A Disposable BioChip for DNA Sample Preparation

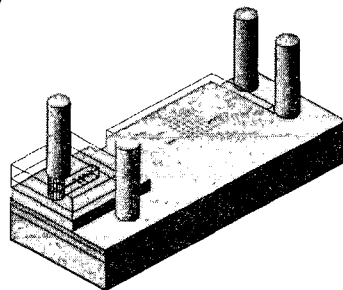**Euisik Yoon**

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KAIST

Portable Microsystem-on-a-Chip

Microfluidics

Micro Pump
Micro Mixer
Micro Filter
Micro Valve

Micro Reactor

DNA Purification Chip
Micro PCR

Micro Detector

Wireless Communication

Micro Power Source

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Microsystem-on-a-Chip Application Using 3-D Microstructures

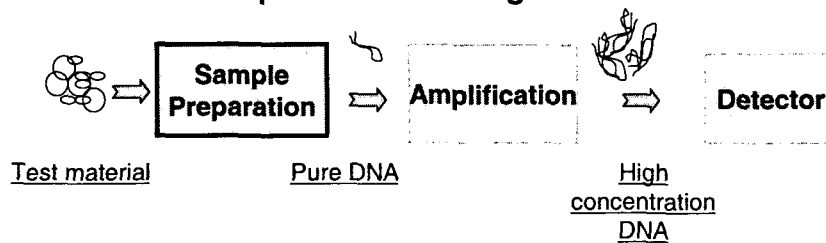- Disposable DNA purification chip

- Micro Mixer

- Micro Pump

- Micro Power Source

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DNA Sample Preparation for Genetic Analysis

- **Process steps of DNA testing**

| Test material | Pure DNA | High concentration DNA |

Sample Preparation ⟹ Amplification ⟹ Detector

- **Sample preparation step**

  □ **Complex, labor intensive, time consuming**

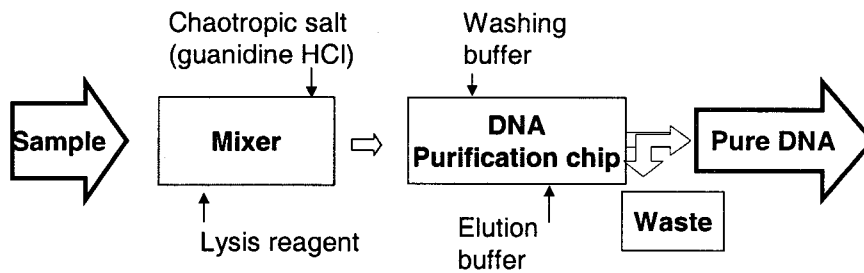 □ **Most difficult step to be automated in DNA testing**

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Proposed Microfluidic Chip for DNA Sample Preparation

- Process steps of DNA testing

Inlet   DNA binding chip   Outlet

Mixer

PDMS

- Work Flow

Sample ⟹ Mixer ⇒ DNA Purification chip ⇒ Pure DNA

Chaotropic salt (guanidine HCl) → (into Mixer)

Washing buffer → (into DNA Purification chip)

↑ Lysis reagent (into Mixer)

Elution buffer ↑ (into DNA Purification chip)

Waste
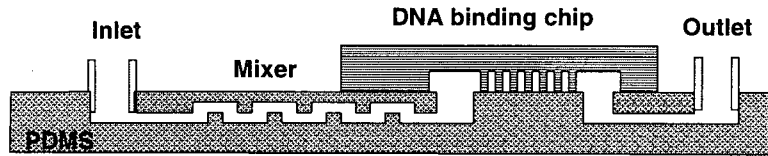
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Mechanism of DNA Binding to Silica (SiO_2)

D.I. Water + DNA + Silica

Silica (SiO_2) —OH H_2O / —OH / —OH H_2O / —OH / —OH H_2O / —OH / —OH H_2O / —OH

H_2O H_2O DNA H_2O H_2O DNA H_2O H_2O H_2O
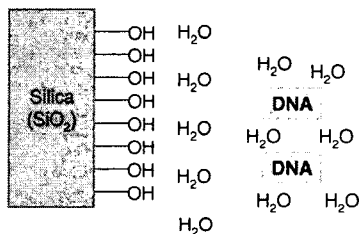
Chaotropic salt (Guanidin HCl, NaI) + DNA + Silica

Silica (SiO_2) —OH----PO_4 \ Sugar / Base / —OH / —OH----PO_4 \ Sugar / Base / —OH / —OH----PO_4 \ Sugar / Base / —OH / —OH----PO_4 \ Sugar / Base / —OH
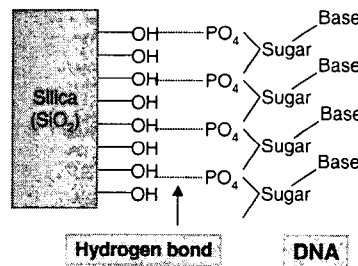
Hydrogen bond   DNA

- Chaotropic salt disruption of the water structure around silica surface and DNA
- Silica and DNA dehydration effects and intermolecular hydrogen bond formation drive DNA adsorption to the silica surface

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DNA Purification Chip Using Photosensitive Glass

- Simple and inexpensive process
- DNA will bind to exposed SiO_2 surface
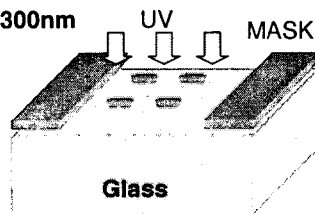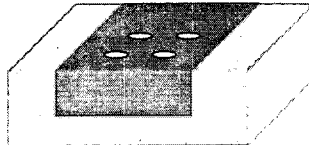- Micro Pillar Structure : Increase the binding surface area

PDMS
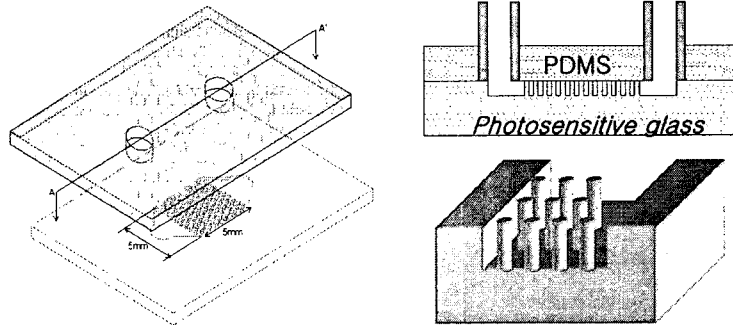
Photosensitive glass

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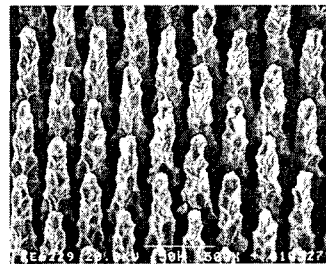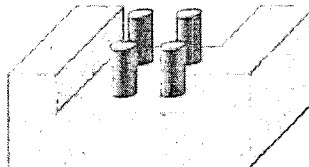# Photosensitive Glass Process for 3-D Microstructures

(a) UV exposure 300nm   UV   MASK

Glass

(b) Crystallization 500~600°C

(c) Etch 10%HF

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Fabrication Results
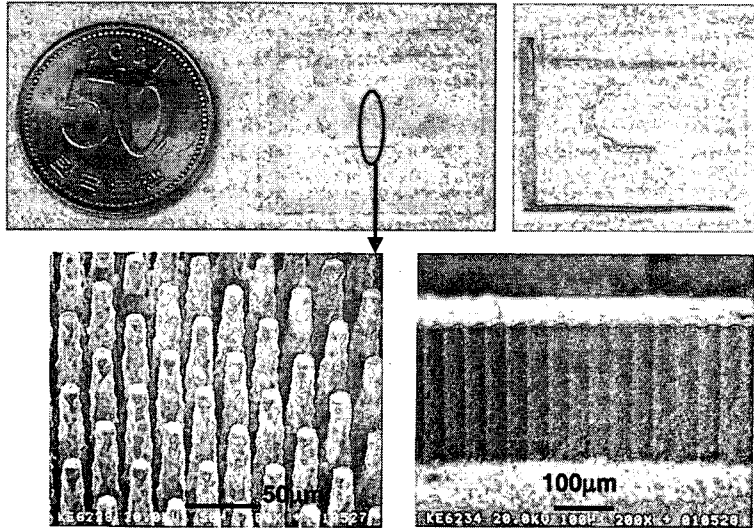
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DNA Purification Chip Test

Syringe Pump

Elution solution
D.I. Water

DNA/salt mixture

Silicone tube

Washing solution
(80% Ethanol)

High concentration input

Electrophoresis
(EtBr stained Gel)
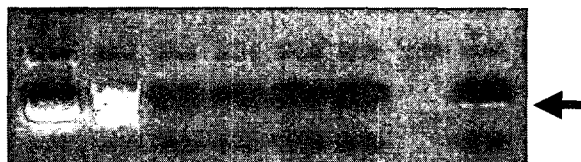
PCR

Low concentration input
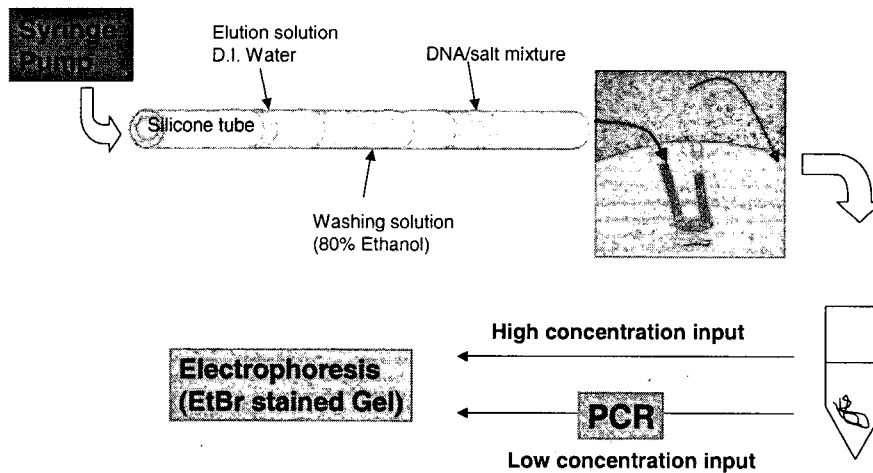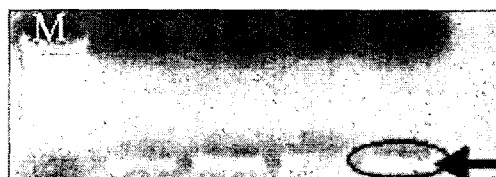
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Characteristics of Fabricated DNA Purification Chip

¦ High concentration input test : 600ng/200ul

¦ Low concentration input test (with PCR) :
100copies/200uL

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Characteristics of Fabricated DNA Purification Chip

	High concentration	Low concentration
Starting DNA	4789bp, plasmid circular dsDNA	
DNA/Salt Mixture	200μL	
DNA concentration	**600ng/ μL**	**100copies/200 μL**
Guanidine HCl concentration	4.8M	4.8M
Wash solution	400 μL 80% Ethanol	
Elution solution	40 μL D.I. Water	
PCR	No	30cycles

■ **Binding Capacity : 15ng/cm^2**

■ **Minimum Extractable Input Concentration :**
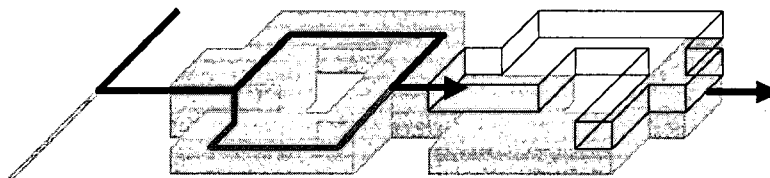**100copies/200 μL (5pg/200 μL)**

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Micro Mixer

■ **Mixing is necessary in the microfluidic systems**

　□ **Biochemistry analysis, drug delivery, sequencing or synthesis of nucleic acids**

■ **Small dimension**

　□ **Low Reynolds number - laminar flow**

　□ **No turbulence**

　□ **Mixing dominated by diffusion**

■ **Active mixer**

■ **Passive mixer**

Passive Micro Mixer with PDMS
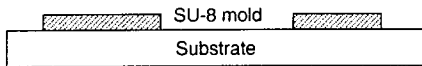
■ **Schematic of Micro Mixer**

• **Easy to fabricate**

• **Low cost**

• **Enhancement of mixing performance by increasing of diffusion area**

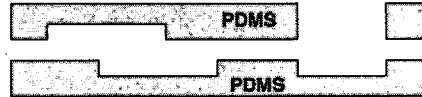• **Easy to integrate with micro fluidic system**

PDMS Microstructures Fabrication Process

1. SU-8 Mold Petterning

SU-8 mold

Substrate

2. Curing PDMS

PDMS

Substrate

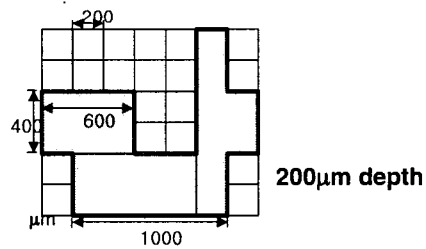**3. O₂ Plasma Treatment**

PDMS

PDMS

4. Bonding

Silicone tube
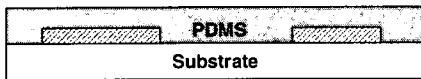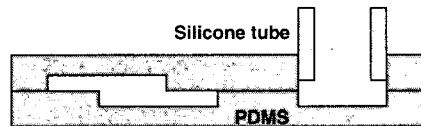
PDMS

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Fabrication of Micro Mixer

■ **PDMS channel structure**

200

400

600

1000

μm

200μm depth
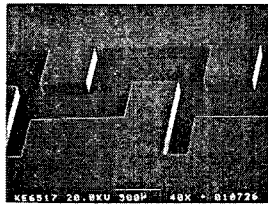
■ **Fabricated micro mixer & test bench**
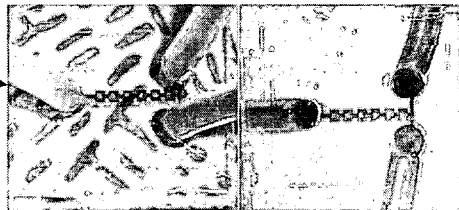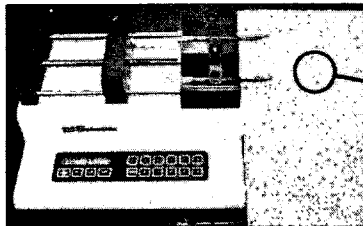
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Mixing Performance Test

■ **Results of mixing test**
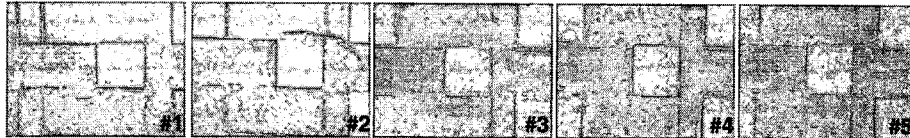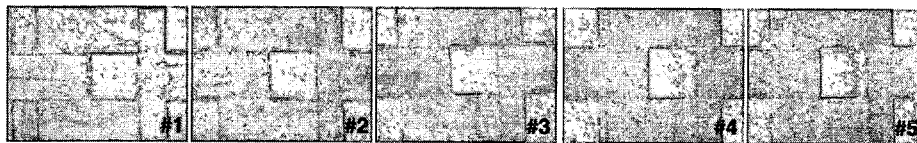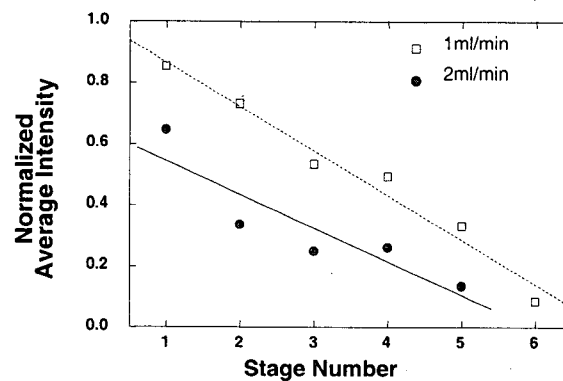**(test solution : Phenolphthalein solution + NaOH solution)**

1mL/min (Re=27)

2mL/min (Re=55)

Characteristics of Micro mixer

❏ **Mixing time 0.12sec (Re=27)**

Micropump

■ Critical component that exerts a pressure on liquids to transport reagents or control liquids

Inlet → Outlet

Micro Actuator

Generalized schematics of membrane type micropump
with passive check valves
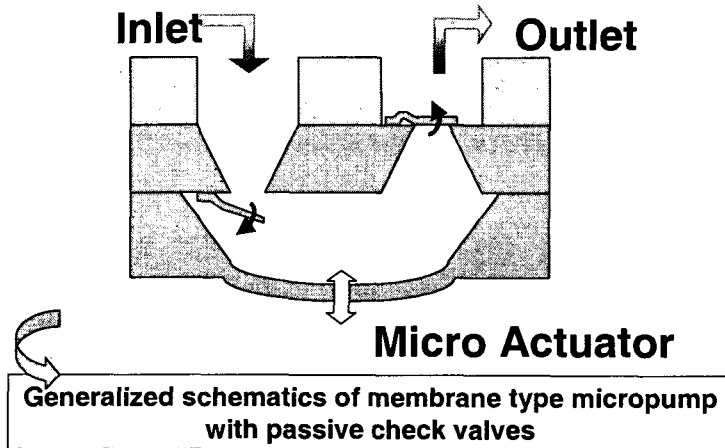
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Micro Actuators

Actuation Type	Pressure	Displacement	Response time	Operation voltage	Power consumption
Piezoelectric (Stack type)	very large	very small	fast	very large	small
Electrostatic	small	very small	very fast	very large	small
Thermo - pneumatic	large	medium	medium	medium	large
Electro - magnetic	small	large	fast	small	large
Bimetallic	large	small	medium	large	medium
SMA	large	-	-	-	large

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Micropump driven by Surface Tension

Electric Potential Gradient	⇒	Surface Tension Variation	⇒	Motion of Liquid Drop

Low Voltage and Low Power Operation

V

Electrode x Electrolyte

Hg

Motion

High surface tension   Low surface tension
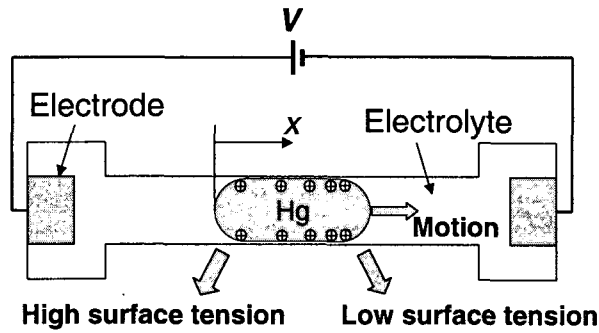
Design and Operation of Micropump

Inlet   Silicone tube channel   Outlet

Cu flap valve

Si

Si

SU-8   (Hg)   SU-8   (Hg)

Glass   Glass

Pt electrode   Electrolyte filling   Silicone rubber membrane

Fabrication Results

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Experimental Results

- $V_{app} = 2.3$ V
- $V_{app} = 2.0$ V
- $V_{app} = 1.7$ V

Flow rate (μl/min)

Frequency (Hz)
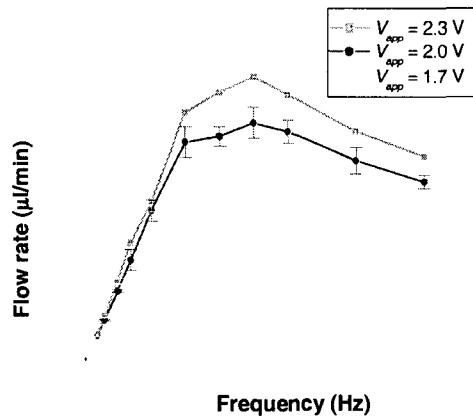
- *Operating voltage : 2.3 V*
- *Power consumption : 170μW*
- *Maximum flow rate : 70 μl/min*

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Micro Power Source

■ **Candidates for micro power source**

Device	Power Density (MW/m³)
Micro-lithium battery	0.4
Micro solar cell	1
Micro-electric motors	1.7
Micro reactors	20
Micro-magnetic motors	200
Micro-combustors	2000

◘ High power density
  - light weight
  - small size
◘ Long operation time

=> *Micro Combustion*
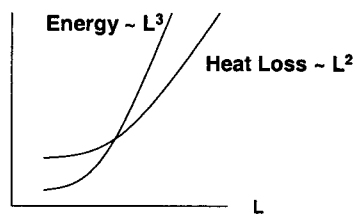 *Engine* is one of the
  prospective solutions due
  to *its high power density*

Scaling of Micro-combustor

■ **Combustion Power vs. Heat Loss**

Energy ~ L^3

Heat Loss ~ L^2

L

■ **Material Selection of Engine Body**
  ◘ Thermal insulator, Electrical isolator → Glass

■ **Scaling Combustor Dimension**
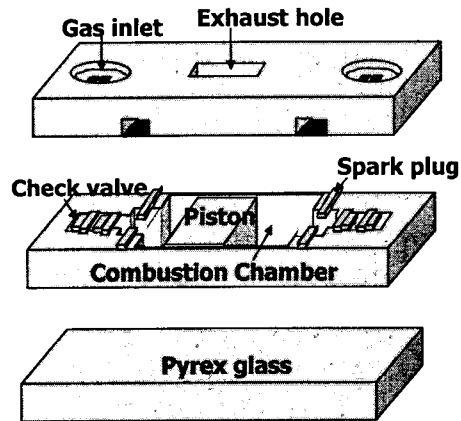 ◘ Larger than critical quenching distance

Micro Combustion Engine

■ **Piston Reciprocating Type Engine**

　□ **Utilization of linear piston movement**

Gas inlet　Exhaust hole

Check valve　Spark plug

Piston

Combustion Chamber

Pyrex glass
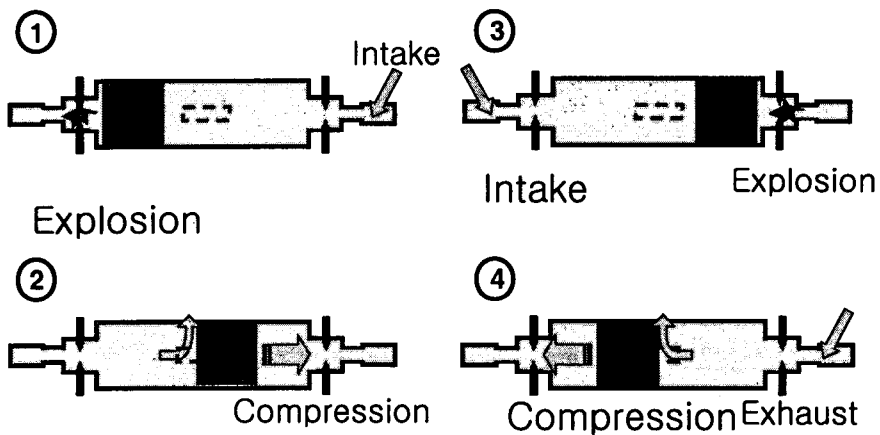
　□ Epoxy bonded 3 layers

　　- 2 photosensitive glasses

　　- 1 pyrex glasses

　□ High aspect ratio

　□ Isolation between substrate

　　and spark plugs

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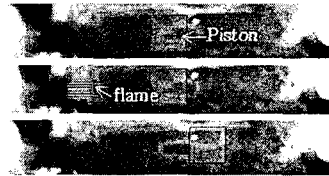# Operation Sequence of Micro Combustion Engine

① Explosion

② Compression

Intake

③ Intake　Explosion
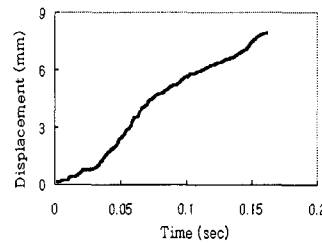
④ Compression Exhaust

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One-shot Combustion Test

- H_2 : Air(27 : 73)
- 1 atm.
- Breakdown voltage = 1670 V

- Displacement curve of piston

< Fabrication Result>   < One-shot combustion test >

Conclusions

- **Simple and low cost technologies for 3-D microstructures**
  - MESD & electroplating
  - PDMS
  - Photosensitive glass

- **Demonstration of several components for Lab-on-a-chip**
  - Disposable DNA purification chip
  - Passive micromixer with PDMS
  - Micropump driven by surface tension variation
  - Micro combustion engine