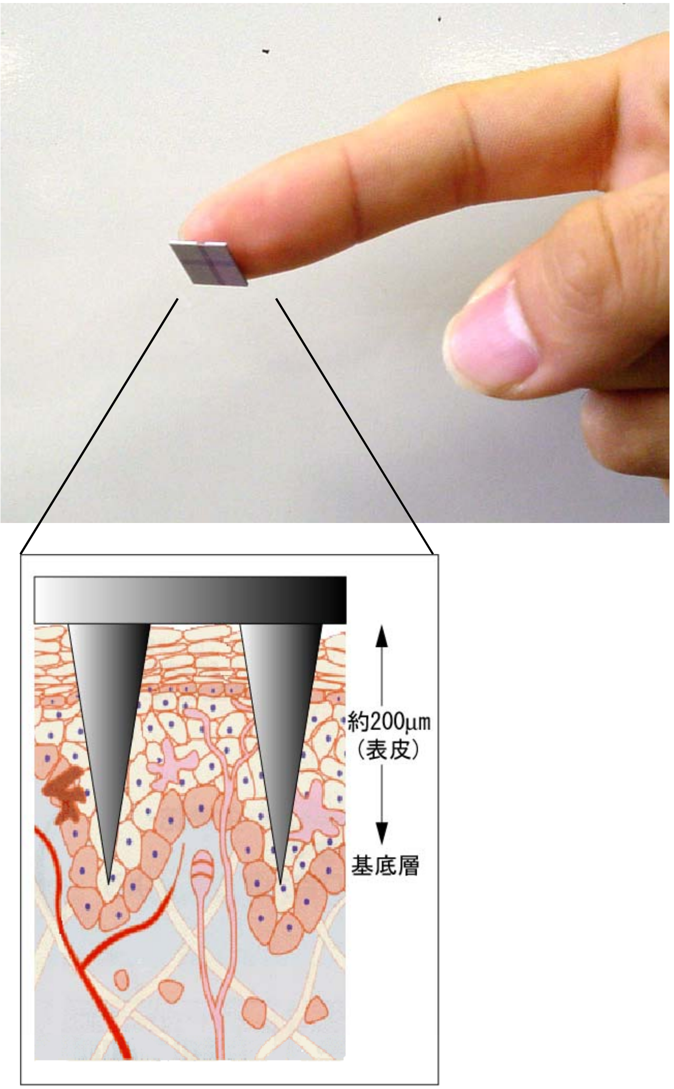
Advanced 6
Advanced MEMS applications
-Micro-needle for trans-dermal DDS-
-Portable biochemical reaction system-

Associate Prof. M. Shikida
Center for Micro-nano Mechatronics
Nagoya University

Micro-needle for medical application

Micro-needle for trans-dermal DDS



Requirements of needle development

✓Sharpness of needle tip

✓Sufficient height for skin penetration

✓High density for drug supply

✓Disposable, low-cost

Micro-needle for medical application

Advanced MEMS fabrication

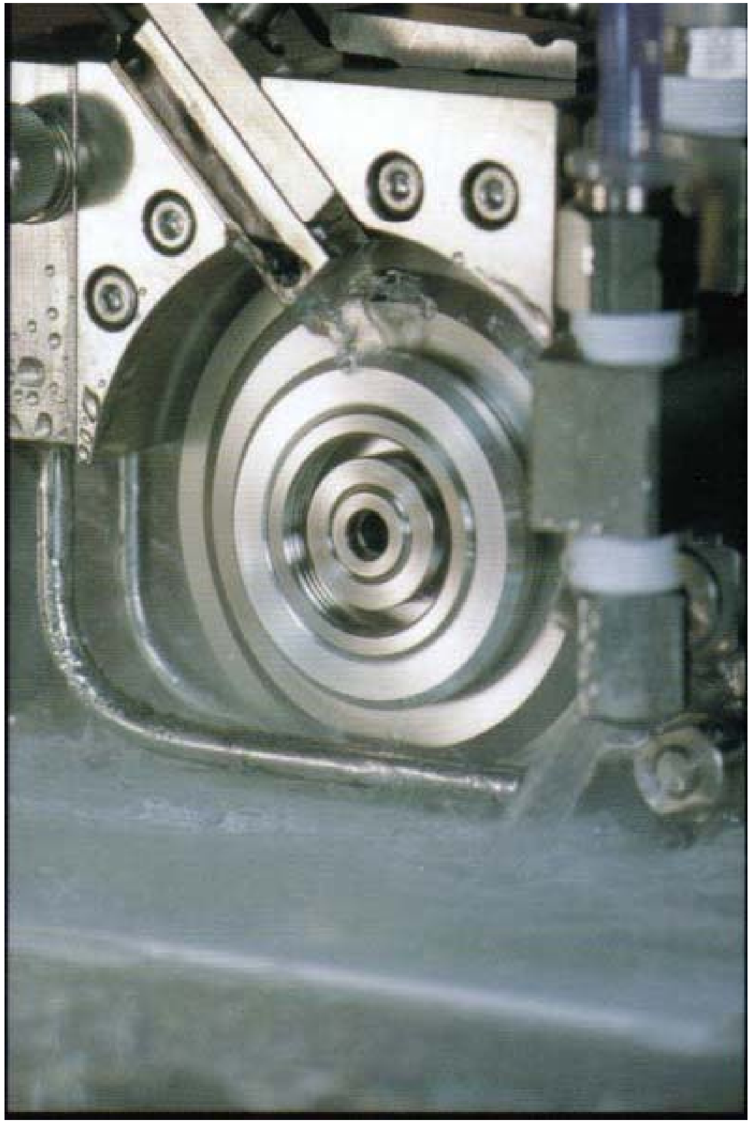
Fabrication step
① 2.5D shape formation by grinding
② 3D shape production by anisotropic wet etching

⇩

Advantages
✓Low facility investment
It can produce MEMS device without using photo-lithography and Deep reactive ion etching.
✓Production of high aspect ratio micro-structure

Micro-needle for medical application

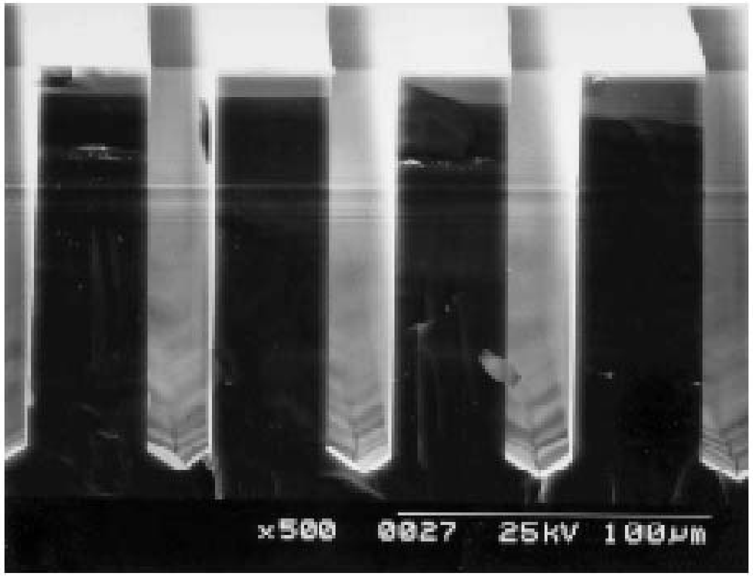
Advanced MEMS fabrication _ Grinding process

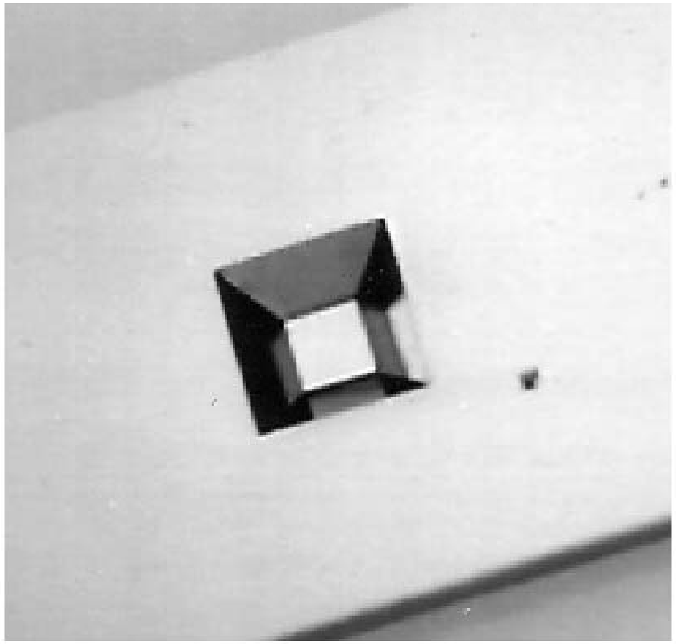


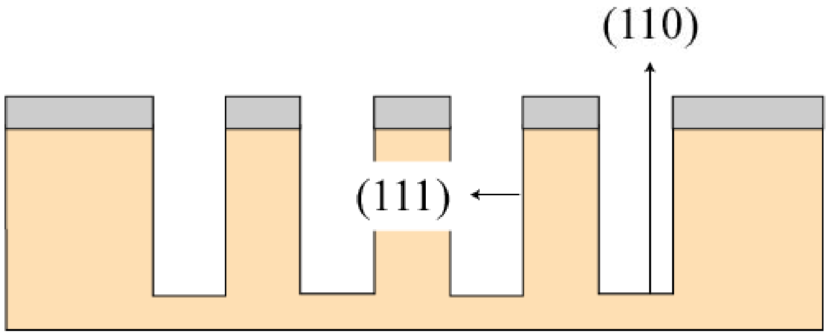
Blade
Thickness：0.025 mm, 0.050 mm
Particle size: #2000

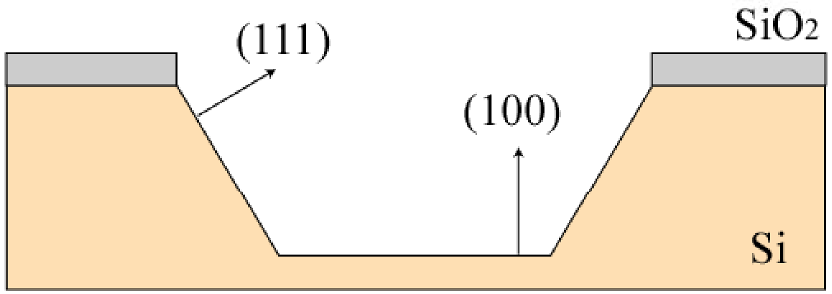
Micro-needle for medical application

Advanced MEMS fabrication _ Anisotropic wet etching







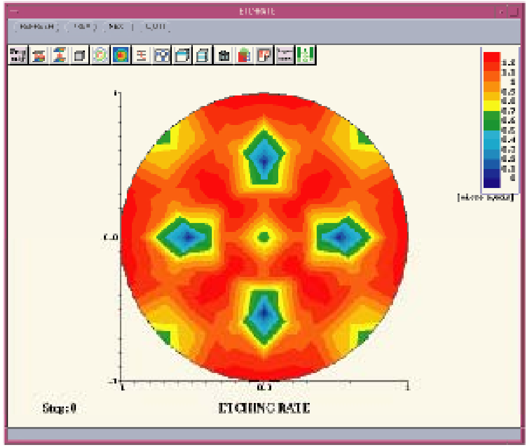


Etching rate depends on crystallographic orientation.

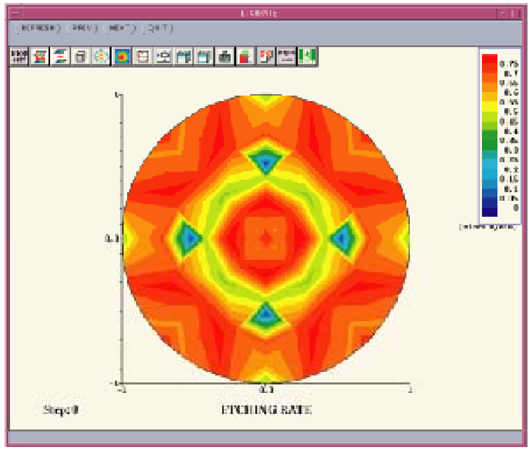
Micro-needle for medical application

Dependency of etching rate distribution

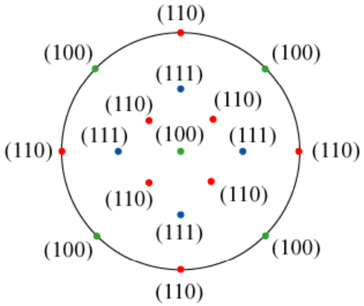
Distribution of etching rate



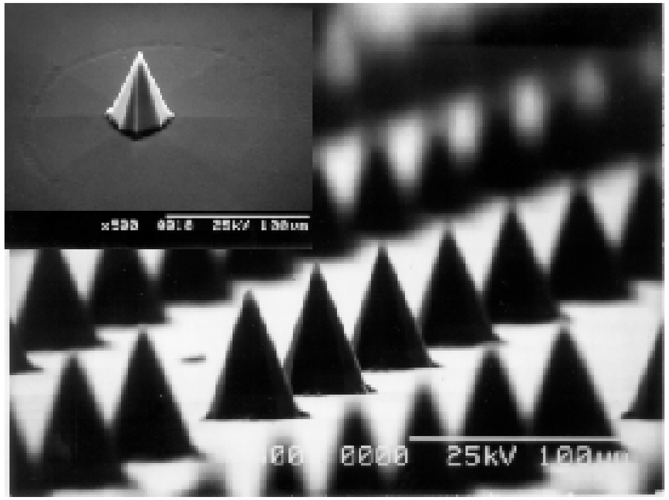
34.0 wt.% KOH (70℃)

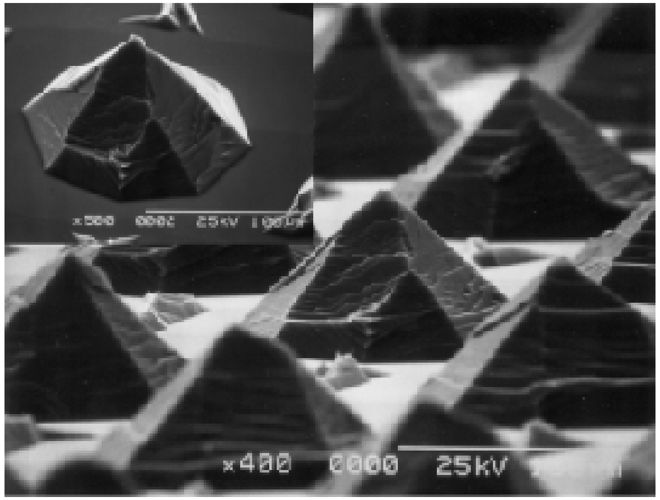


10.0 wt.% TMAH (80℃)



Fabricated needle shape

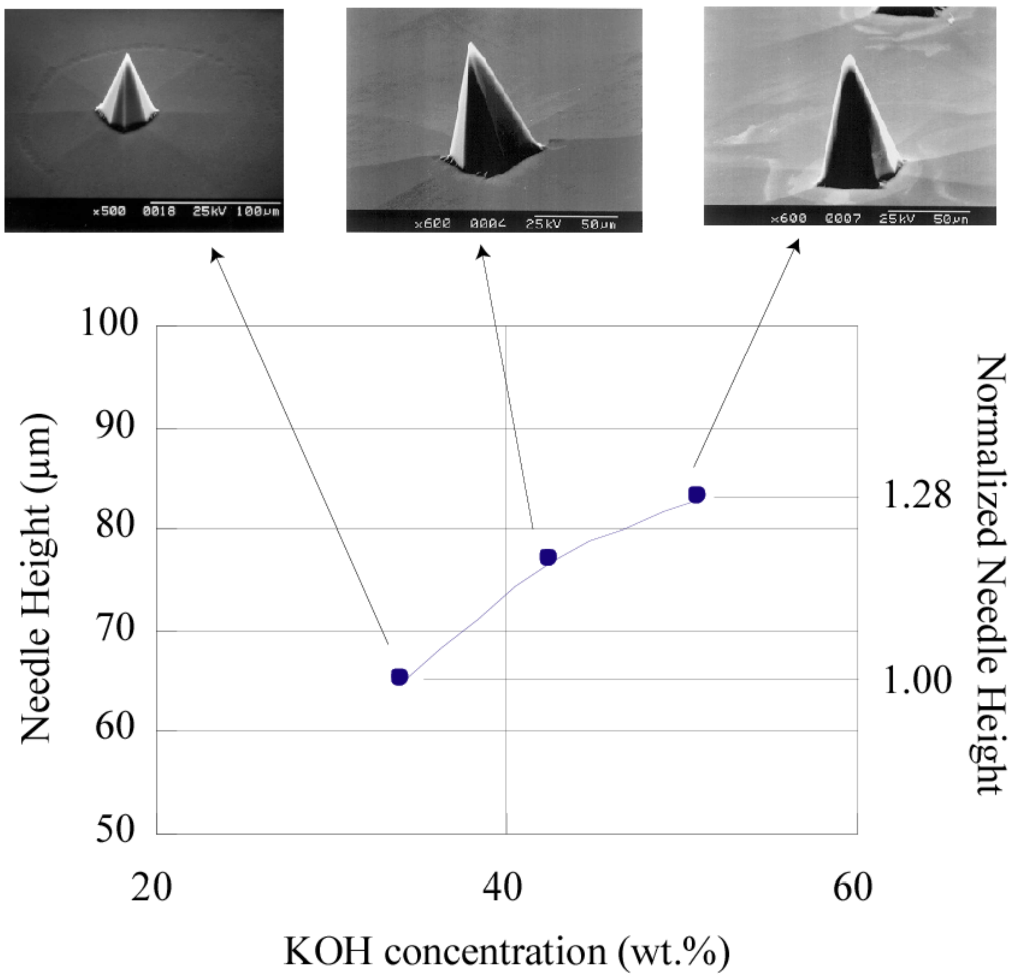




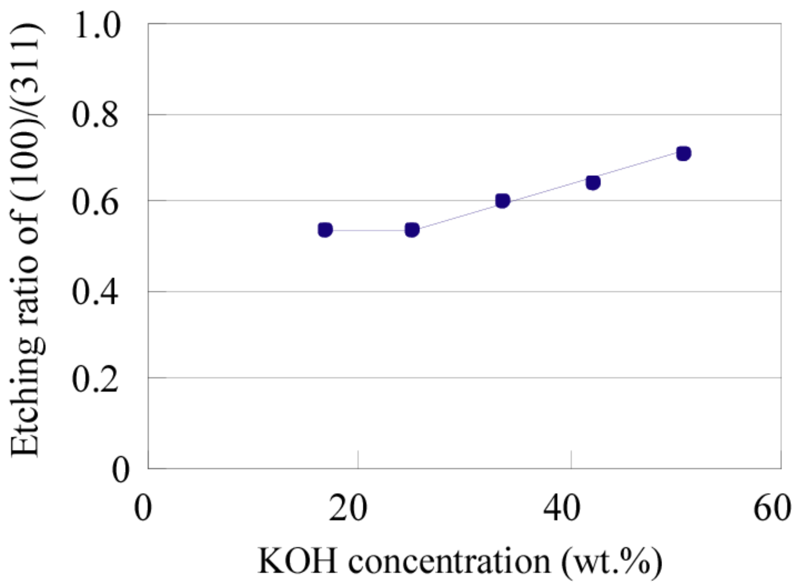
H. Sasaki, et al., IEEJ Trans Electrical Electronic Eng., 2, 2007, 340-347

Micro-needle for medical application

Dependency of concentration



KOH concentration (wt.%)	Etching rate (μm/min) (100)	(311)	Etching Ratio (100)/(311)
17.0	0.713	1.344	0.531
25.5	0.759	1.430	0.531
34.0	0.629	1.065	0.591
42.5	0.473	0.747	0.633
51.0	0.265	0.380	0.697



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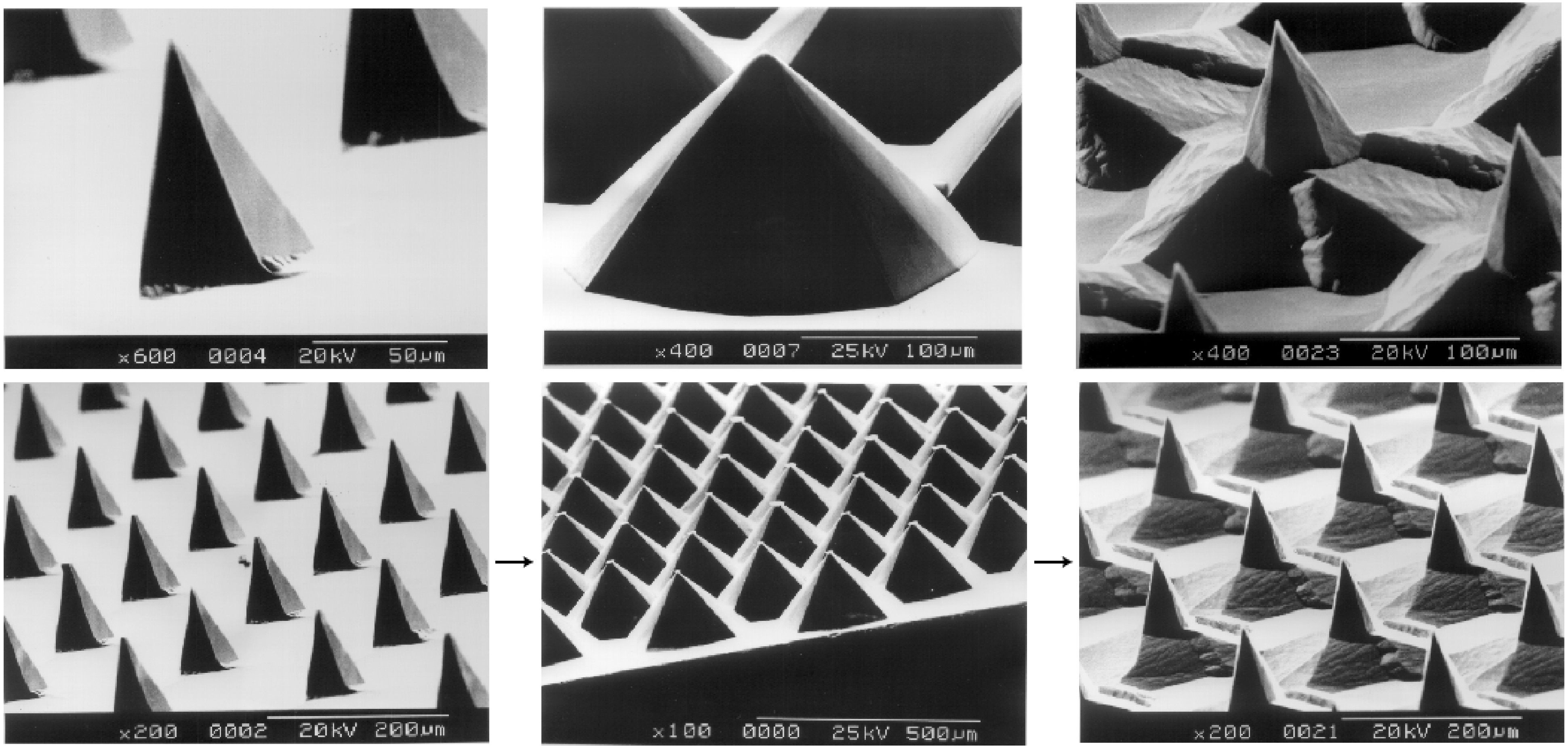
Micro-needle for medical application

Shape change with change of etching solution

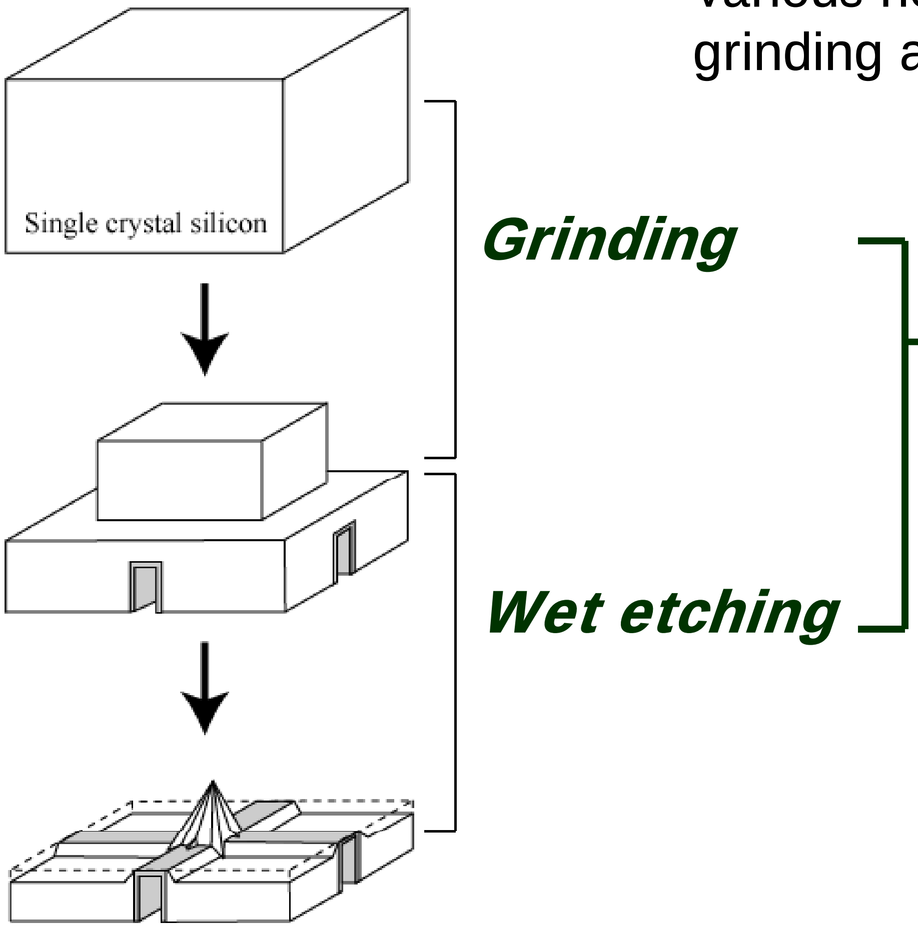


51.0 wt.% KOH (69 deg-C) → 25.0 wt.% TMAH with surfactant (75 deg-C) → 51.0 wt.% KOH (71 deg-C)

Windmill shaped mask pattern

Micro-needle for medical application

Advanced MEMS fabrication



Various needle shapes are produced by combing grinding and wet etching processes

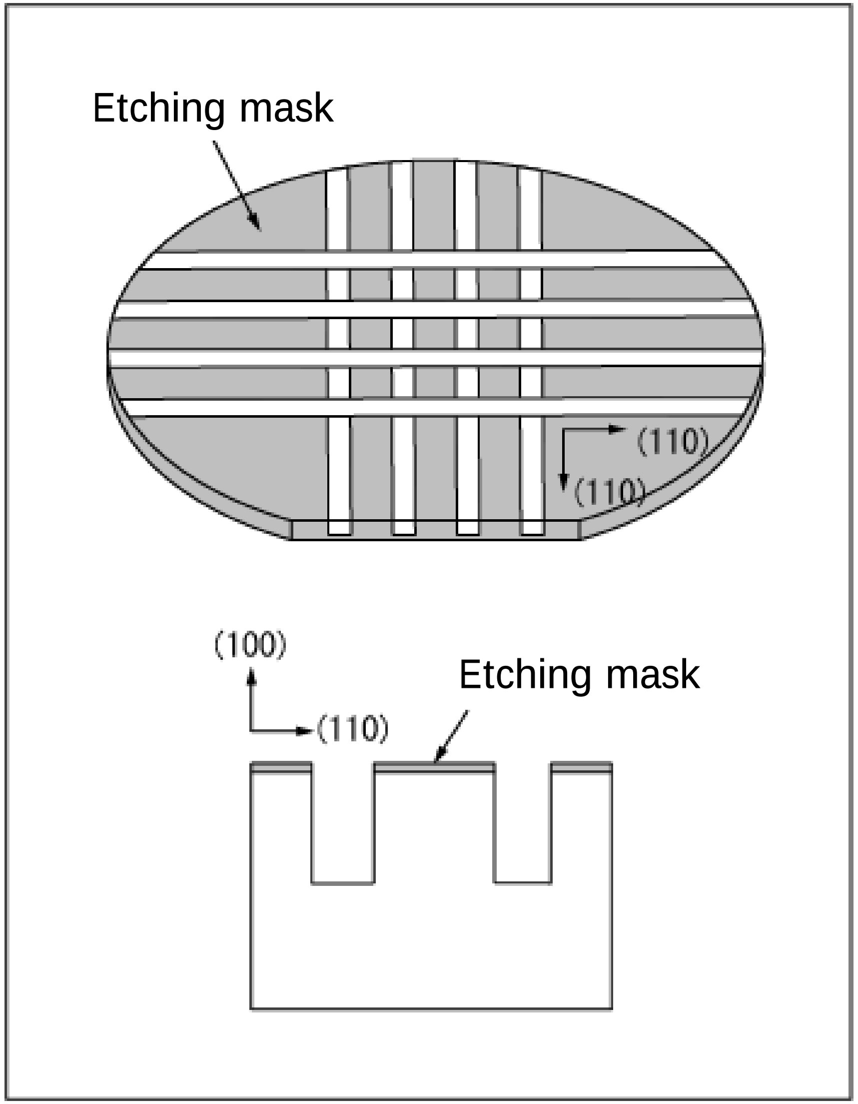
Solid-type
- ✓Pyramid (Si)
- ✓Candle (Si)
- ✓Spike (Si)
- ✓Straight (Si)
- ✓Pen (Si)

Hollow-type
- ✓Pyramid (Si)
- ✓Candle (Si)
- ✓Straight (Ni)
- ✓Flat (Ni)

Micro-needle for medical application

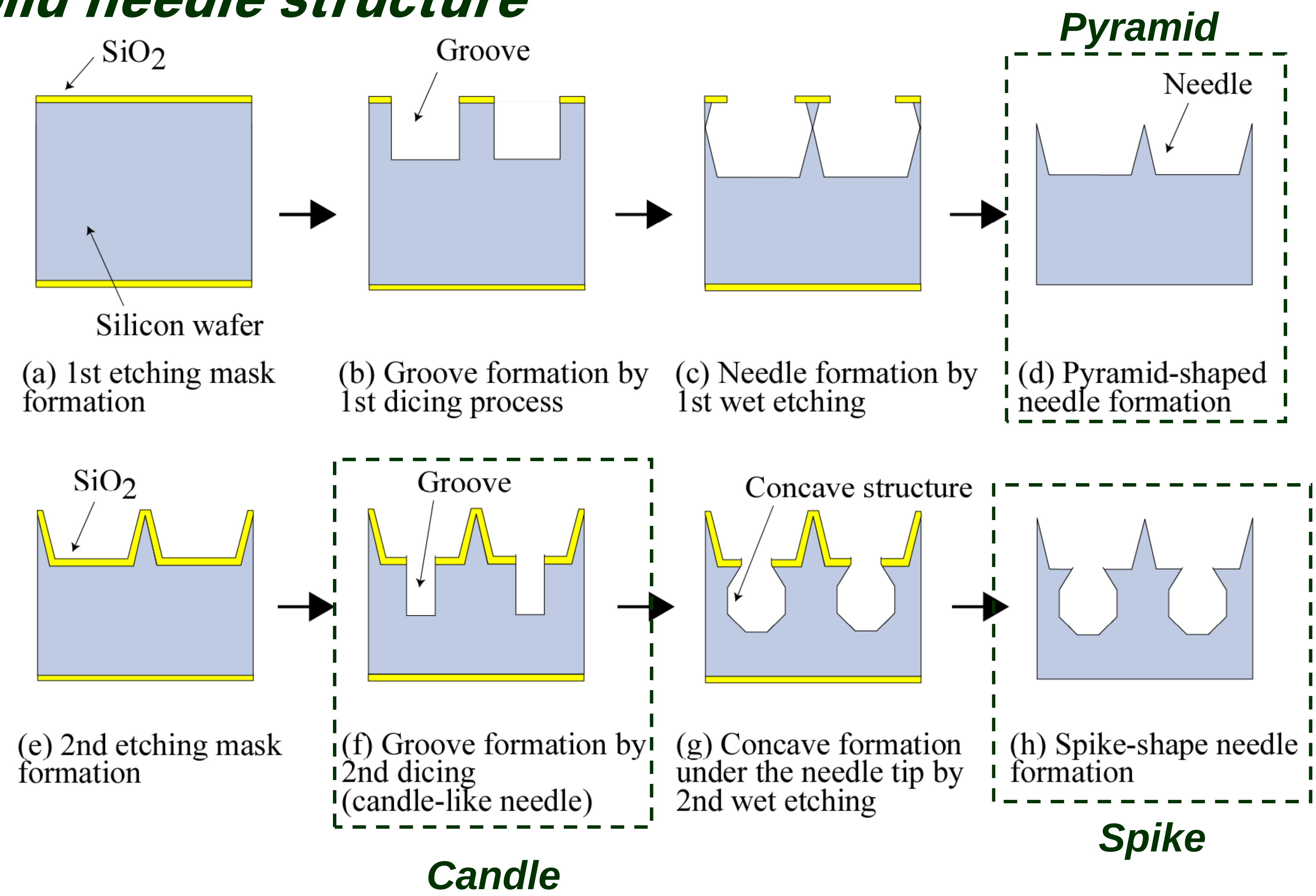
Advanced MEMS fabrication _ Recipe

- ✓ Si(100) wafer
- ✓ Blade
  - ✓ #2000 (4/6 micron)
  - ✓ Thickness： 0.025, 0.050 mm
- ✓ Grinding
  - ✓ Direction <110>
  - ✓ Groove depth：40 - 400 μm
  - ✓ Groove width：30 - 180 μm
  - ✓ Pitch：70 - 200 μm
  - ✓ Cutting speed：5 mm/s
- ✓ Etching: KOH40%, 70℃



Micro-needle for medical application

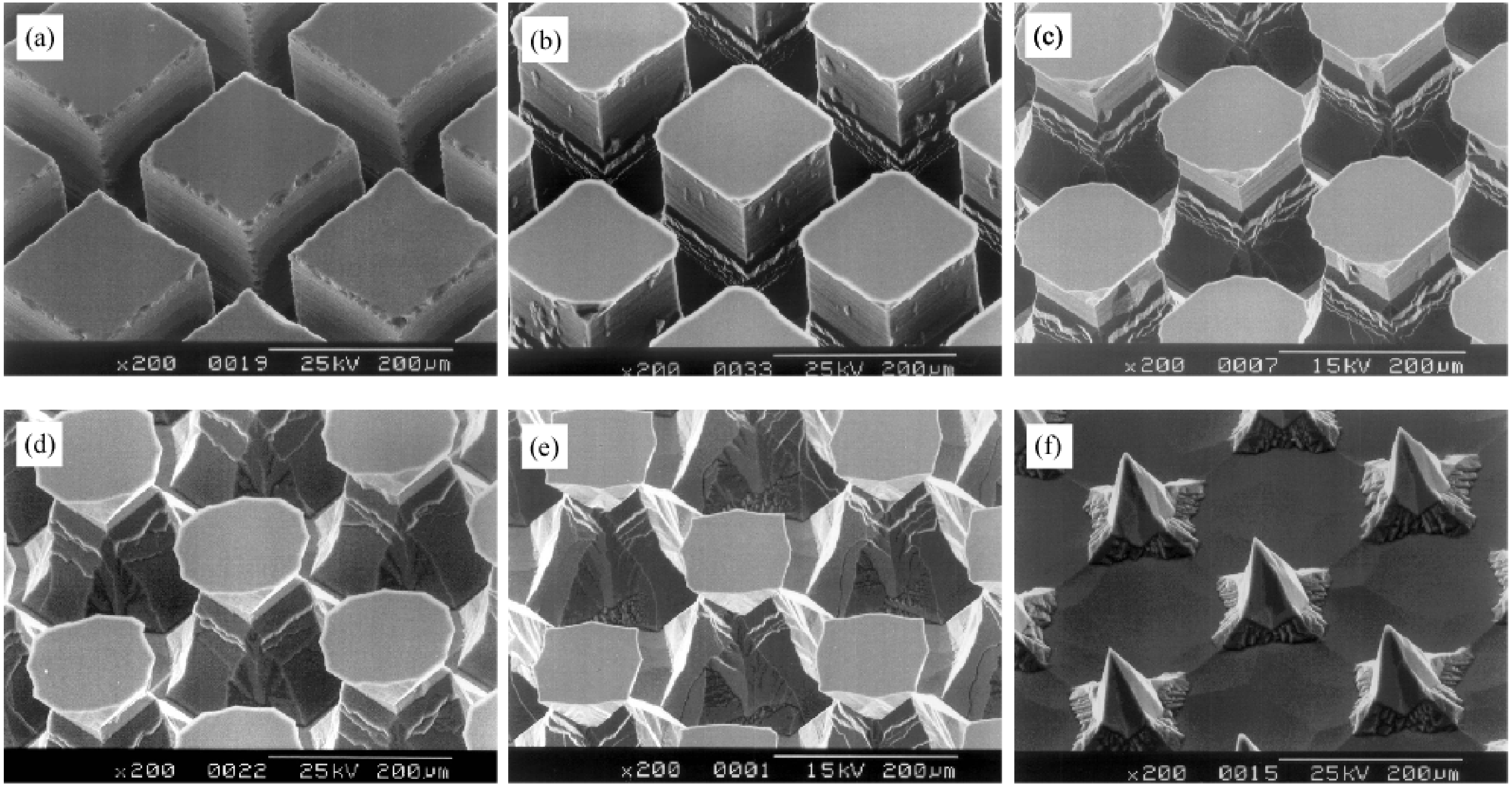
Solid needle structure



M. Shikida, et al., Sensors and Actuators A, 116, 2004, 264-271

Micro-needle for medical application

Solid needle structure _ shape change during etching

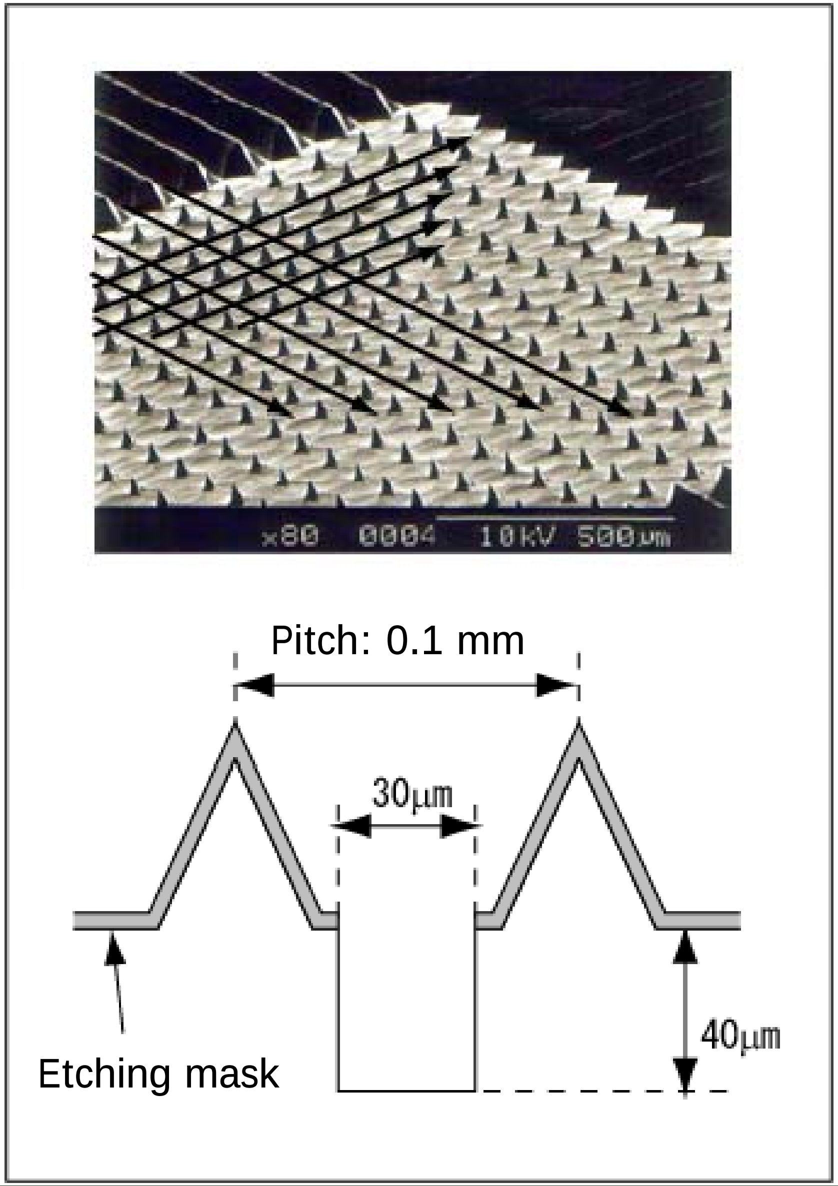


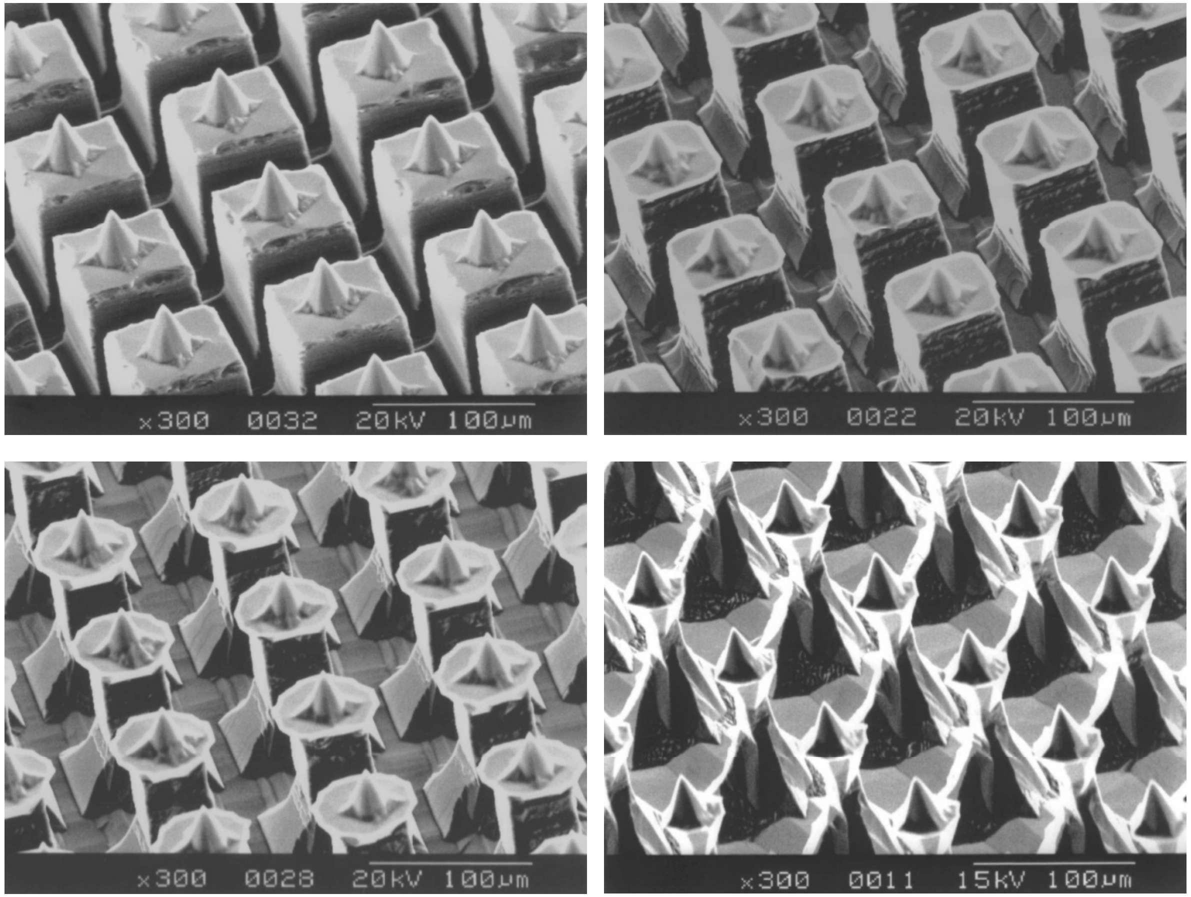
Etching time：(a) 0 min, (b) 15 min, (c) 30 min, (d) 40 min,(e) 50 min, (f) 105 min

<u>**M. Shikida, et al., Sensors and Actuators A, 116, 2004, 264-271**</u>

Micro-needle for medical application

Solid needle structure _ shape change during 2nd etching

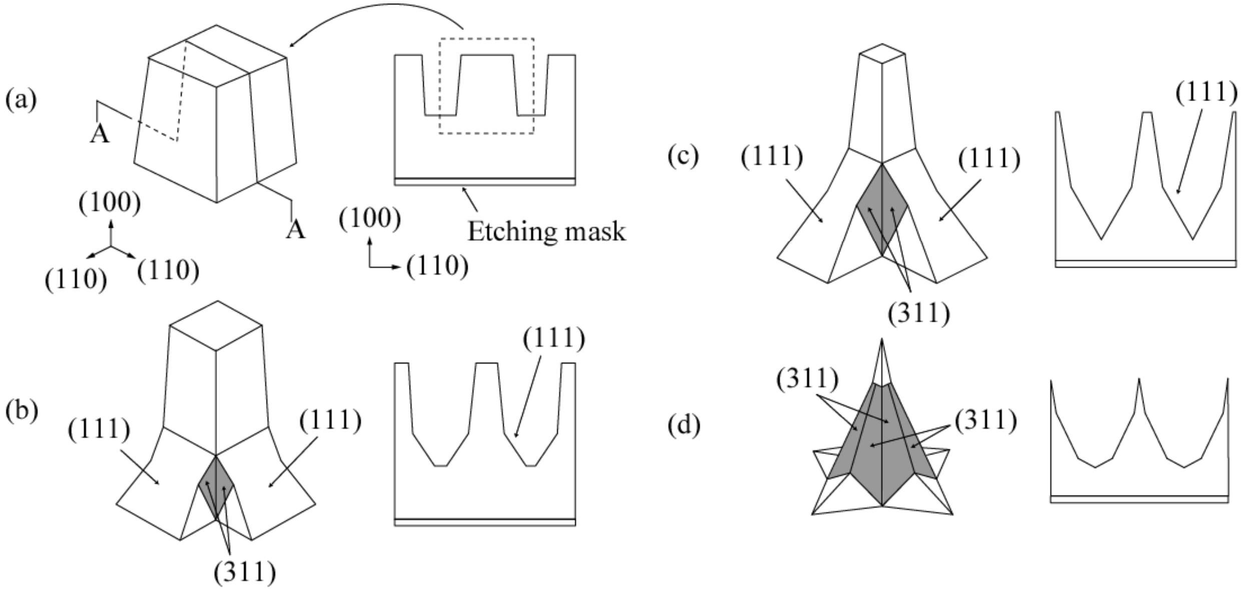


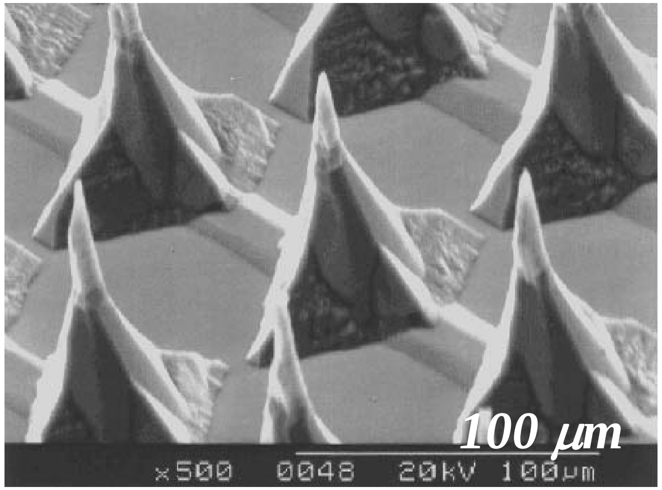


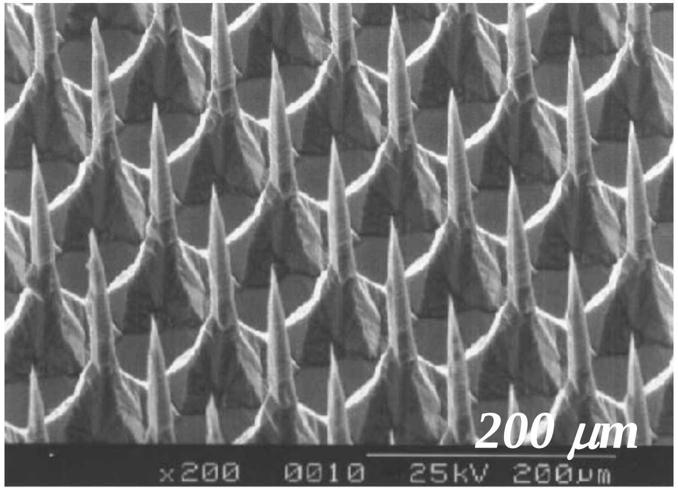
Etching time：0 min, 5 min, 10 min, 20 min

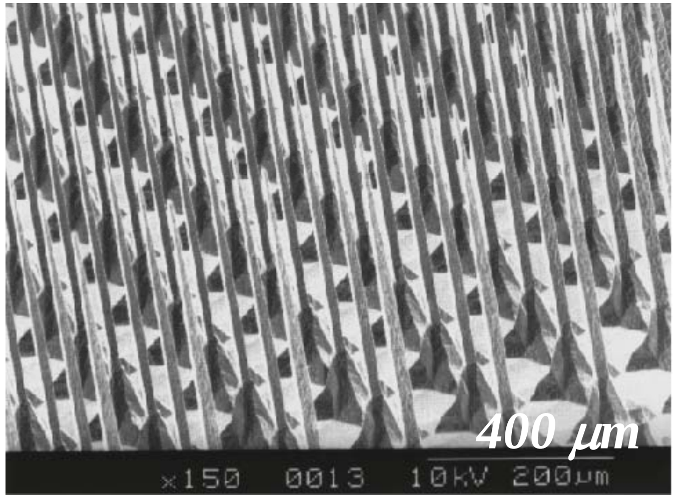
Micro-needle for medical application

Solid needle structure _ straight









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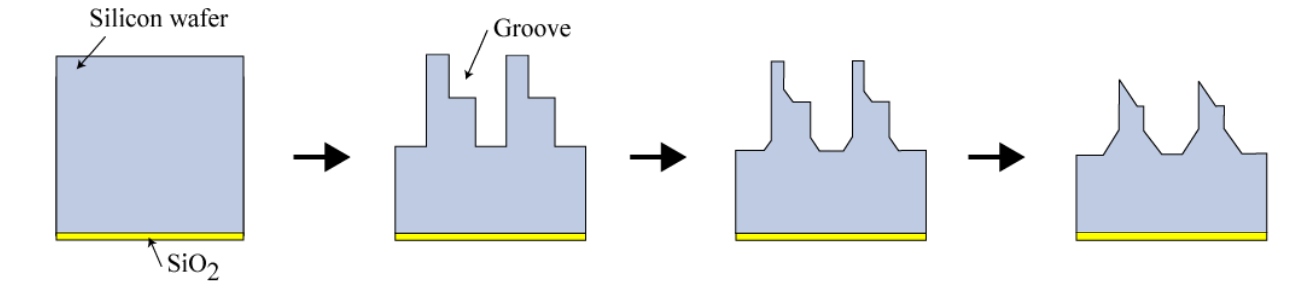
Micro-needle for medical application

Solid needle structure _ Pen-shape



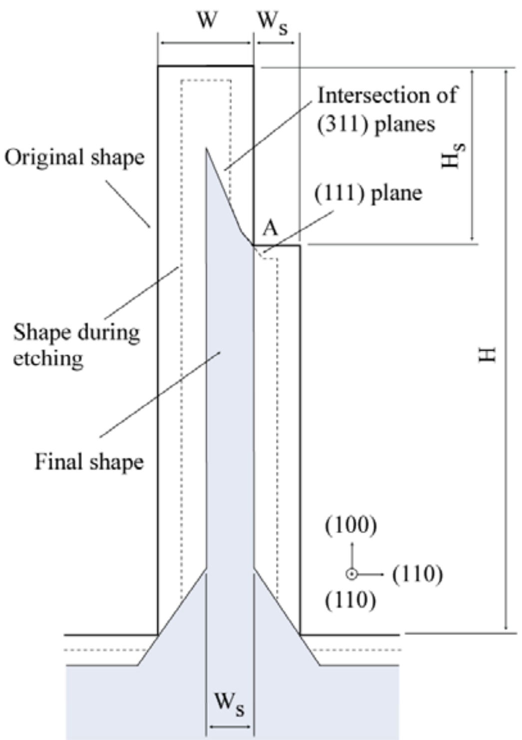
(a) Etching mask formation on the rear side

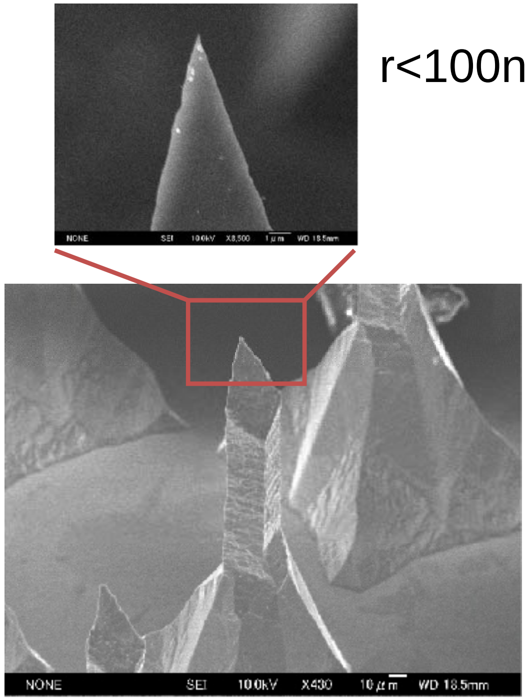
(b) Step shaped post structure formation by dicing

(c) Side etching by anisotropic wet etching

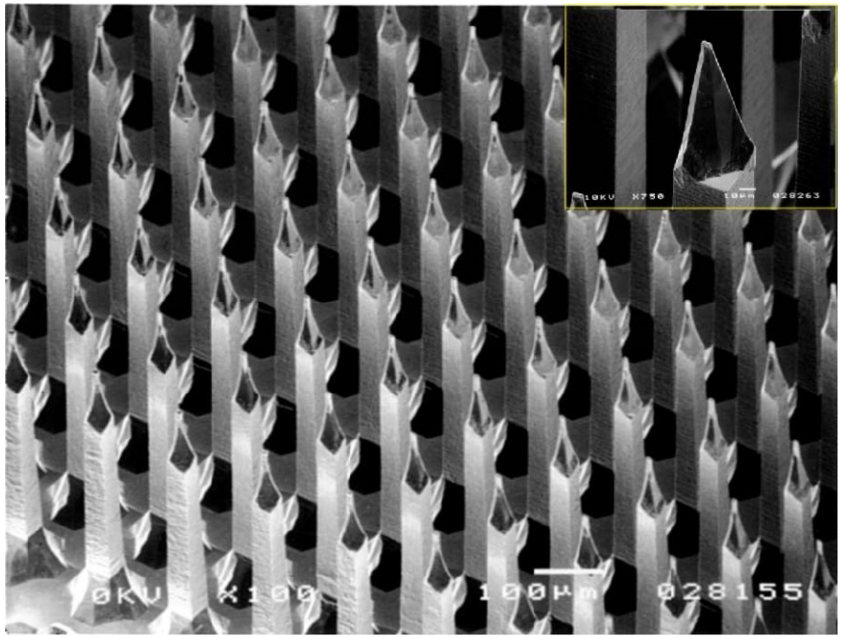
(e) Pen-shaped microneedle formation by wet etching

Pitch:100 μm, Height: 300 μm





r<100nm

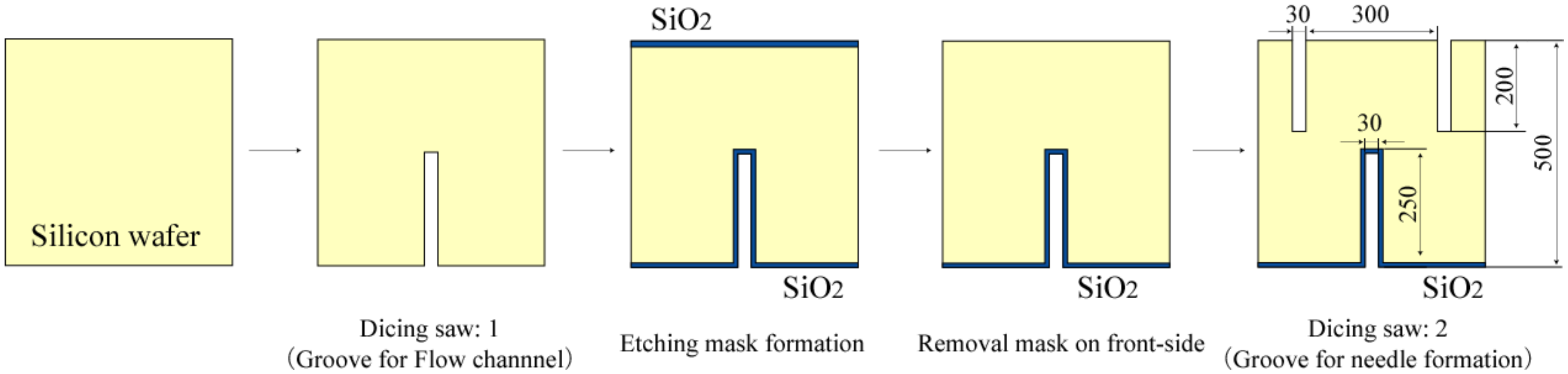


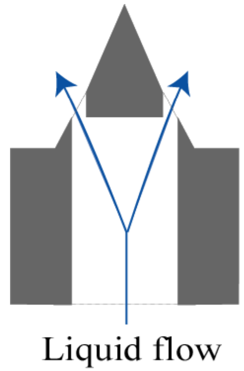
M. Shikida, et al., J. Micromech. Microeng., 14, 2004, 1462-1467

Micro-needle for medical application

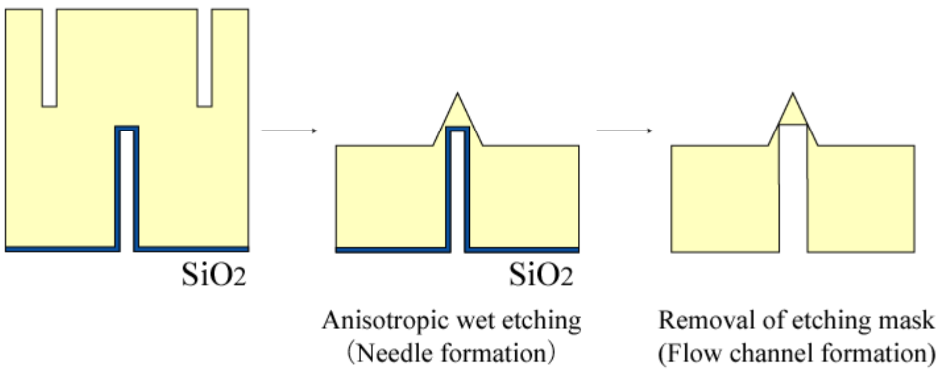
Hollow needle structure

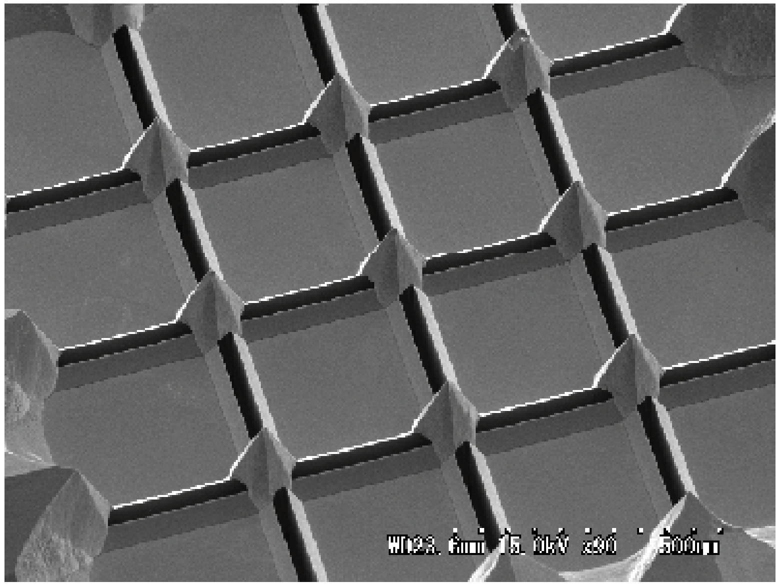
(a) 2.5-dimensional shape formation by mechanical process





(b) Needle formation by anisotropic wet etching

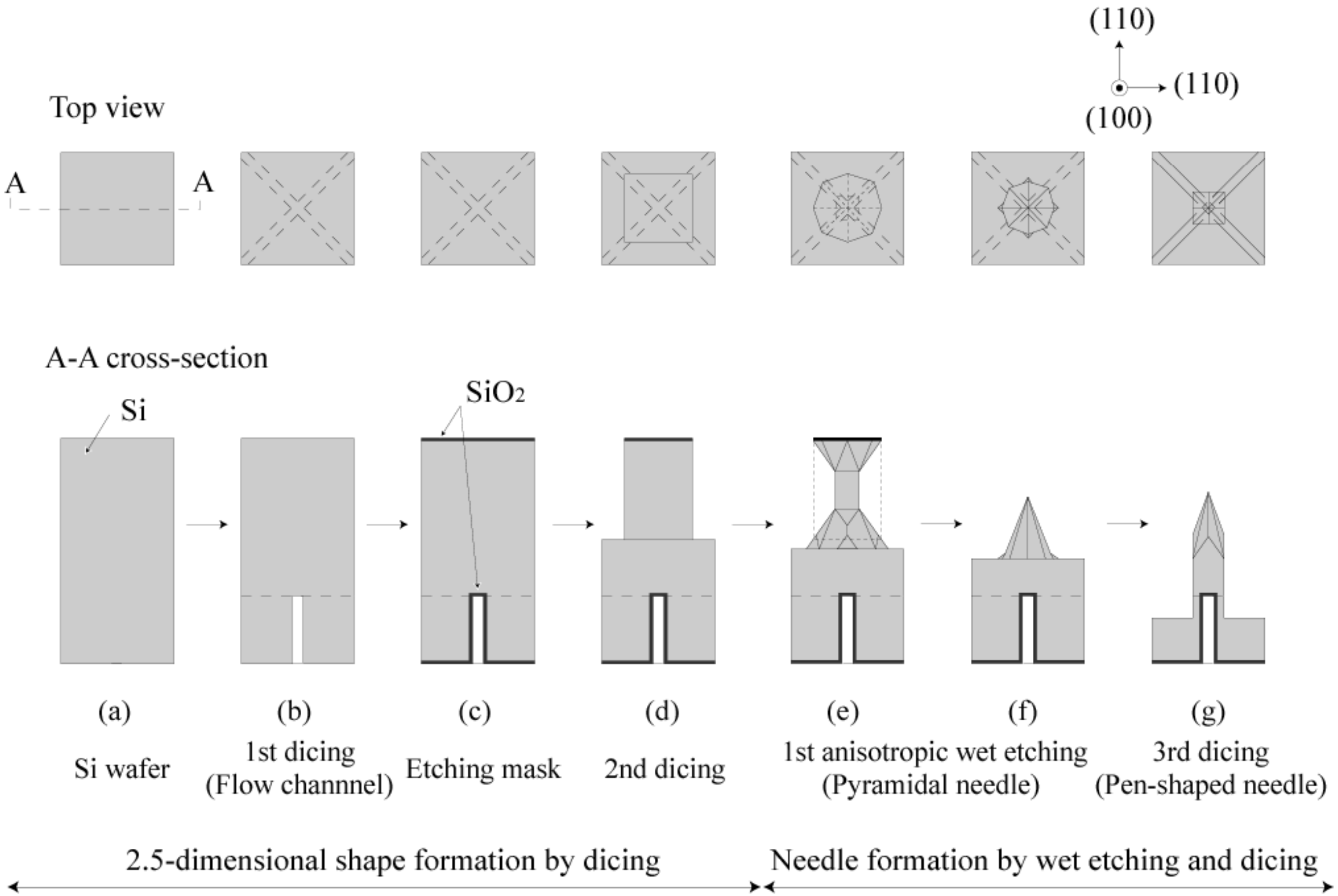


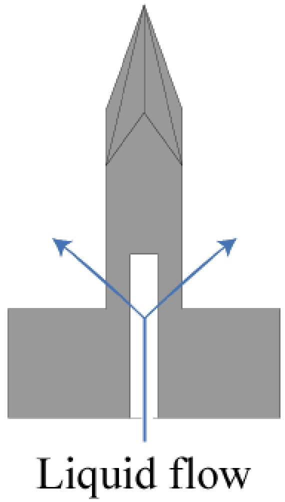


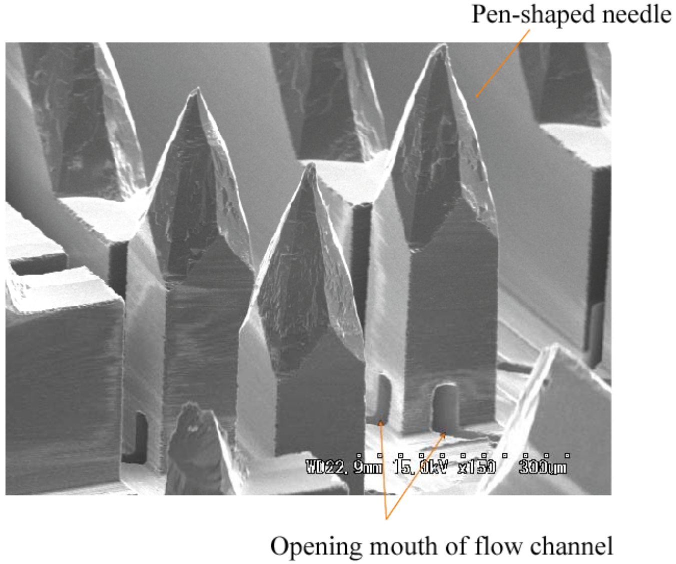
M. Shikida, et al., J. Micromech. Microeng., 16, 2006, 1740-1747

Micro-needle for medical application

Hollow needle structure





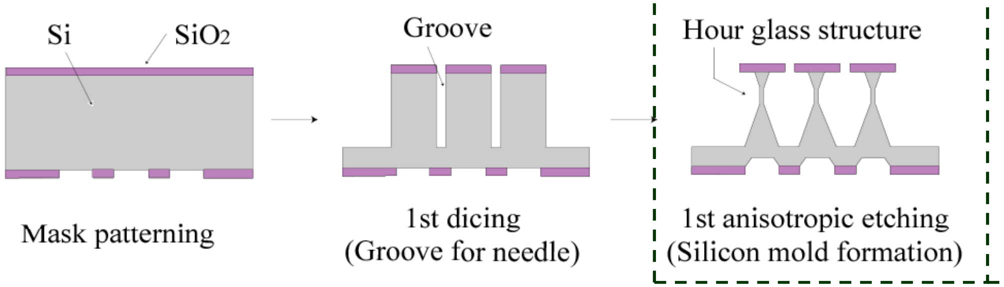


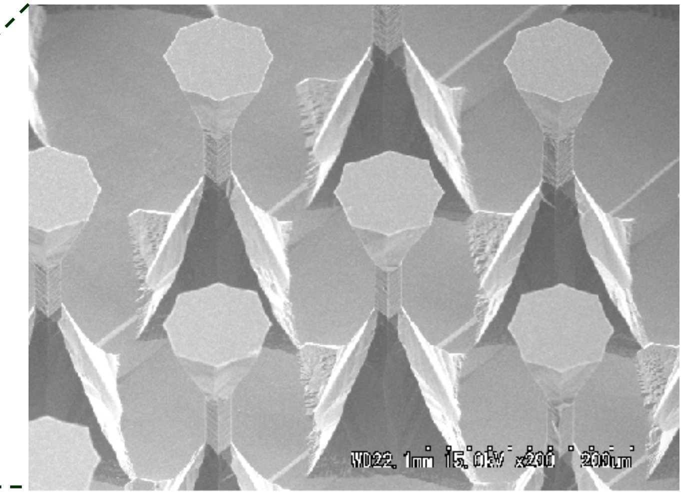
<u>M. Shikida, et al., J. Micromech. Microeng., 16, 2006, 1740-1747</u>

Micro-needle for medical application

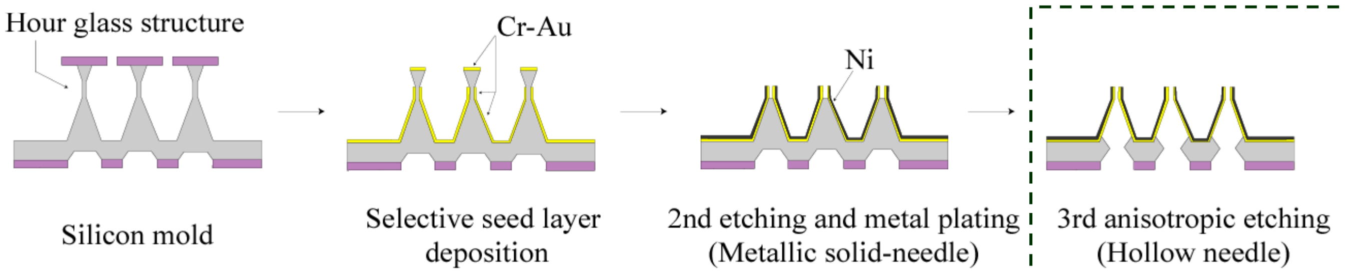
Hollow needle structure

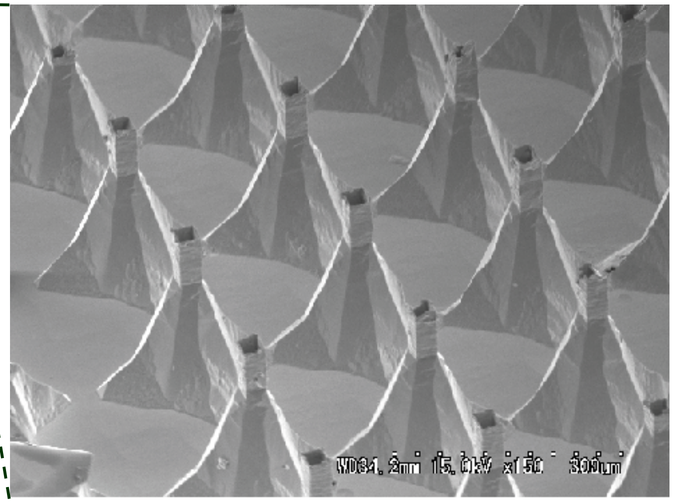
(a) Si mold formation by mechanical dicing and wet etching





(b) Pyramidal-shaped hollow needle formation by metal deposition and etching





M. Shikida, et al., J. Micromech. Microeng., 16, 2006, 2230-2239

Portable biochemical reaction system

Miniaturization of biochemical analysis system

⬇

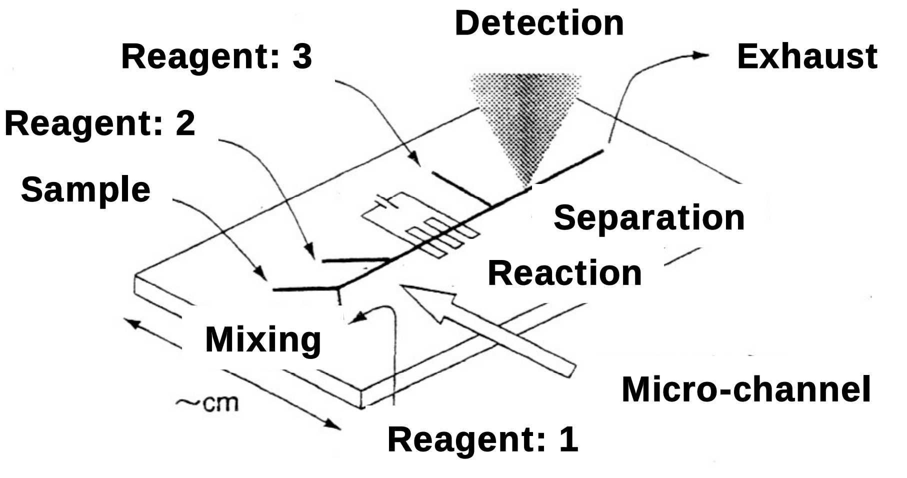
✓Reduction of reagent and waste
→ Reduction of environmental load
✓Portability（in-situ monitoring）
- ✓Medical doctor can give a diagnosis at clinic
- ✓Clinic can monitor health condition of a patient
- ✓Patient can do routine self-examination at home

✓Batch fabrication by MEMS technologies
- ✓Reduction of analysis time by parallel processing
- ✓Low cost

✓Reduction of heat capacity → Rapid reaction

Portable biochemical reaction system

Conventional Miniaturization of analysis system



Schematic view of conventional Micro-TAS

Passive elements:
- ✓Channel
- ✓Reactor
- ✓Heater

Active elements:
(Fluid machine)
- ✓Valve
- ✓Pump

Passive elements: channel, reaction-chamber

→Possible of their miniaturization

Active elements: pump, valve

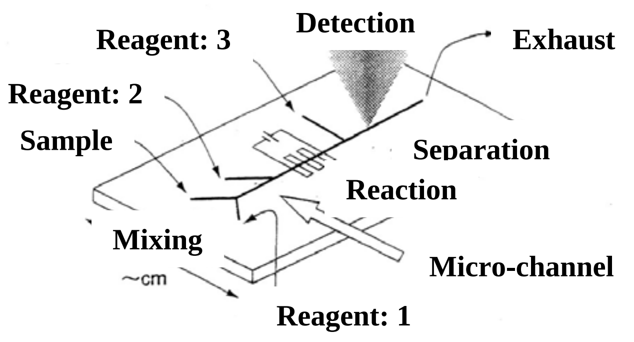
→**Difficult to obtain sufficient output power**

➡ ***Difficult to miniaturize whole system by conventional MEMS technologies***

Portable biochemical reaction system

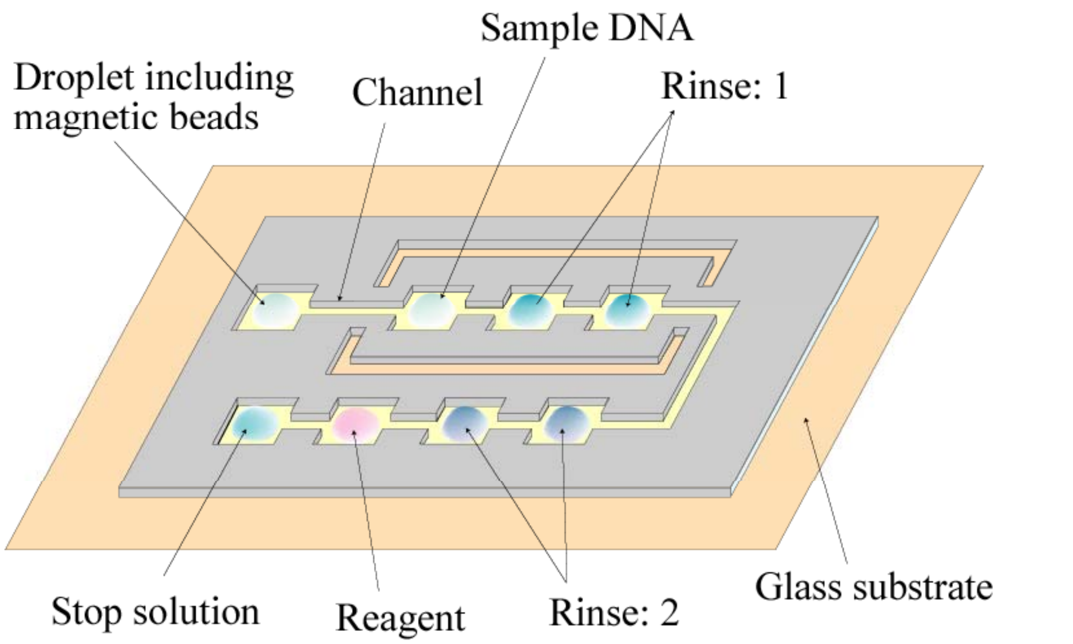
Droplet based reaction system

Continuous flow



Schematic view of conventional Micro-TAS

Droplet manipulation

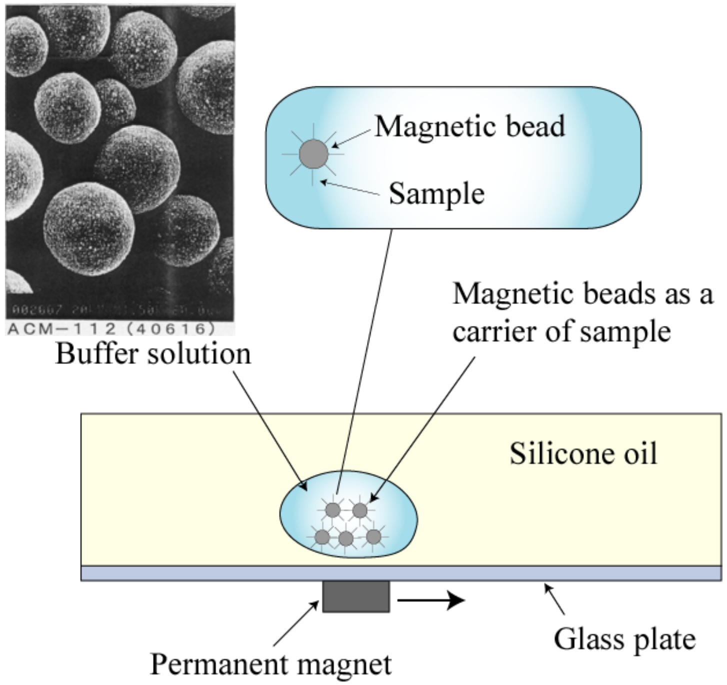


(1) Building reaction systems by a series of chemical droplets

(2) Proposal of magnetic beads as a sample carrier

Portable biochemical reaction system

Magnetic beads handling



(1) Magnetic beads
Works as a sample carrier

(2) Magnetic driving force
→enable a handling of electrolyte solution

(3) Droplet formation by two solution
Hydrophobic treatment of glass surface
→enable a forming of lubricant film on glass surface

→ This system can manipulate magnetic beads without sticking onto glass surface

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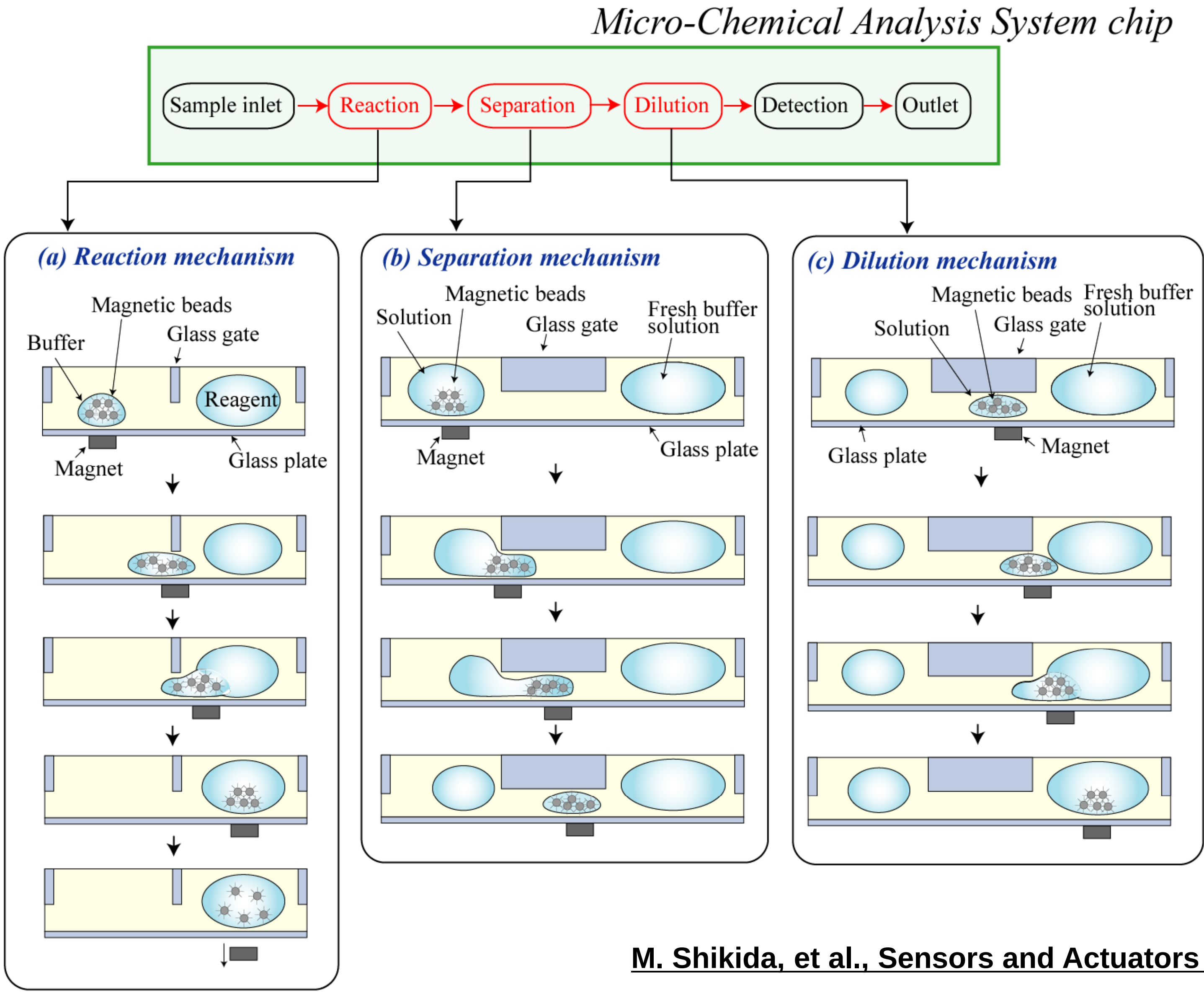
Portable biochemical reaction system

System configuration example



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Portable biochemical reaction system

Advantages

(1) Can miniaturize whole system, because it does not require active fluidic elements

(2) Can transfer magnetic beads selectively between droplets

(3) Can control dilution ratio by changing droplet volume (for example: x1000)

Portable biochemical reaction system

Beads: composite of magnetite and phenol-resin

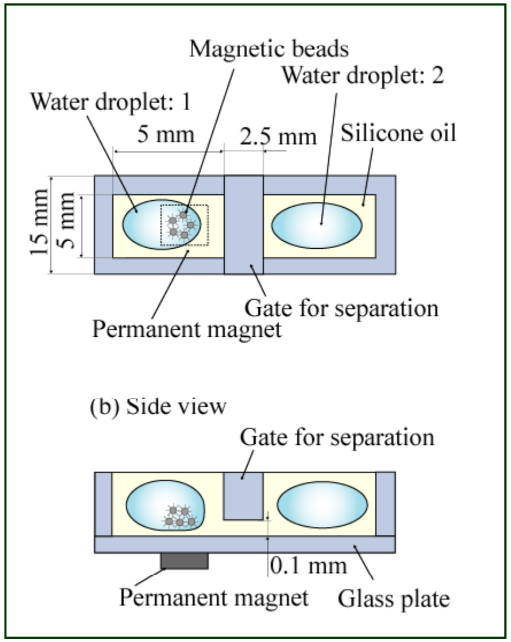
- ✓ Ferromagnetic material：Magnetite (diameter: 20nm)
- ✓ Resin：Phenol-resin（binder）

Magnetic properties

- ✓ Diameter d: 5.9-32.7 μm
- ✓ Density ρ : 3.62 g/cm^3
- ✓ Coercive force Hc: 3.6-5.9 kA/m
- ✓ Residual magnetization σ_r: 2.9-5.9 Am^2/kg
- ✓ Saturated magnetization σ_s: 73.2 Am^2/kg (0.33 Wb/m^2)

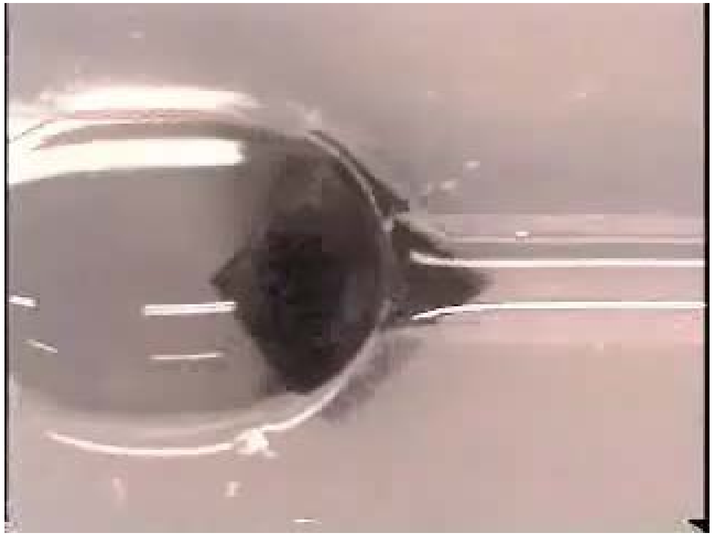
Portable biochemical reaction system

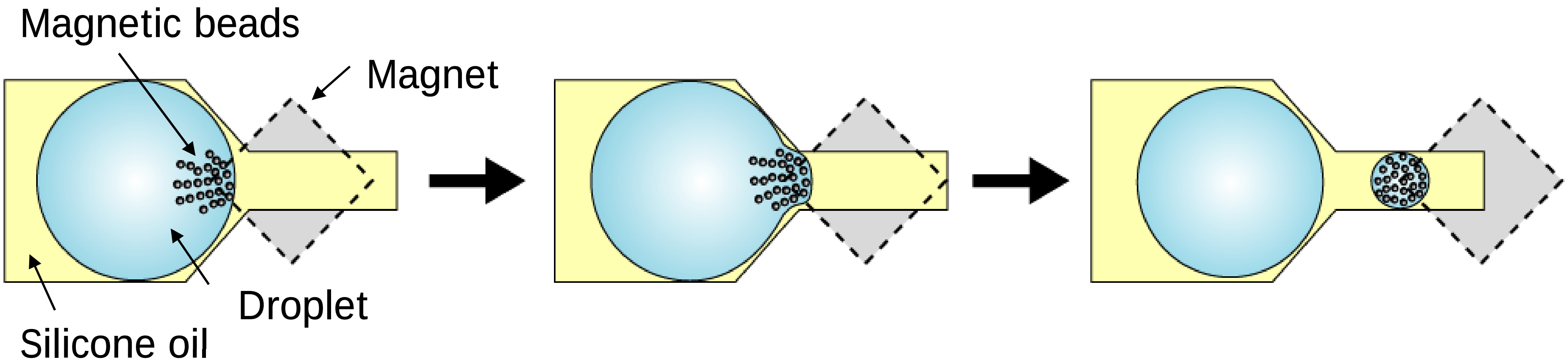
Magnetic beads operation



Planar type

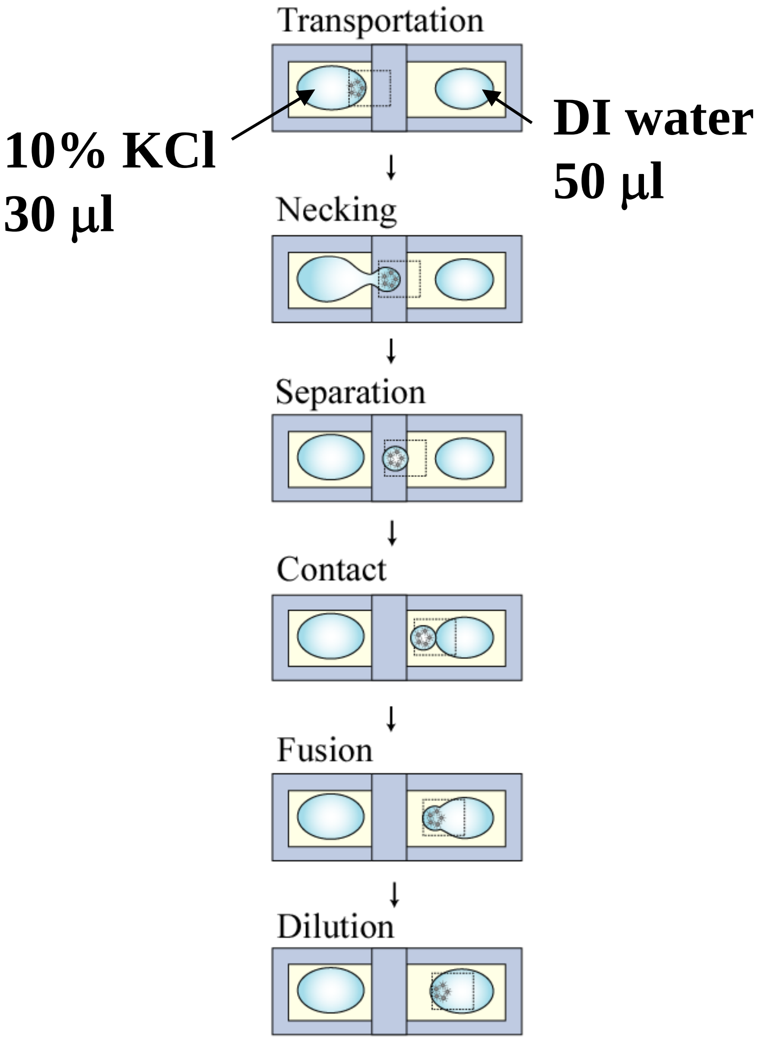
Enable batch fabrication by resin mold



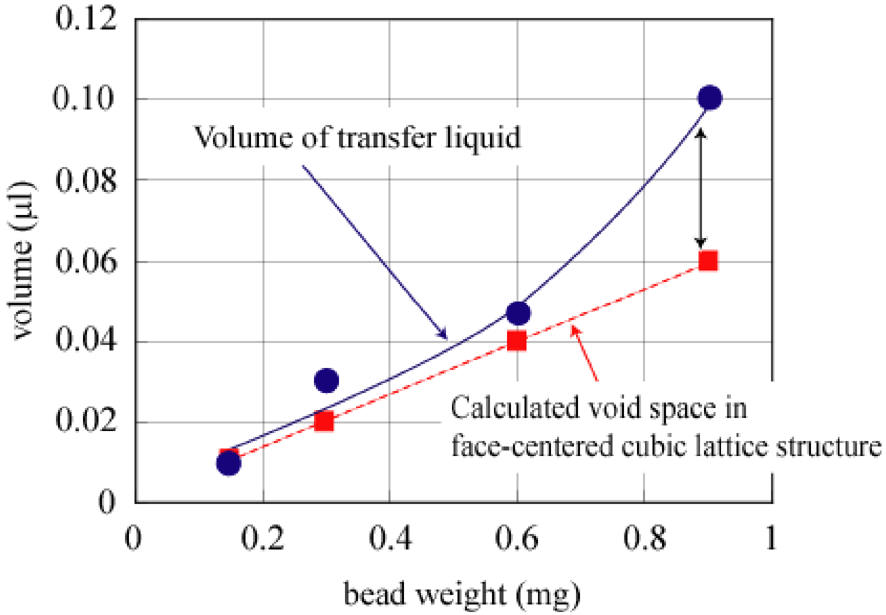


Portable biochemical reaction system

Associated fluid volume by beads extraction



(b) Schematic procedure of experiment
(Beads separation and dilution)



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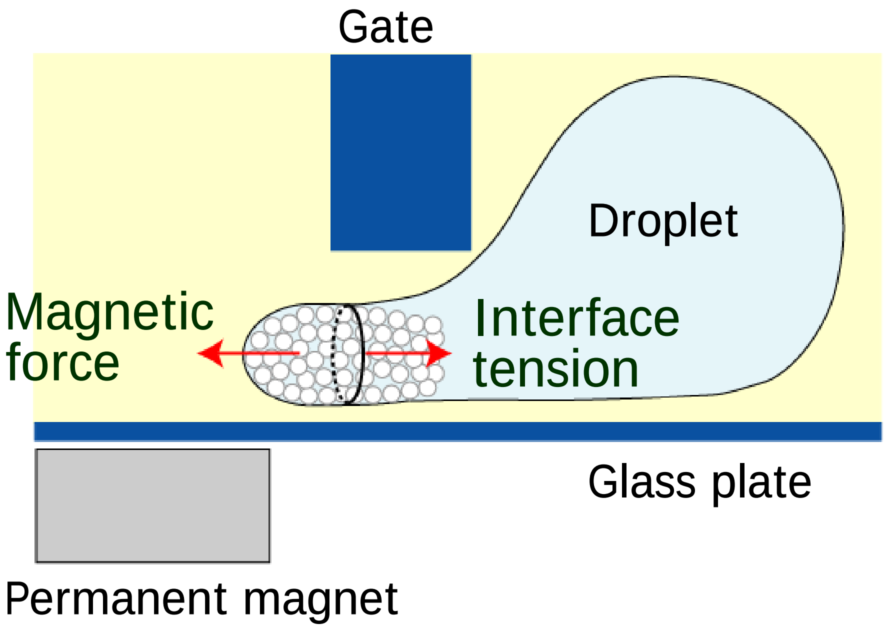
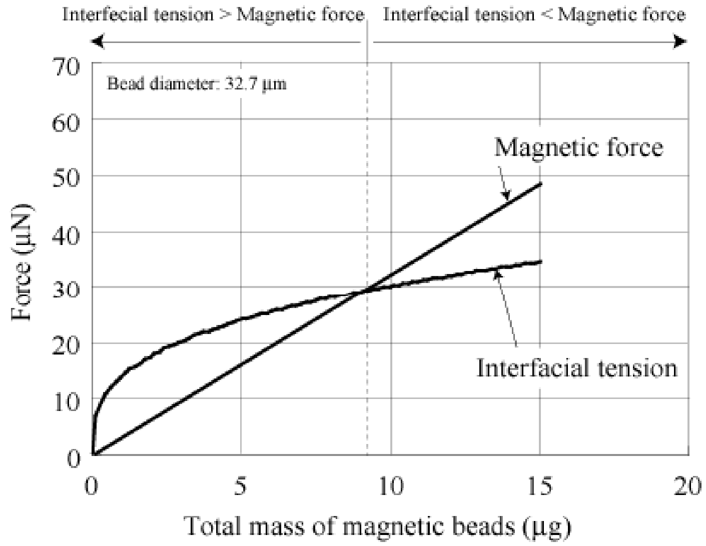
Portable biochemical reaction system

Mechanical model for extraction





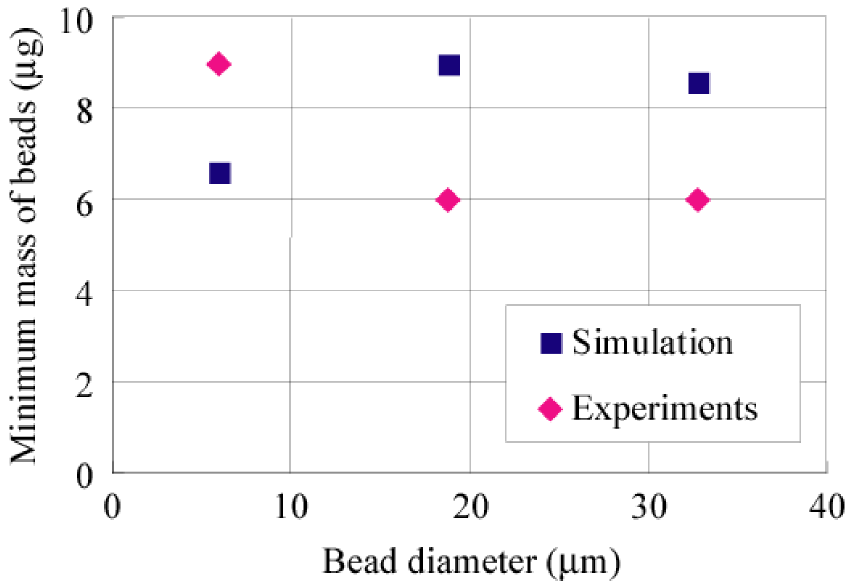
Magnetic force

$$F_m \propto V = \frac{M}{\rho}$$

vs.

Interface tension

$$F_i \propto V^{\frac{1}{3}} = \left(\frac{M}{\rho}\right)^{\frac{1}{3}}$$



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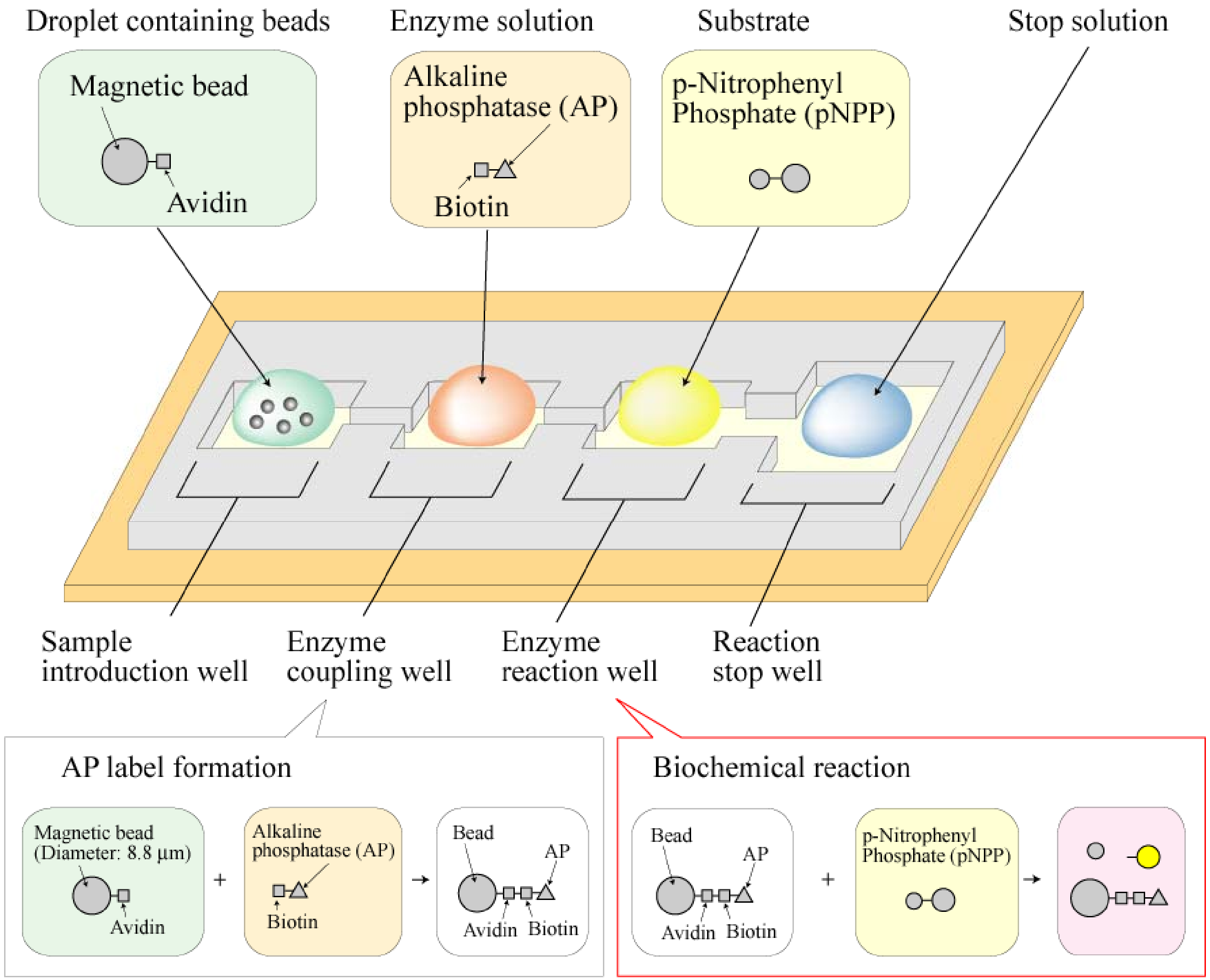
Portable biochemical reaction system

Enzymatic reaction by magnetic beads



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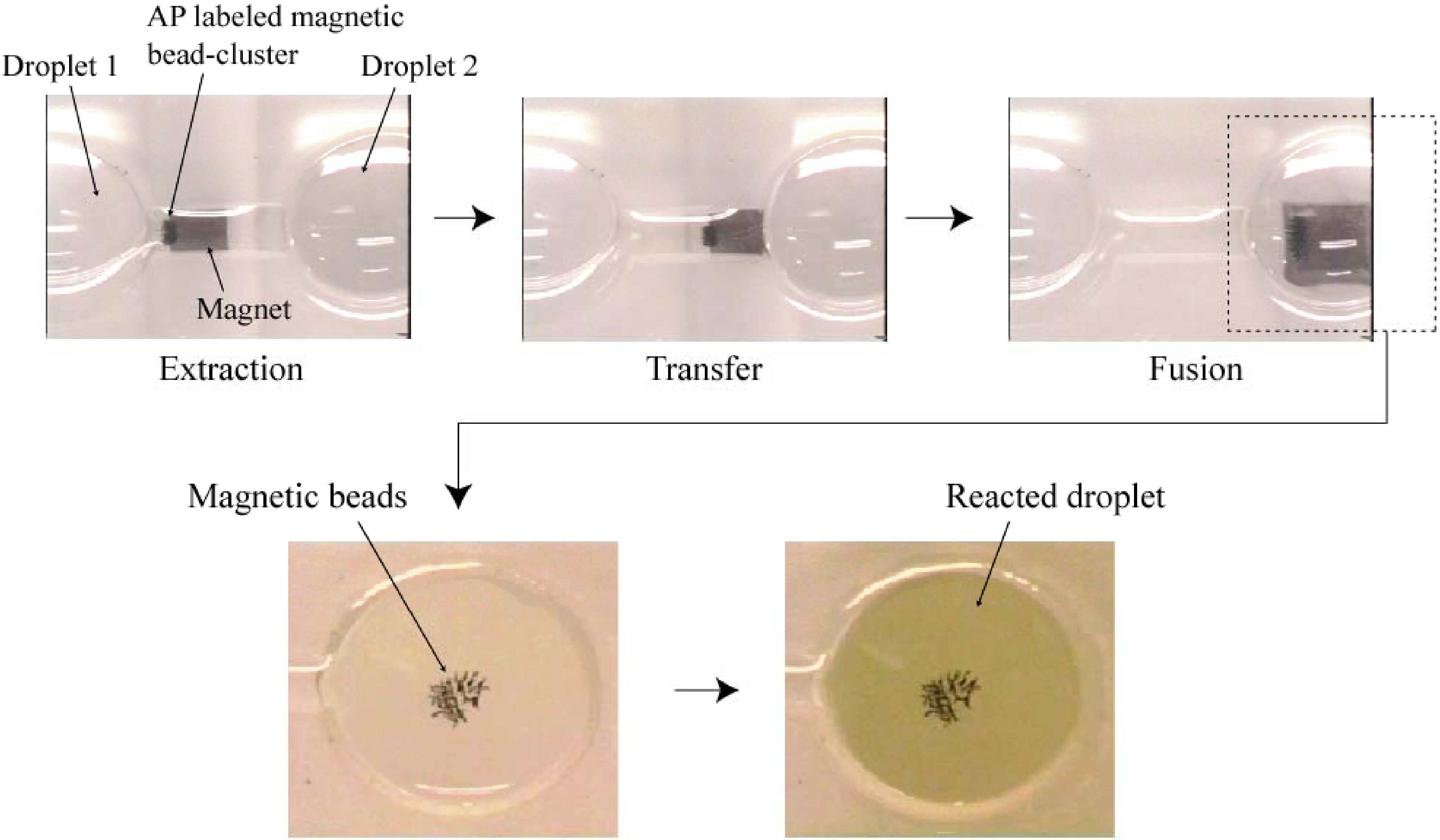
Portable biochemical reaction system

Enzymatic reaction



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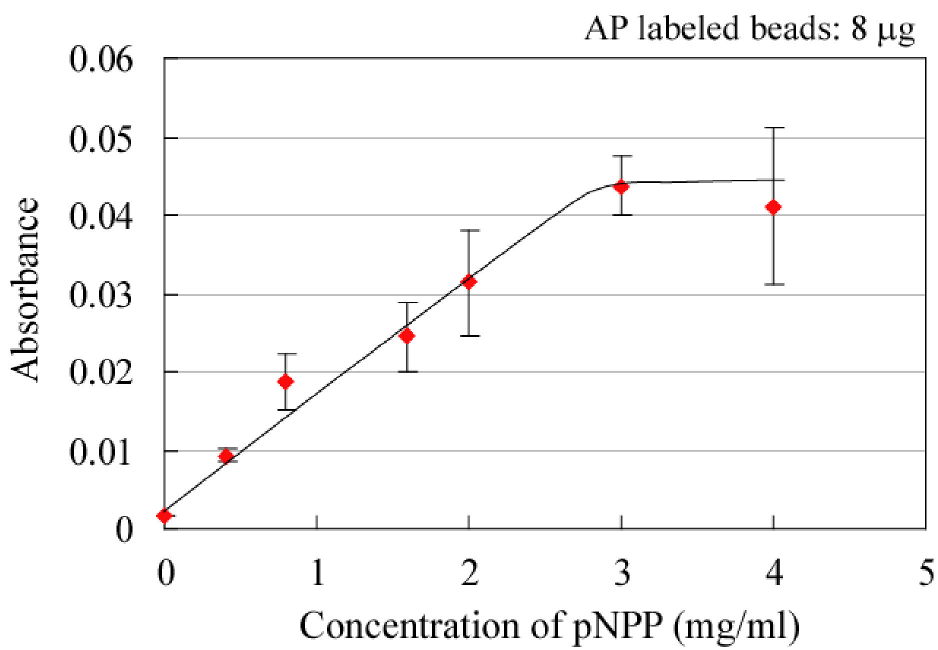
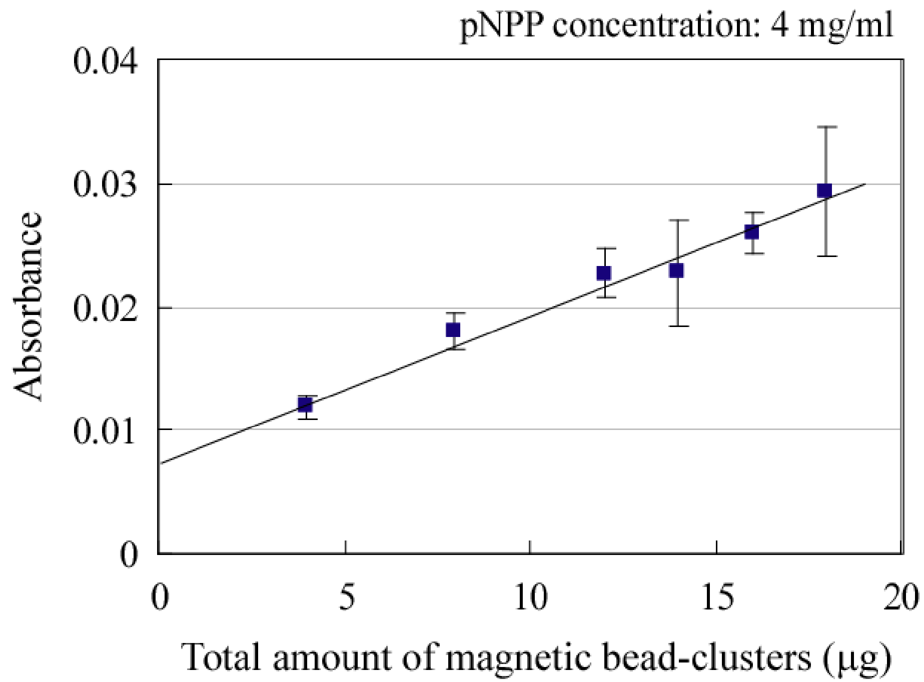
Portable biochemical reaction system

Enzymatic reaction





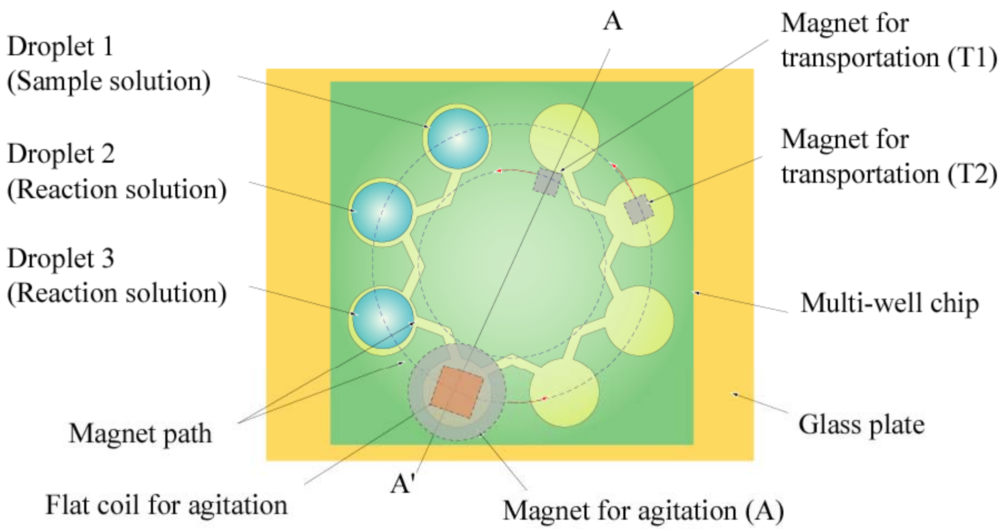
Beads labeled by enzyme : 8 μg
Reaction time : 20 min.

Substrate concentration : 4 μg/ml
Reaction time : 20 min.

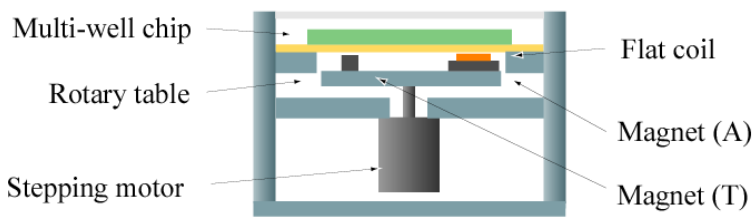
M. Shikida, et al., J. Micromech. Microeng., 16, 2006, 1875-1883

Portable biochemical reaction system

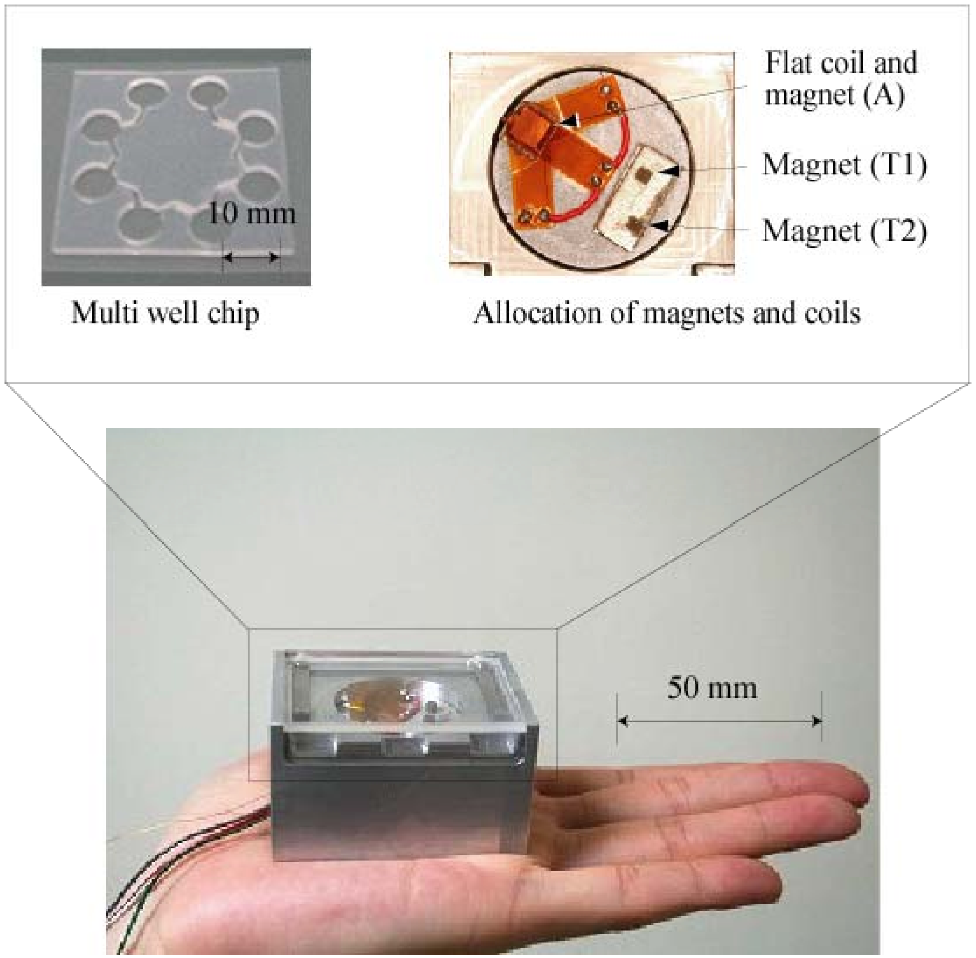
Palm-top sized beads handling system



(a) Chip design and magnets



(b) A-A' Cross-section view of the



<u>M. Shikida, et al., J. Micromech. Microeng., 18, 2008, 035034 (8pp)</u>