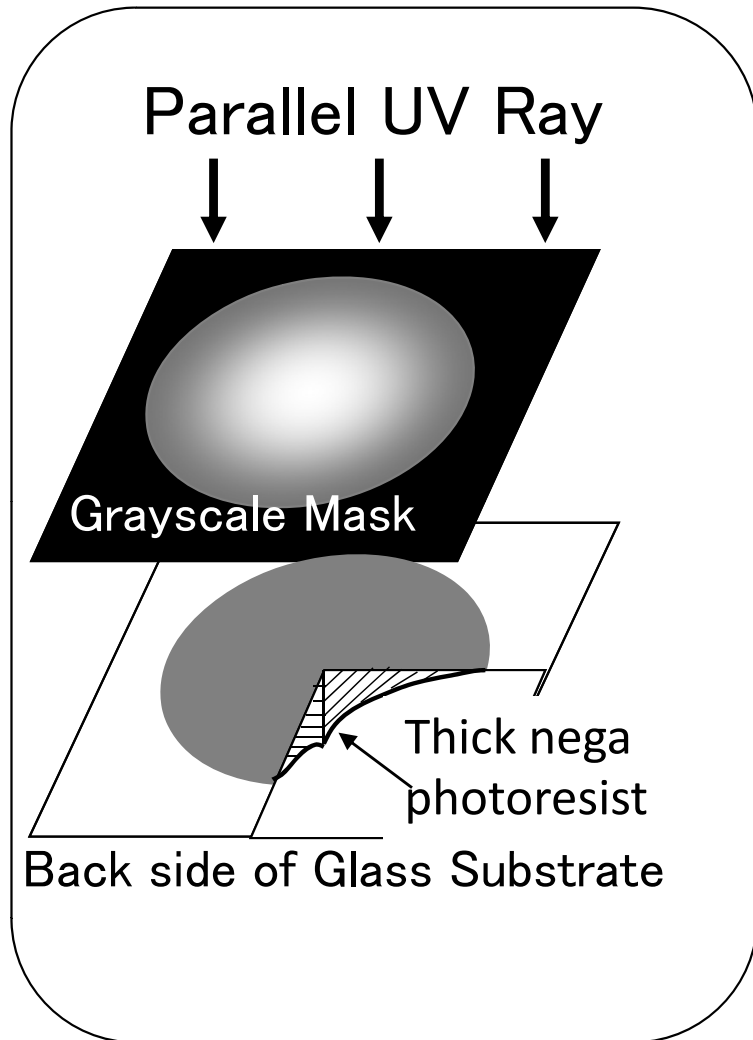
Depth of Resist

The Transparent Depth [mm] of 1/e of Intensity of UV light Radiated on the surface of resist

$$E_c = E_0 \times \exp(-G_d / D)$$

Critical Amount of Exposure Until the Curing of the Liquid Resist

$$G_d = D \times \ln(E_0 / E_c)$$



The relationship between Amount of Exposure E_0 and the Depth of Cured Resist G_d [mm]

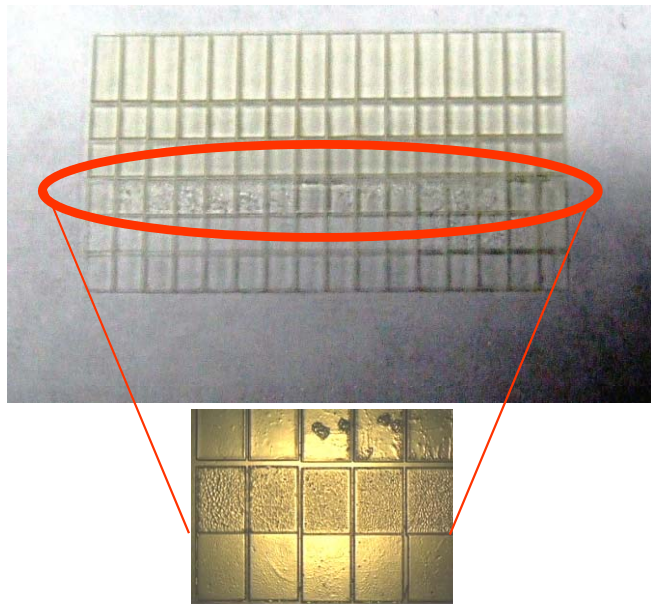
Calibration of Grayscale Photolithography

The Cured Depth G_d [mm] of KMPR at a given amount of exposure E_0 [mJ/cm²] at the critical amount of exposure E_c [mJ/cm²]:

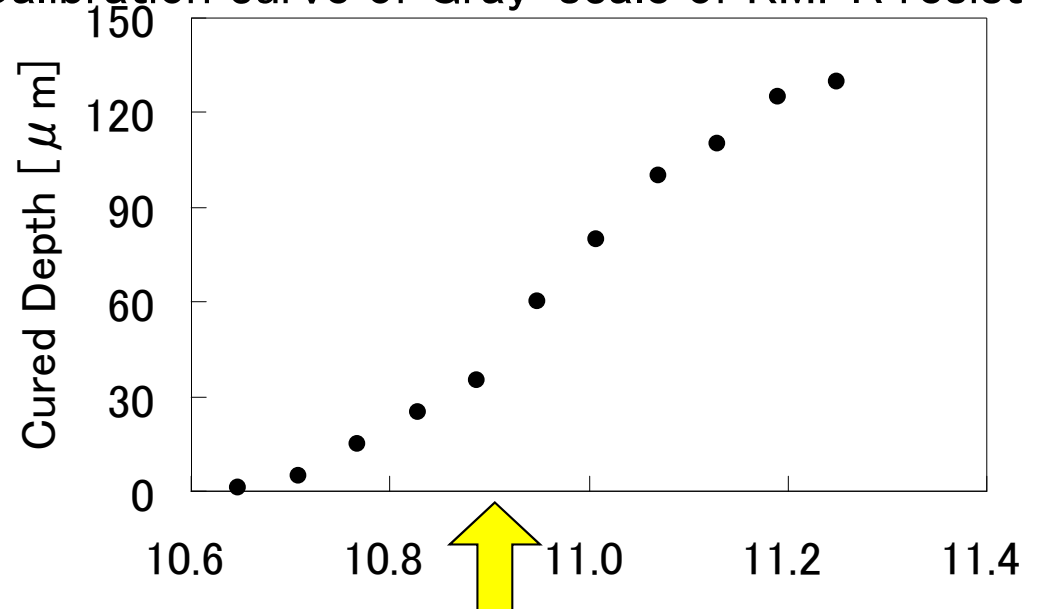
<Theory of Lambert-beer>

$$\begin{cases} E_c = E_0 \times \exp(-G_d / D) \\ G_d = D \times \ln(E_0 / E_c) \end{cases}$$

Depth of penetration when the Intensity of UV become 1/e of surface of resist



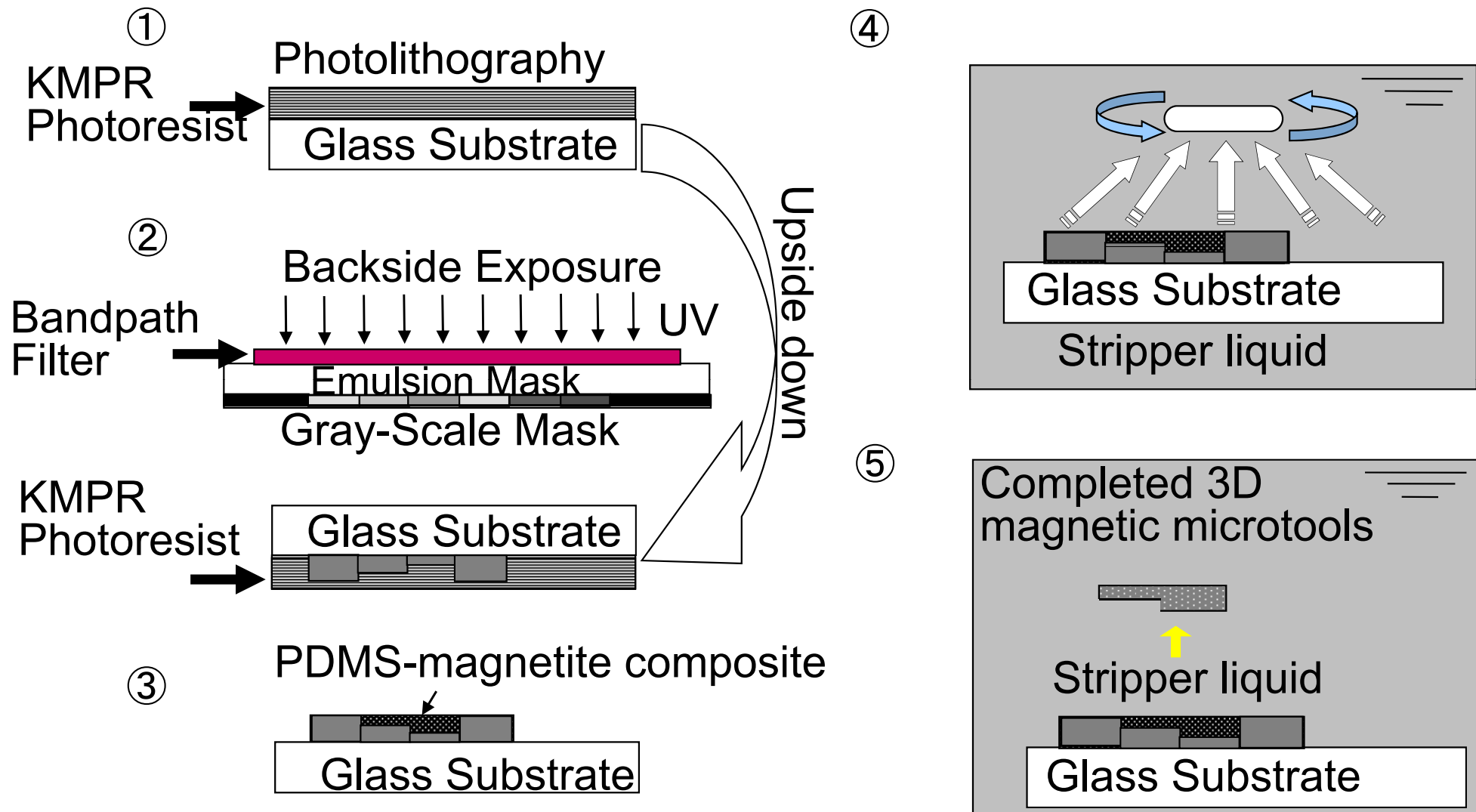
Calibration curve of Gray-scale of KMPR resist



Sudden change of thick negative photoresist of KMPR in the range of 70-75% of Gray-scale

Calculated UV lamp Power [mW/cm²]
Recalculation of the UV lamp power corresponding to the Grey Scale of 70-75%

Fabrication Method of 3D-Microtool



Yamanishi et. al. *JMEMS*, Vol.19(2), p.350-357, (2010).

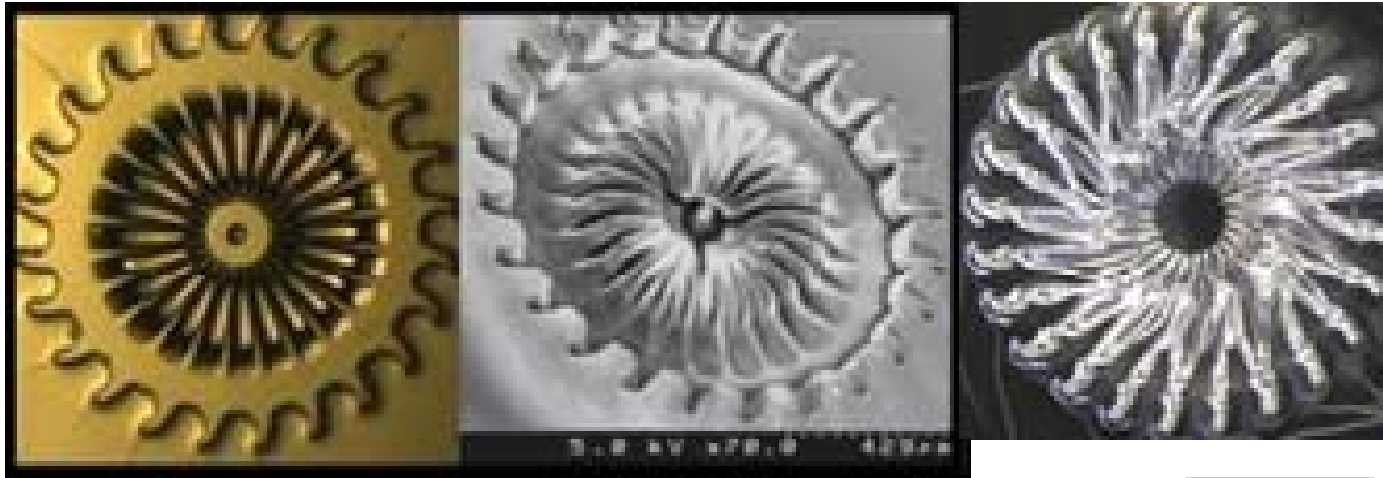
MMT : Magnetically Driven Microtool



Fabricated 3D-MMT

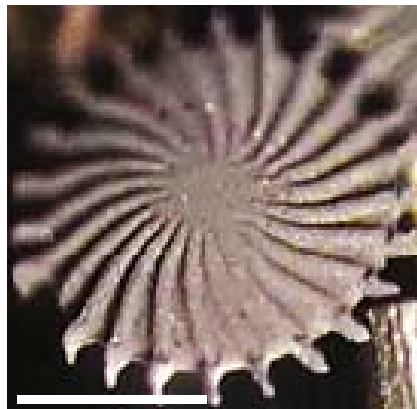
- Gray-scale pattern of KMPR for molding

Yamanishi et. al. JMEMS, Vol.19(2), p.350-357, (2010).



500 μm

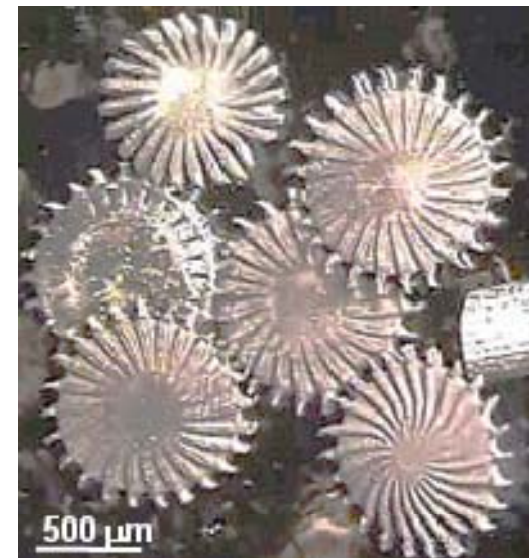
- 3D-MMT after production



500 μm



500 μm

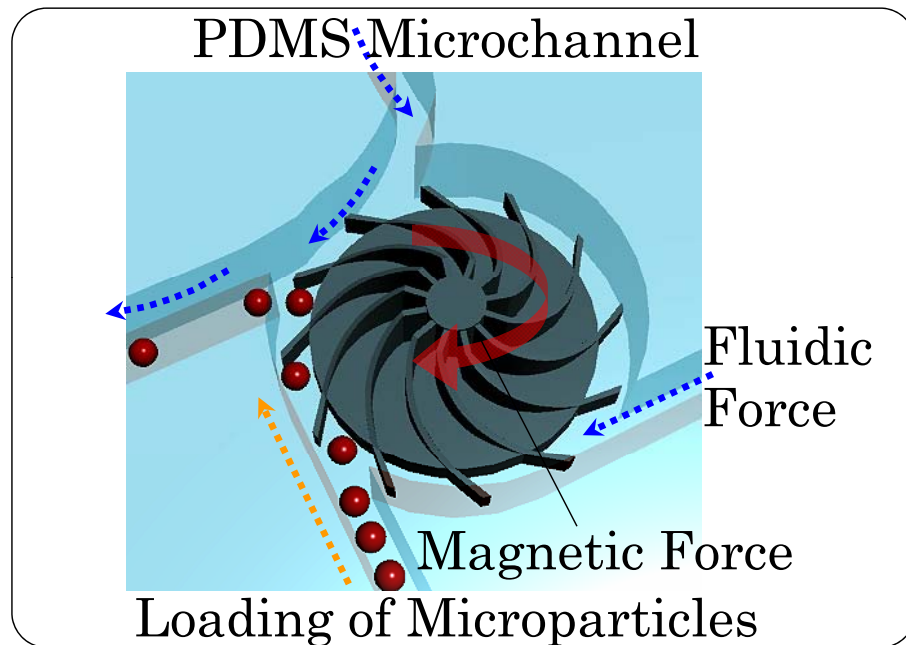


500 μm

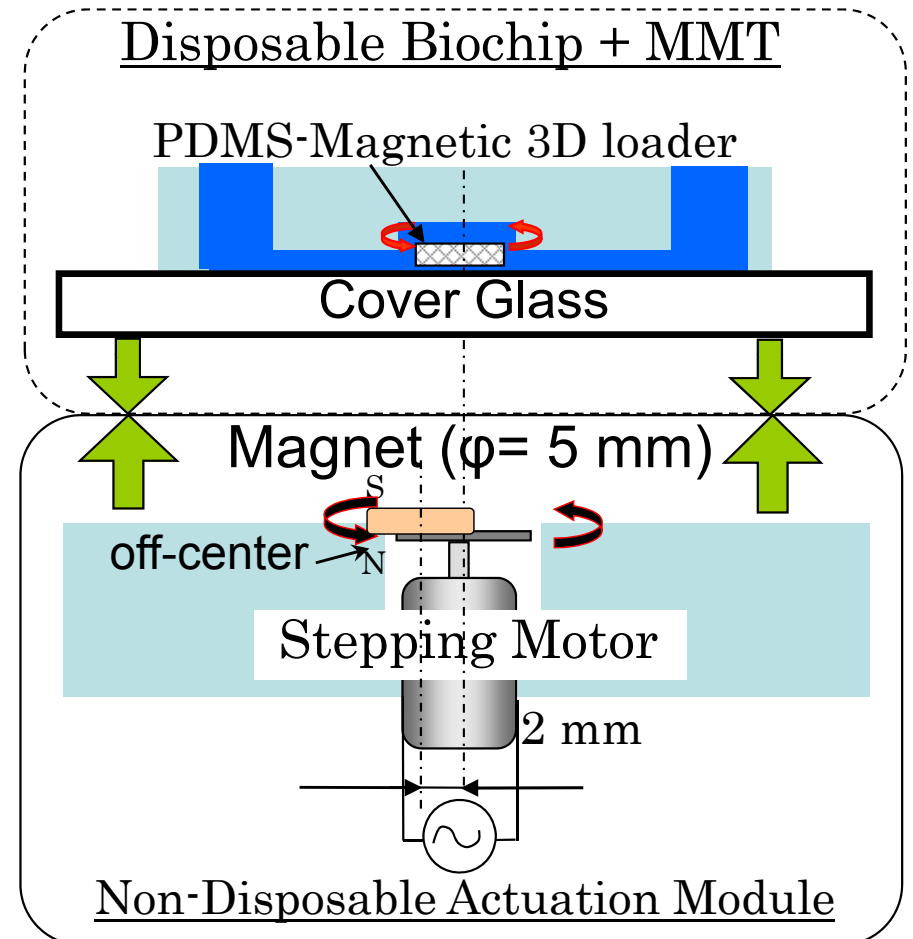
* The gap of height ≈ 110 mm

Application of 3D-MMT

- Particle Loader with External Magnetic Field



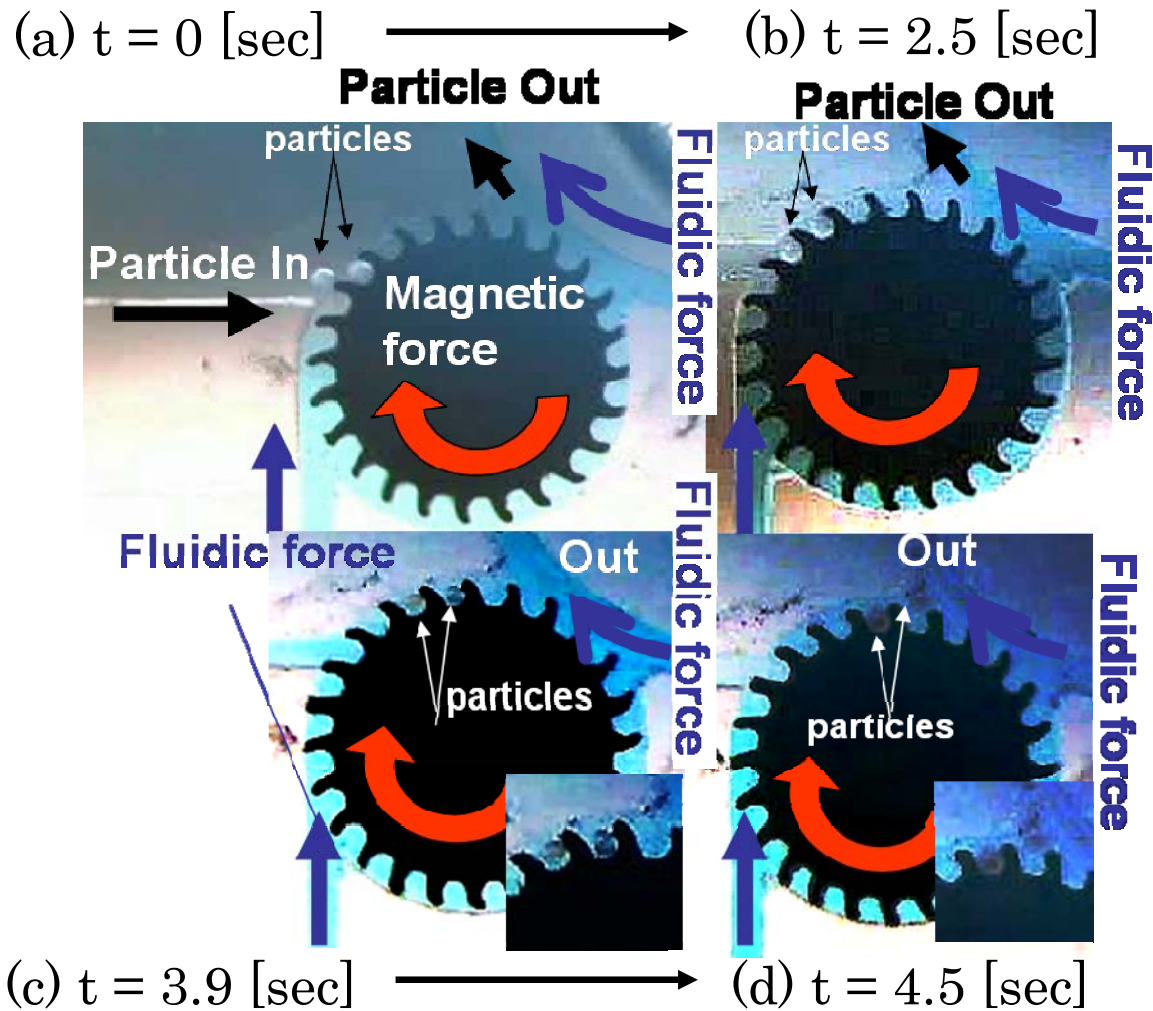
Combination of
Magnetic and Fluidic Force



Yamanishi et. al. JMEMS, Vol.19(2), p.350-357, (2010).



Operation of 3D-MMT Loader



【Microloader】



200 μm

3D-MMT could load particles one by one successfully

Yamanishi et. al. JMEMS, Vol.19(2), p.350-357, (2010).



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Gray-Scale Lithography (Maskless Exposure Method)

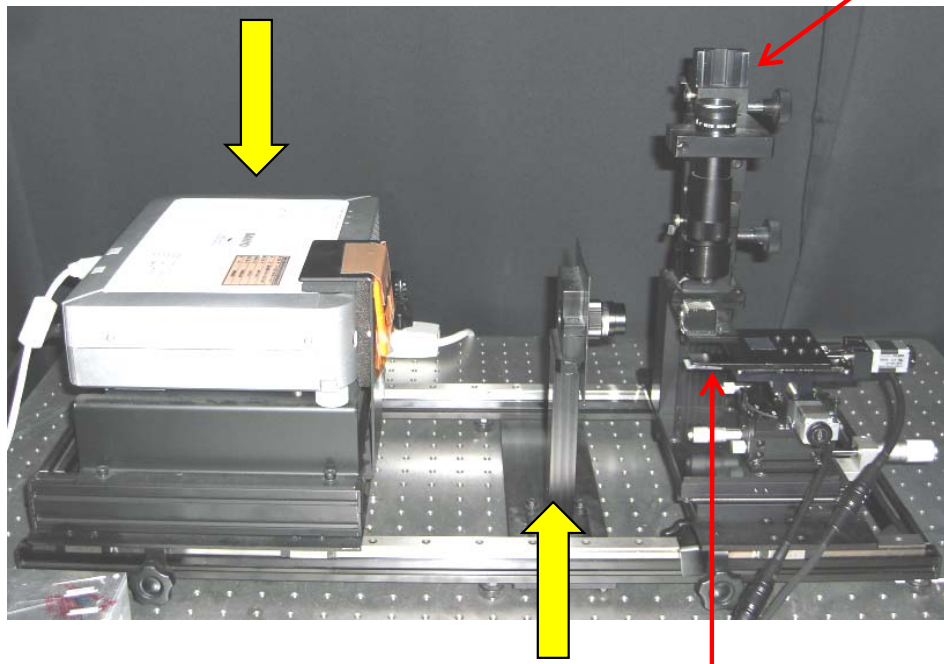


Maskless Exposure Machine

Advantages of Maskless Exposure Technique by using General LCDP

- Low cost and very simple method for gray projection
- Easy to revise the mask
- Relatively large mask can be produced (5×5 cm)

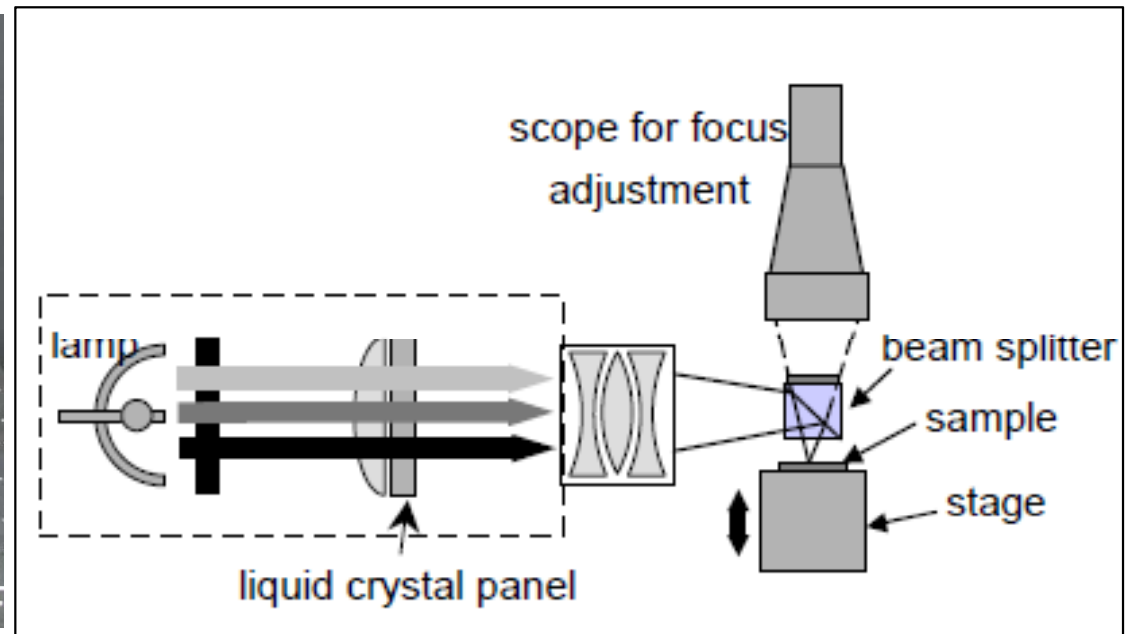
Commercial Liquid crystal device projector (LCDP)



Objective Lens

Sample Stage

Scope for focus adjustment



K. Itoga et al., *Biomaterials*, 25, p.2047-2053, 2004



Background (Removal of Zona Pellucida)

【Zona Pellucida (Protection of Oocyte)】

• Advantage of Removal of Zona Pellucida

1. Automation of Enucleation

⇒ Simplify the Automation of Enucleation Process

2. Fertility Treatment

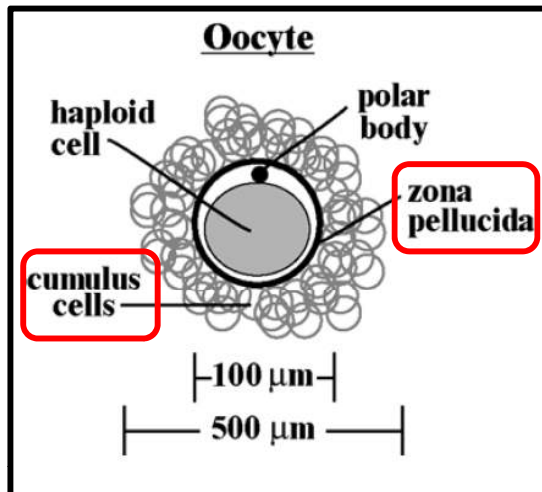
⇒ Improvement of Development Rate for Fusion Process

Conventional Enucleation

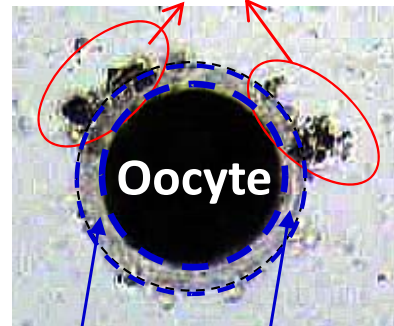


Takahashi et. al.

50 μm

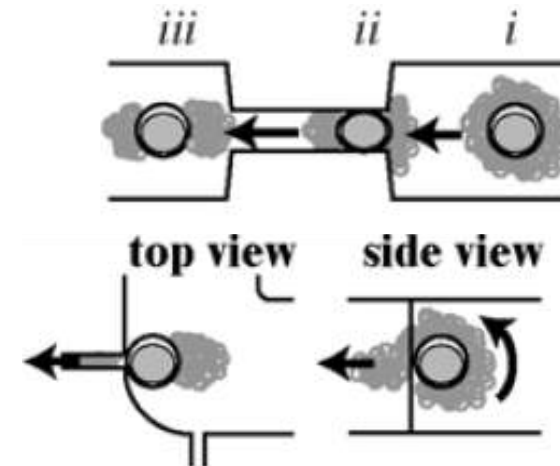


Cumulus Cells



Zona Pellucida

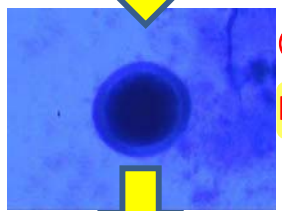
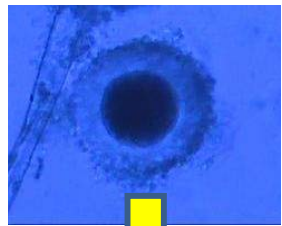
Automation of Removal Cumulus Cells



Beebe et al.(2001)Biomedical Microdevices 3, p.219-224

Conventional Method of Removal of Zona Pellucida

Removal of zona pellucida by glass capillary



① Removal of Cumulus Cells
Hyaluronidase Treatment

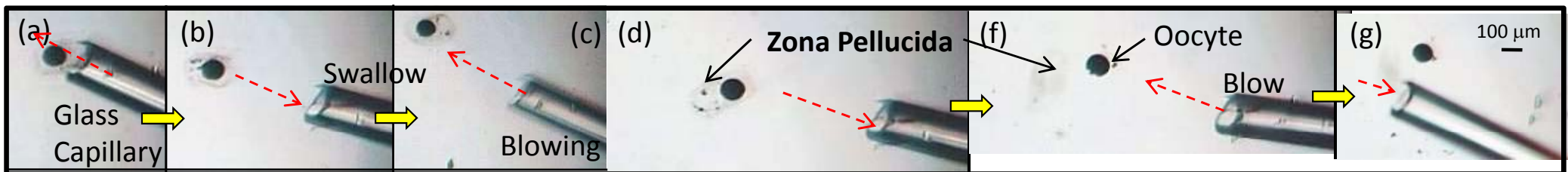


② Removal of Zona Pellucida
Pronase Treatment

Requirement of zona pellucida



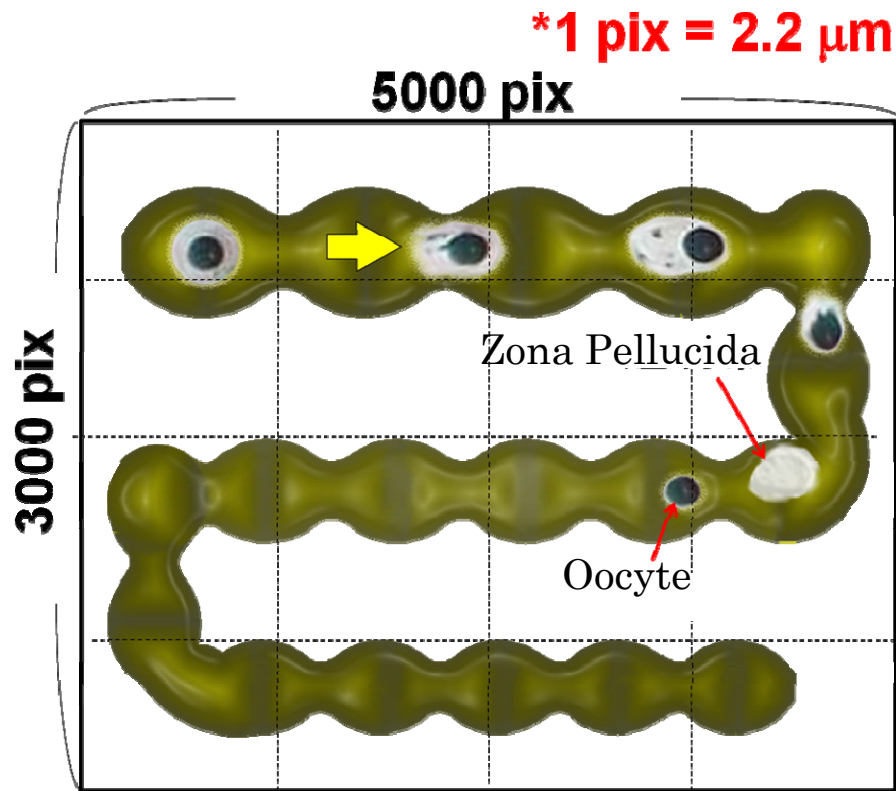
Removal of Zona Pellucida by Repetitive Motion of Swallowing and Blowing with Glass Capillary



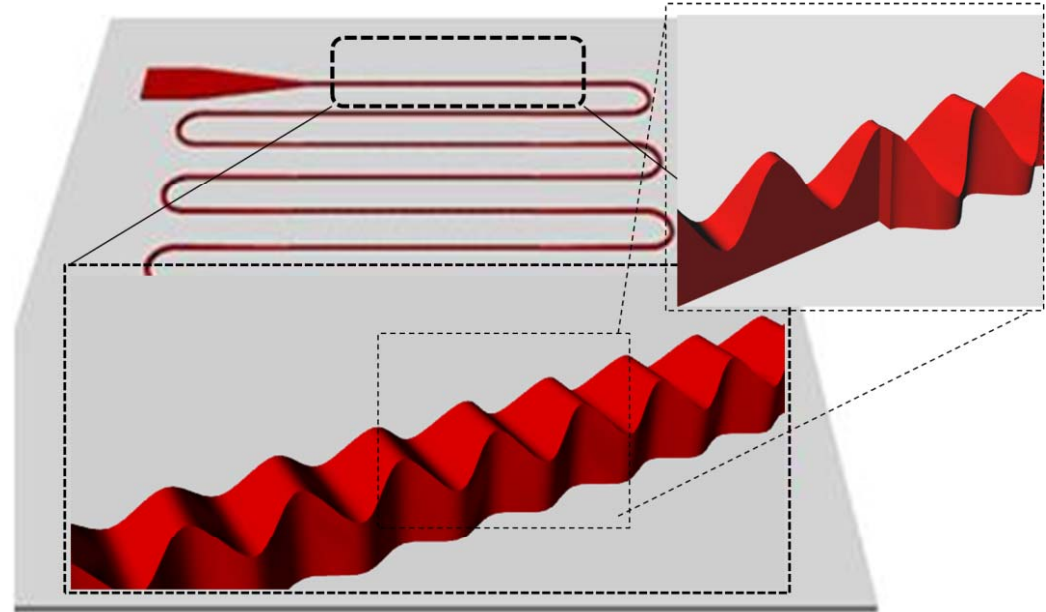
【Problem】

- Require long time to remove zona pellucida
- Multiple treatment is difficult (**Not Mass-productive**)

Removal of Zona Pellucida by 3D Microchannel



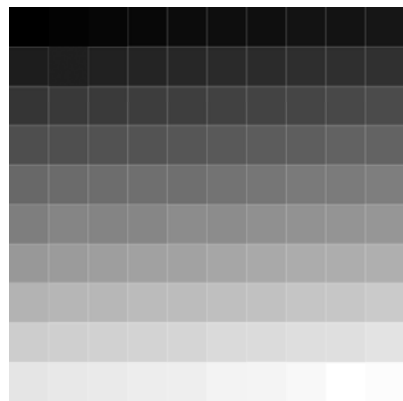
Height and width reduced sinusoidally with a phase shift each other



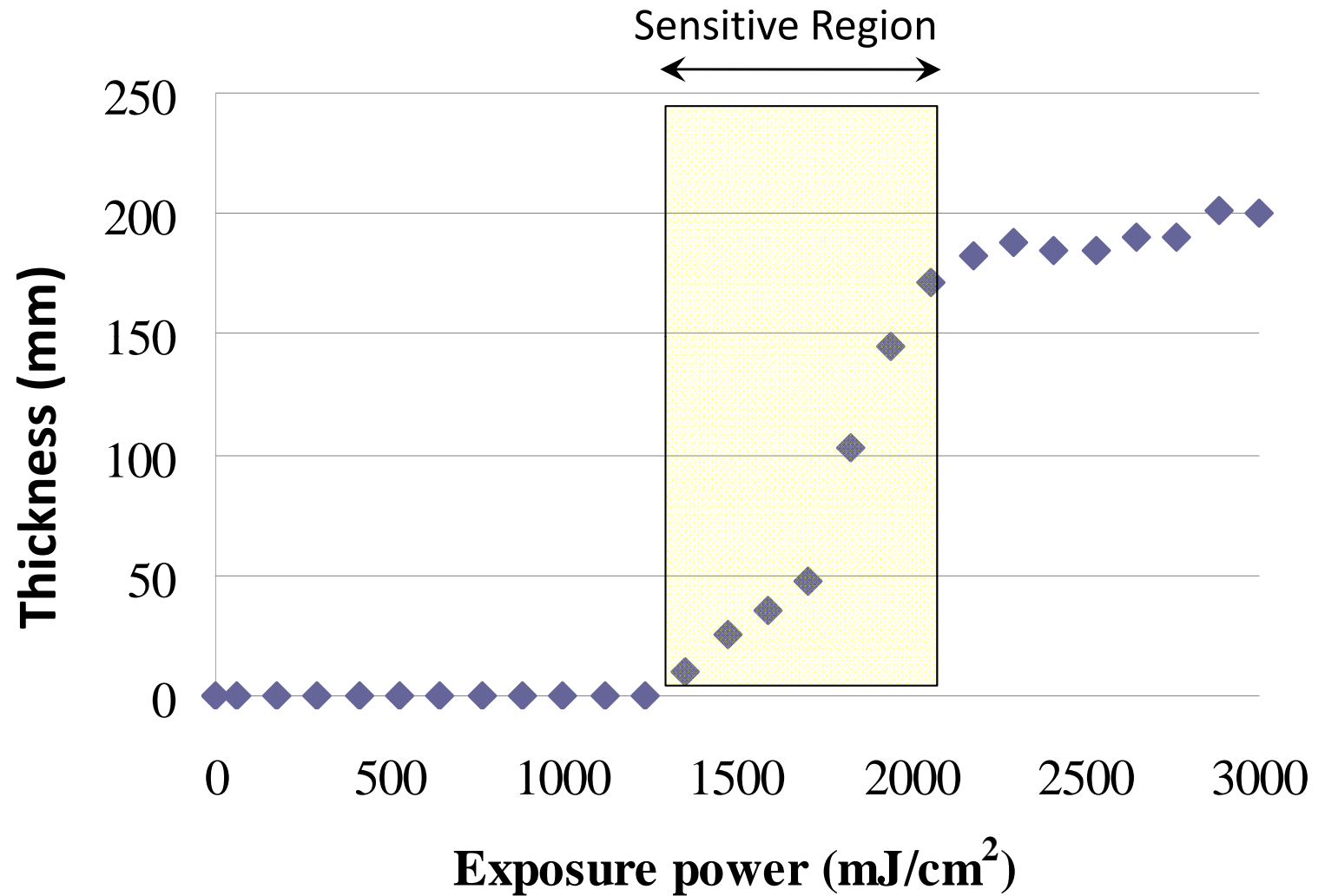
1. Height and width of the microchannel was designed to reduce **sinusoidally** along the path **with a phase shift** each other
2. Height or width of the microchannel **gradually reduced** below the size of oocyte to provide the **mechanical stimuli** effectively by the friction between the microchannel and oocyte.

Grayscale calibration

- Thick Negative -photoresist (TSMR-iN1000PM photoresist)



Projection of
256 steps of
Grayscale

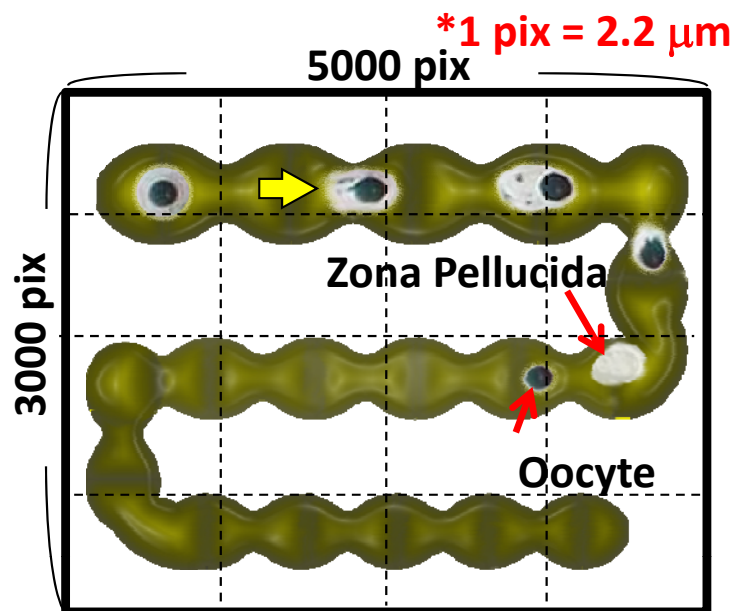
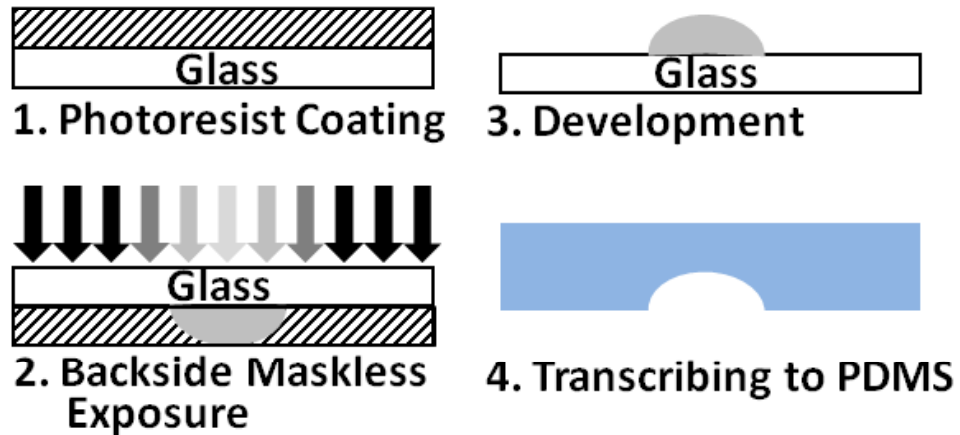


Evaluation of the Amount of exposure as a function of the photoresist cure depth.

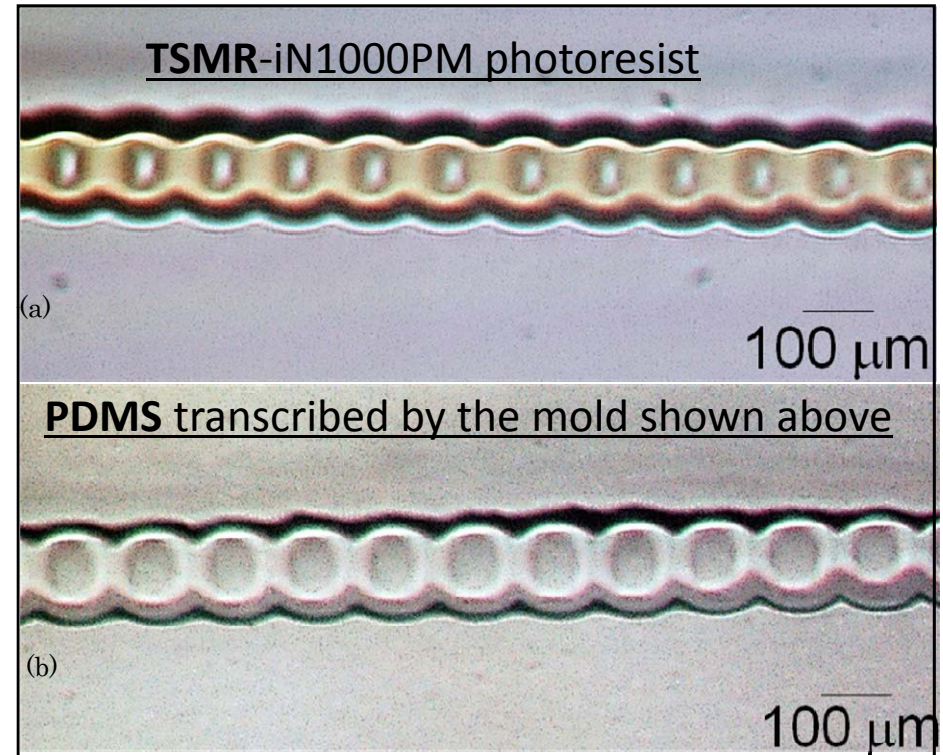


Process flow to fabricate 3D microchannel

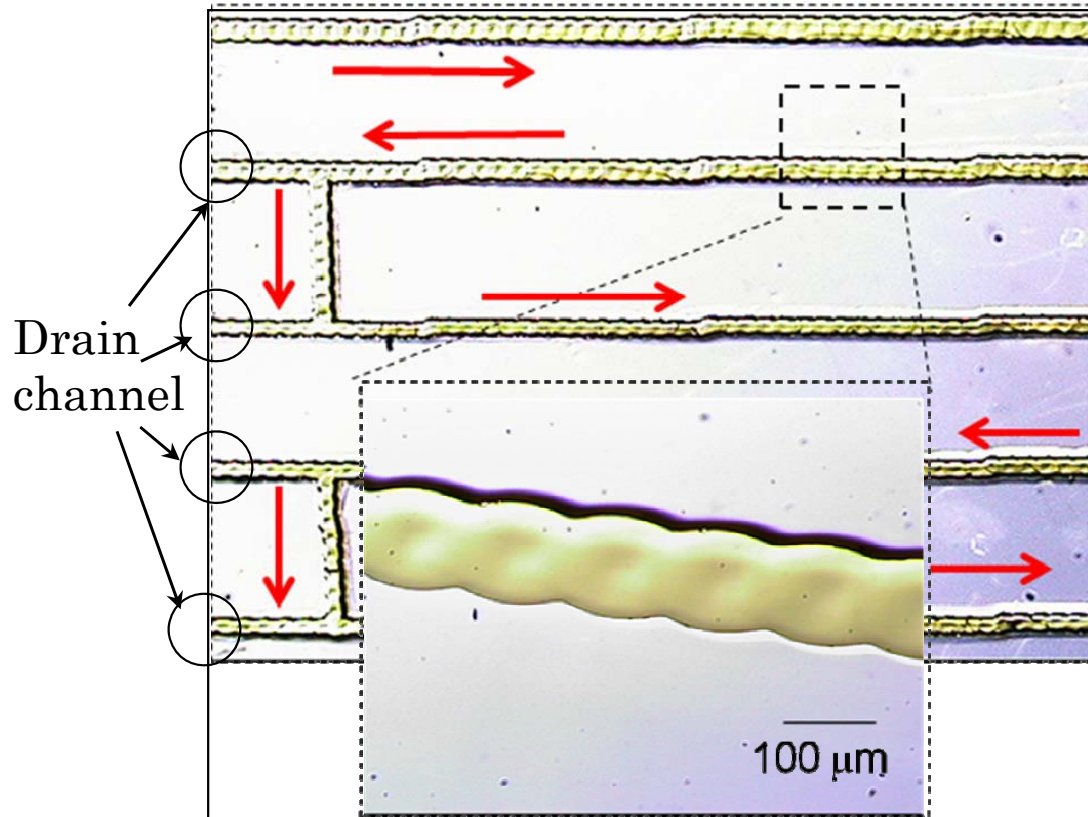
Backside Exposure techniques to fabricate 3D Microchannel



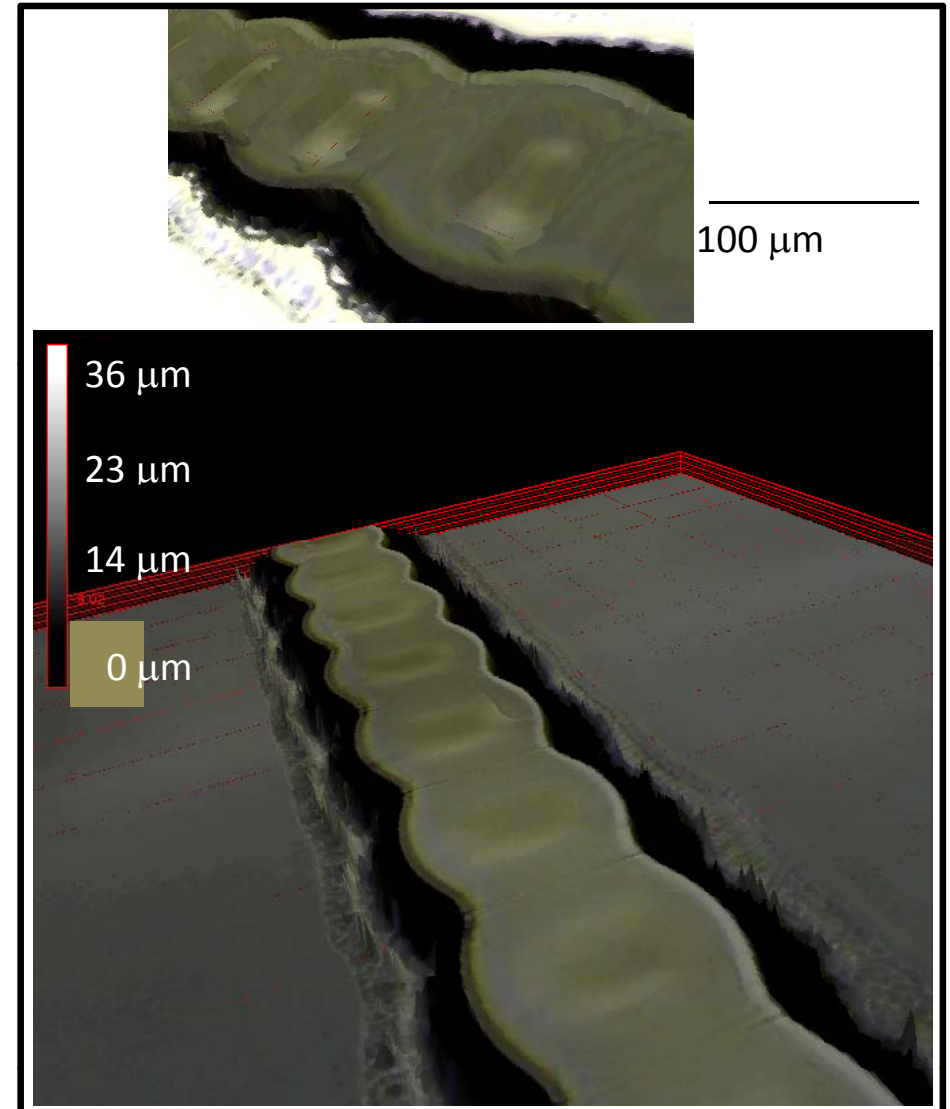
Fabricated 3D Microchannel



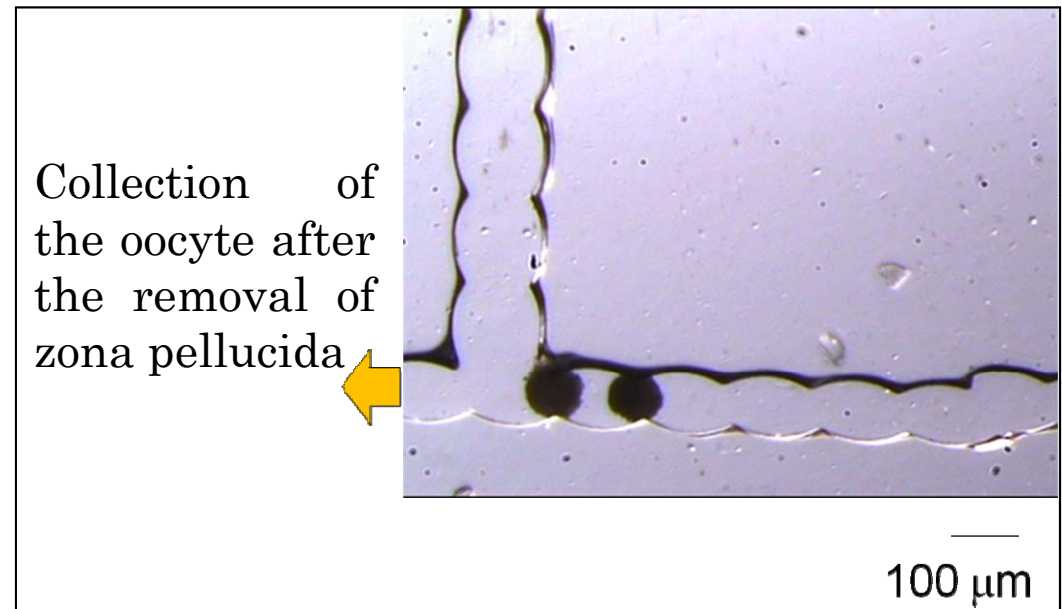
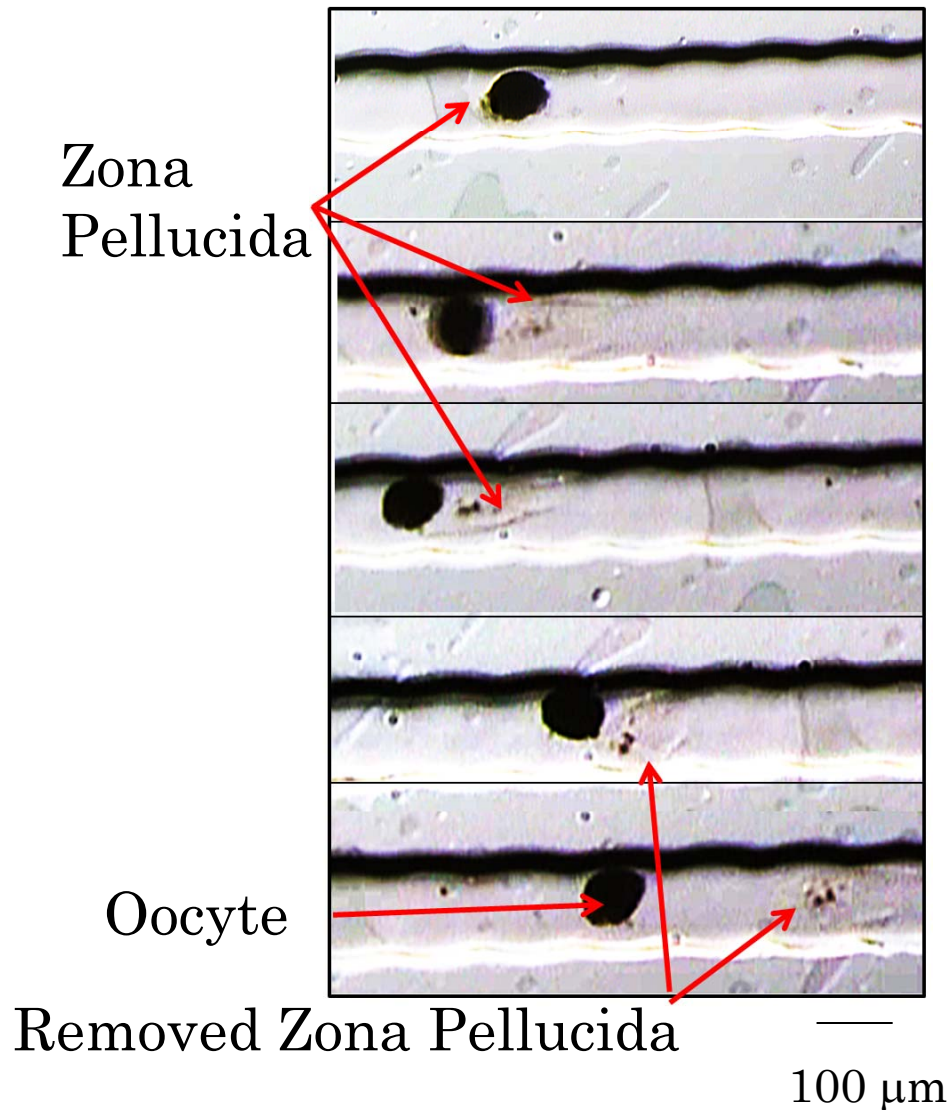
3D Microchannels to Remove Zona Pellucida



Surface Condition Measured by Laser Scanning Microscope



Application : Removal of Zona Pellucida



3D-Microchannel could remove zona pellucida of oocyte successfully

