MEMS for Bio Applications

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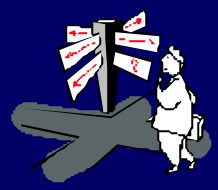
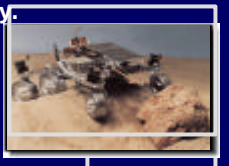


Applications of MEMS

Applications of MEMS

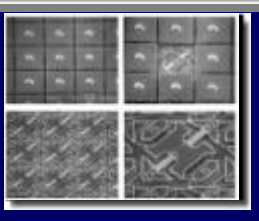
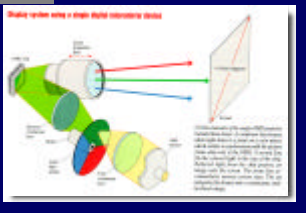
- MEMS has been developed as a break-through technology.





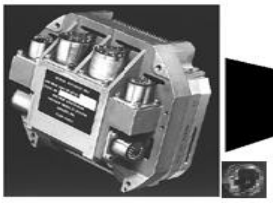

- Pressure sensors
- Accelerometer
- Gyroscope
- Digital Micromirror Device
- Inkjet Head
- Optical Switch



Conventional vs. MEMS Inertial Measurement Units

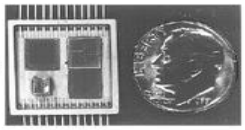
Conventional



Mass : 1587.5 grams
Size : 15 cm x 8 cm x 5 cm
Power : 35 W
Survivability : 35 G's
Cost : $ 20,000

MEMS

Inertial Measurement Unit



Mass : 10 grams
Size : 2 cm x 2 cm x 0.5 cm
Power : ~ 1 mW
Survivability : 100 kG's
Cost : $ 500

- The merits of MEMS are to be small, light, cheap, multi-functional and integrated with mechanical and electronic components.

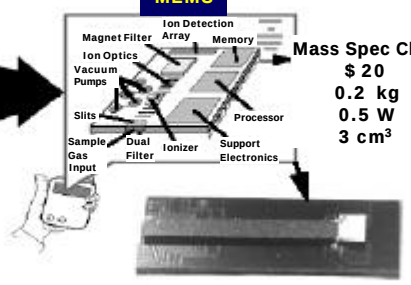
From DARPA

Mass Spectrograph on a Chip

Conventional

$ 17,000
70 kg
1,200 W
20,000 cm^3

MEMS



Mass Spec Chip
$ 20
0.2 kg
0.5 W
3 cm^3

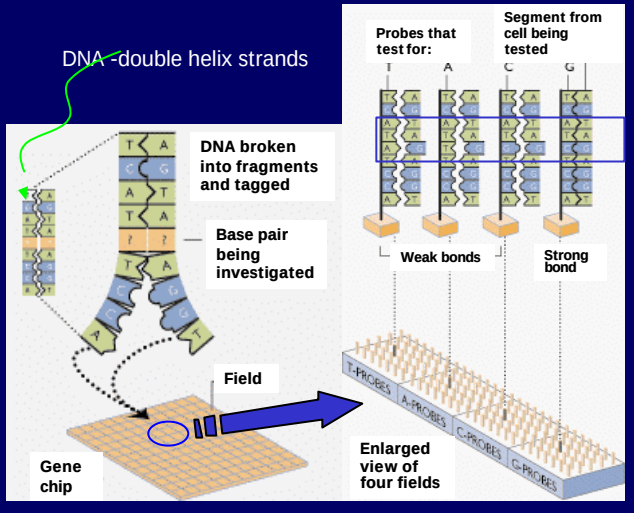
From DARPA

- Mass spectrograph on a chip will be integrated with vacuum pumps, ionizer, an ion detector array, and control electronic circuits.
- The MS on a chip enables potable measurement units and point-of-care will be available.

- BioMEMS provides new methodologies to the biotechnology.
- For examples, lab-on-a-chips, Affymetrix DNA chips, and high throughput screening chips continue to evolve the biotechnology.

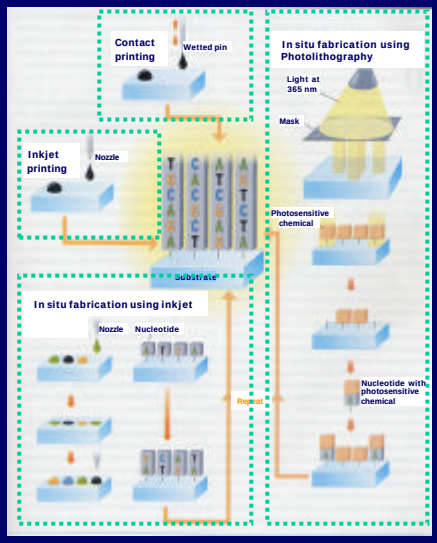
Bio Applications : Peptide Micro Array Synthesized using Micromirror Array

DNA Micro Array



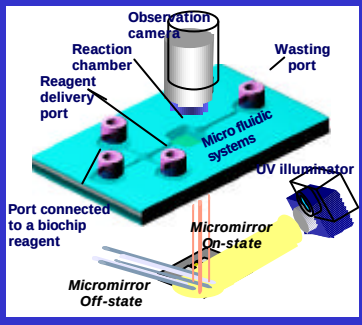
- **DNA micro arrays**
  - DNA sequencing assay
  - Microfabrication
    - (a) Contact printing
    - (b) Inkjet printing
    - (c) In situ fabrication using inkjet
    - (d) In situ fabrication using photolithography
- **Merits**
  - One chip assay
  - Performance is improved
  - Assay time and cost are reduced
  - Easy manipulation

Making Micro Arrays

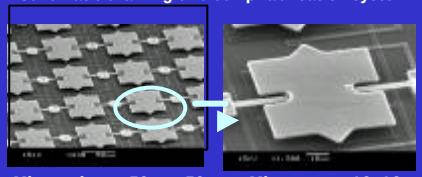


- **Making micro arrays**
  - Just printing
    - (a) Contact printing
    - (b) Inkjet printing
  - In situ fabrication
    - (c) In situ fabrication using inkjet
    - (d) In situ fabrication using photolithography
- **In situ fabrication using photolithography**
  - Light at 365nm is shone through a mask.
  - The light releases the capping chemical, exposing parts of the substrate.
  - A solution is then washed over the substrate.
  - The nucleotides attach to the unprotected sites, adding their own capping layer.
  - The process is repeated, building up sequences of DNA.
- **Suitable to mass production with the same sequence.**

Synthesis of Peptide Micro Array using Micromirror Array



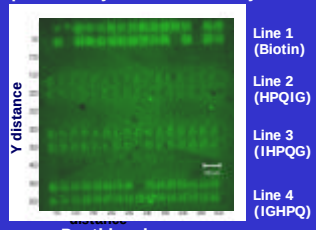
Schematic drawing of biochip fabrication system



Mircromirror : 50 ㎛ x50 ㎛ Mirror array-16x16

3 x 3 units operation (1 unit : 2 x 2 mirrors)

Photoresist(AZ1512) patterns produced by micromirror array



Peptide micro array

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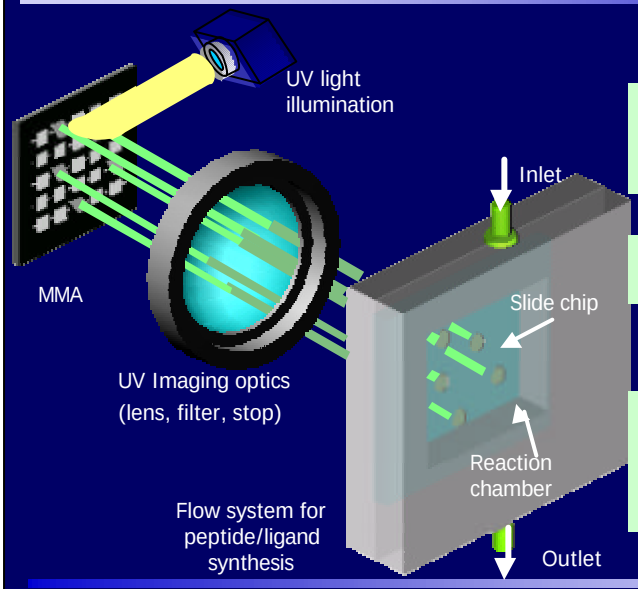
MMA Systems for Peptide Synthesis on a Chip



- Virtual mask pattern generator
  - Micromirror array(MMA)
- UV imaging optics for MMA photolithography
- Flow cell for surface synthesis chemistry
  - Reagent delivery to the flow cell

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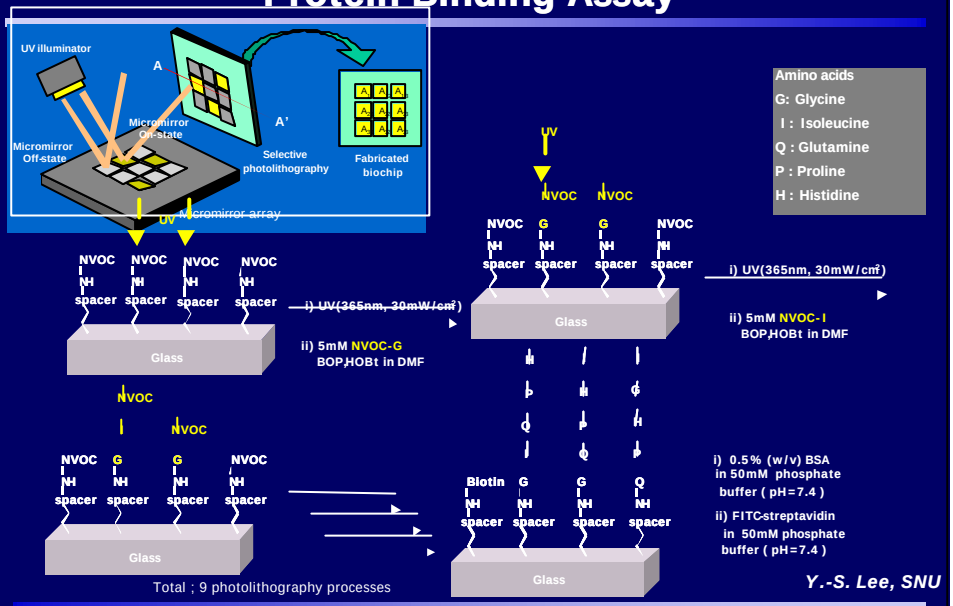
Peptide Array Synthesis on a Chip using MMA and Protein Binding Assay



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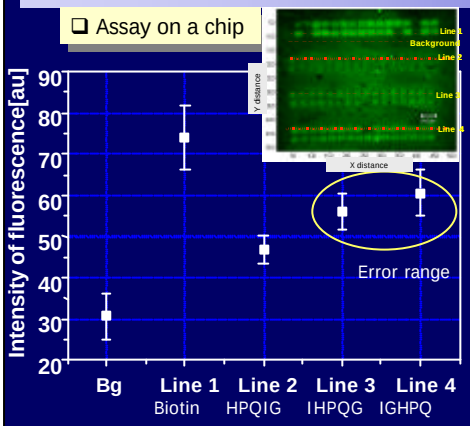
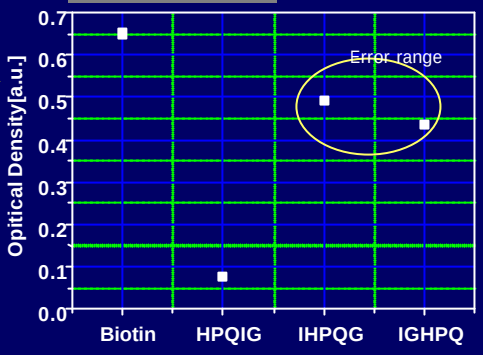
Ligand Interaction using MMA

❑ Assay on a chip



❑ Assay on beads



- ❑ Fluorescence assay v s Enzyme assay
- ❑ Sensitivity & S/N
- ❑ One chip analysis v s 4 times ELISA with sophisticated controlled condition

Assay time(labor) reduced (<1/7days), Convenience(automated synthesis by MMA systems), Improvement of assay reliability by comparison on a chip

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Merits of the Synthesis using MMA

	On resin(bead)	On surface(chip)	Comments
	NH_2	NH_2	
Surface density	0.1 mmol/g	1 nmol/ cm^2	
Quantity	resin 500 mg	5 mM solution in 200 μℓ flow cell	
Required amino acid	150 μ mol / reaction	1 μ mol / reaction	
Application example	GIQPH QPHGI GQPHI	GIQPH QPHGI GQPHI	100 mg resins for each penta peptide for 3 kinds of sequence G:Glycine, I: Isoleucine, Q: Glutamine, P: Proline, H: Histadine
Reagent quantity (Amino acids)	15 times x 150 μ mol = 2250 μ mol	15 μ mol	3 sequences x penta peptide = 15 times
Assay time (labor)	~ 7 days	< 1 day	affinity assay of streptavidin

- The MMA system provides the flexibility on biopattern design and fast turn-around analysis.

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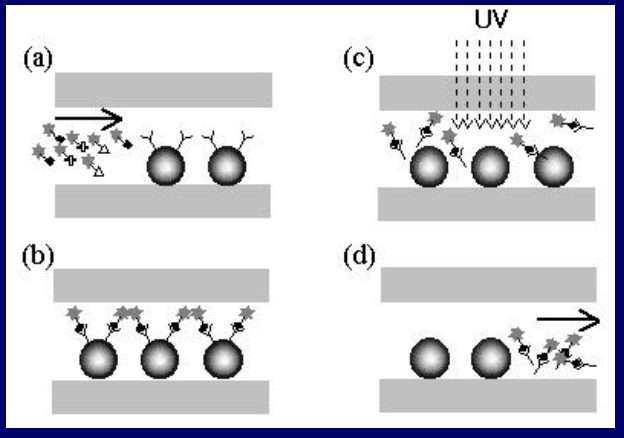
Bio Applications : Bead Affinity Chromatography Chips

Bead Affinity Chromatography (BAC)

- BAC chips are based on the idea using a large surface area of beads to analyze bio target molecules in a low concentration.
- Silicon and glass based micromachining makes the reaction chamber packed micro beads and micro channels.



(a) Injection biosamples
(b) Concentration & separation of target protein
(c) Elution of target protein using UV cleavage
(d) Analysis of target protein using mass spectrometry or fluorescence

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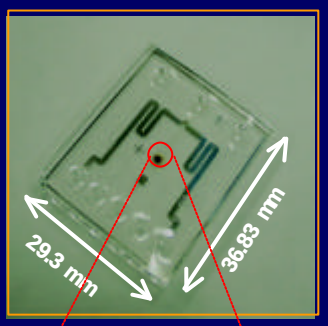
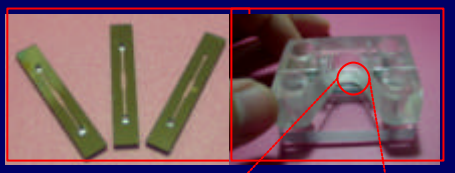
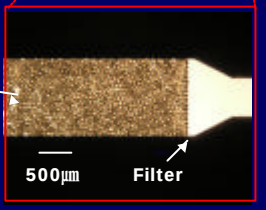
Micro Bead Affinity Chromatography Chips





Micro Beads

Left : magnetic bead
Right : CutiCore bead



Reactor depth 50㎛
Total volume : 1 ㎕

Reactor depth 100㎛
Total volume : 0.4 ㎕

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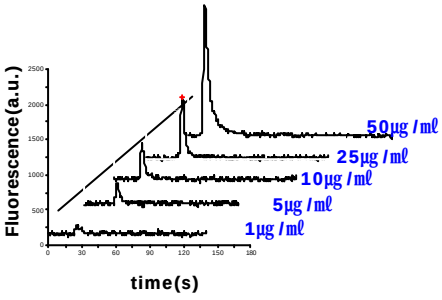
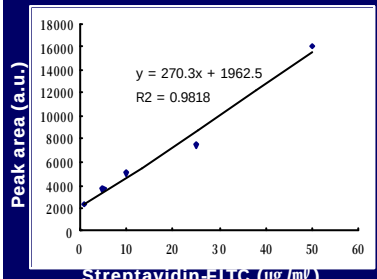
Quantitative Analysis
Streptavidin-Biotin Model System

- Packed bead (40 ㎕ of 0.33 % bead suspension), BSA blocking (20 min),
- Sample injection and reaction (30 min), room temperature
- Streptavidin-FITC (1 - 50 ㎍/㎖) / PB (pH 7.4)
- UV irradiation for 30 min and elution with PB

Chromatogram of eluted protein





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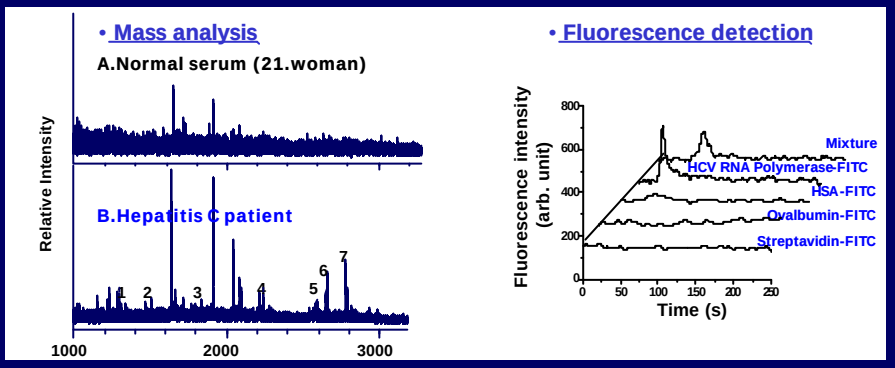
HCV RNA Polymerase Detection and Analysis by MALDI-TOF & Fluorescence

- To show the feasibility, we tested the HCV RNA polymerase detection.
- With MALDI and fluorescence detection, HCV RNA polymerase are detected, even in cocktailed samples.



1.1311.961(LPINALSNSLLR)
2.1511.846(YLFNWAVKTKLK)
3.1835.717(WEYVLLFLLLADAR)
4.2234.996(LNAACNWTRGERCDLEDR)
5.2585.975(SLTERLYIGGPLTNSKGQNCGYR)
6.2651.06(CRASGVLTTSCGNTLTCYLKASAACR)
7.2779.324(ALDCQIYGACYSIEPLDLPQIIER)

❖ 100 - 200 fmol/μℓ of HCV RNA polymerase was detected

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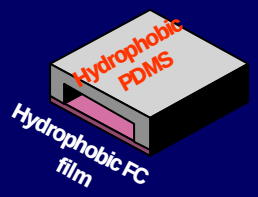
Bio Applications : Enzyme Reaction in a Micro Fluidic System

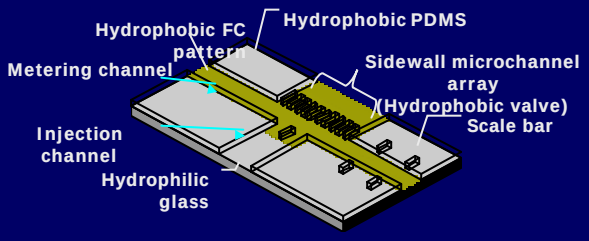
Variable Metering using a T-shaped Microinjecor with Sidewall Microchannel Array

- Nanoliter droplets are controlled using the surface property such as hydrophobic and hydrophilic.

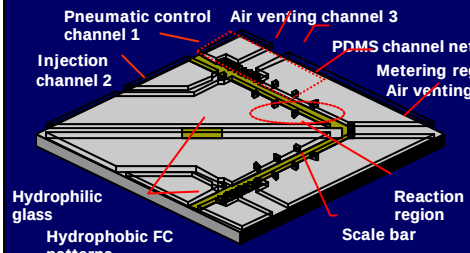


$$P = g\cos q_{PDMS}\left(\frac{2h+w}{hw}\right) + g\cos q_{FC}\left(\frac{w}{hw}\right)$$

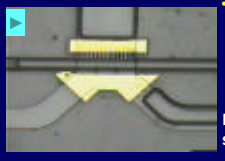
A negative pressure indicates a repellent force at the solid-liquid-gas interface.

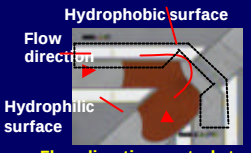


Enzyme Reaction in a Micro Fluidic System

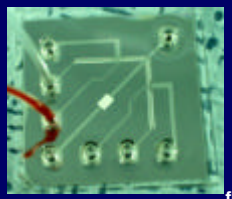


• Nanolitermeasuring step

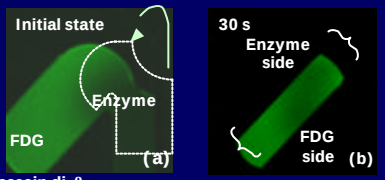




• Flow direction control step



Fabricated device



fluorescein di-ß-galactopyranoside

Reaction on a micro fluidic system

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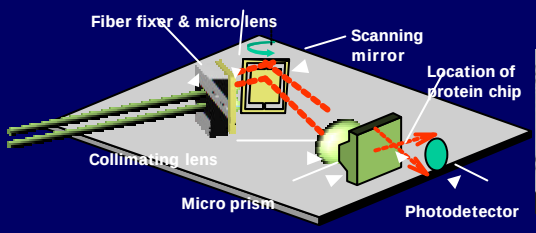
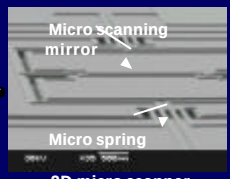
Bio Applications : Measurements using Optical MEMS Components

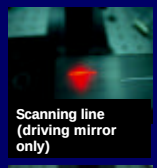
Bio Measurements using Optical MEMS

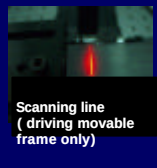


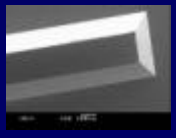
Schematic drawing of Bio Measurements



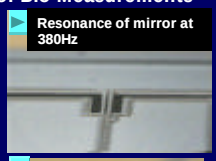
2D micro scanner
Mirror : 3.5 mm x 3.5 mm







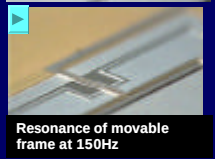
Micro prism (PMMA) fabricated using hot embossing



1. 2D surface scan (silicon spring)
2. 1:2 freq. ratio (silicon spring)
3. 1:2 freq. ratio (polymer spring)
4. 2:5 freq. ratio (polymer spring)

Lissajous pattern illuminated using micro scanner

Micro lens (PMMA)



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Summaries

- MEMS technology provides the strong methodologies to biotechnology, life science and chemical engineering.
- Nanotechnology will also be a break-through technology to biotechnology.

- Acknowledgements
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- Co workers
- Prof. Yoon-Sik Lee, Prof. Byung-Gee Kim (SNU), Prof. Hoseong Kim (ChungAng Univ.)
- Post Doc. Researchers : Dr. Kooknyung Lee, Dr. Sangho Lee, Dr. Chang-Soo Lee (SNU).
- Graduate Students: Minsoo Kim, Suhyung Cho, Woojae chung (SNU), Yongyoon Kim (ChungAng Univ.).