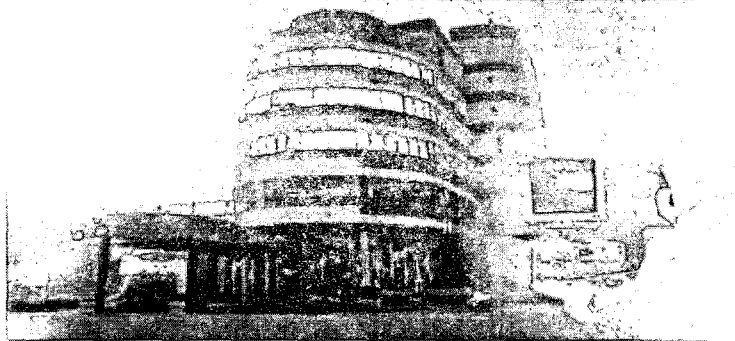


Samsung Advanced Institute of Technology



Geunbae Lim

limmems@sait.samsung.co.kr

MEMS & Micro Fluidics

차세대 생물산업 핵심기술 개발

- 산업 자원부 차세대 신기술 개발사업 from 1999.12-

총사업개발비 : 2000년 55억, 2001년 65억, 2002년 72억

DNA Chip 개발

MEMS기술을 이용한 DNA Lab on a Chip System 개발

ECL방식에 의한 DNA Chip 개발

유전정보를 활용한 Oligomer합성과 cDNA/Oligo DNA Chip System 개발

유전자 전달체

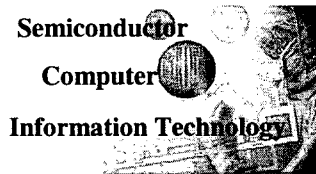
재조합 아데노바이러스 유전자전달체를 이용한 암 및 심혈관 치료제 개발

리포솜 유전자 전달체를 이용한 혈액질환 및 간암 치료제 개발

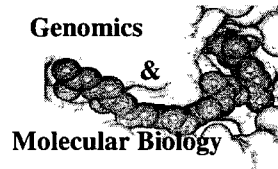
차세대 렌티바이러스 벡터제조 및 이를 이용한 유전자 치료제 개발

신규 아데노부속바이러스 유전자 전달체 및 아데노류 바이러스 제조기술 개발

Technology of the 21st Century



Technology Fusion

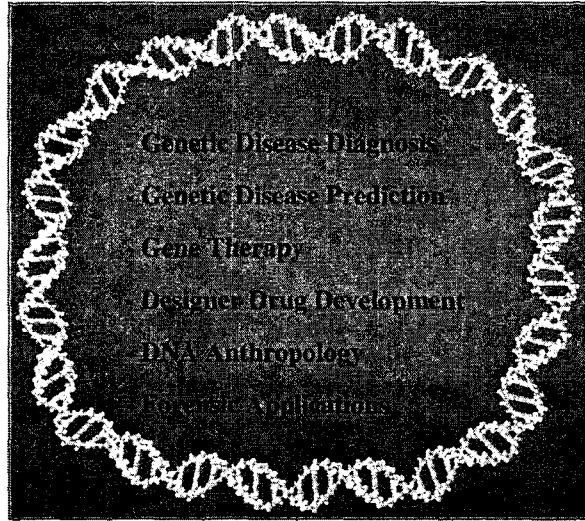


DNA Chip

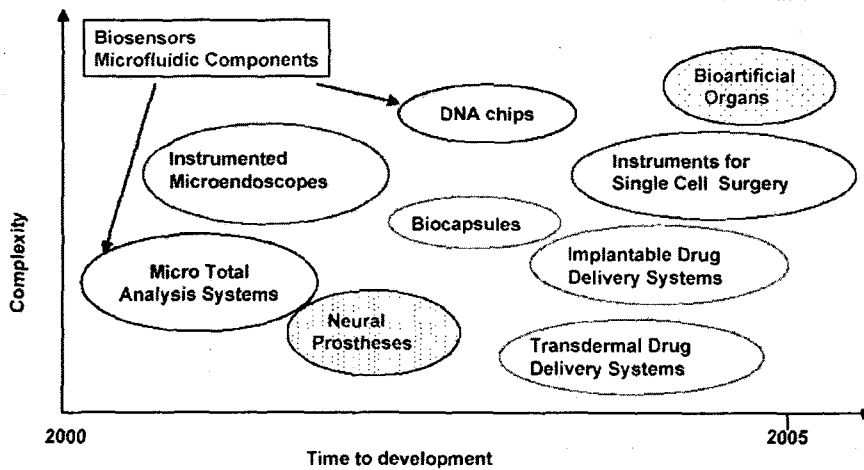


Microfluidics / Microelectronics / Optics / Biology / Chemistry

Why DNA Chip?

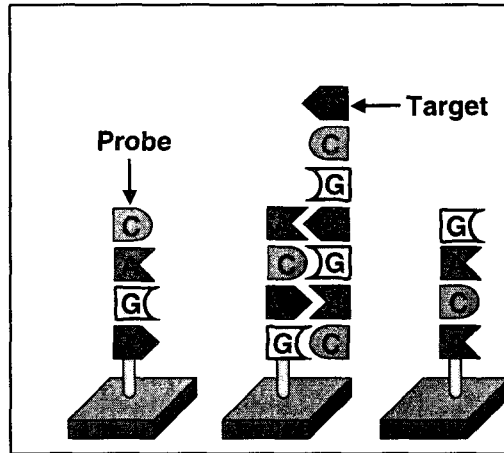


MEMS in biomedical application

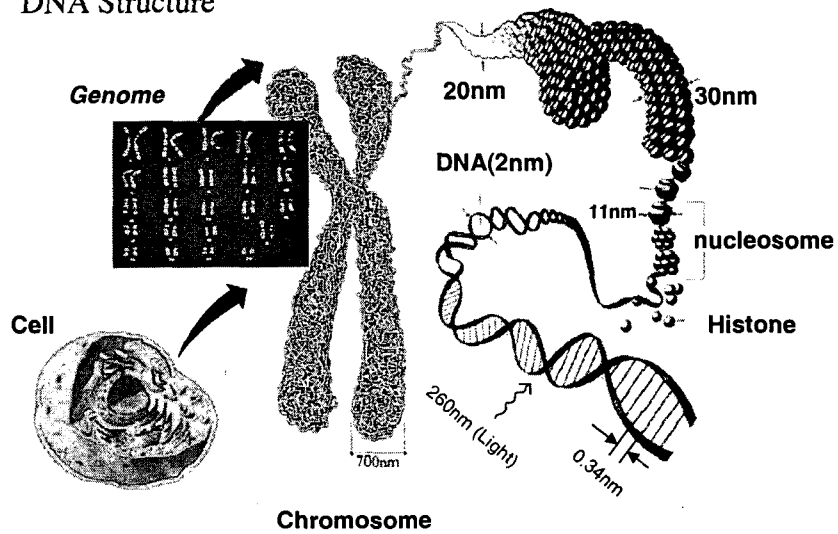


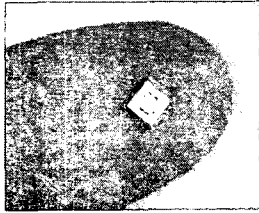
DNA Array 방법의 원리

기본 원리 : 특정 DNA 염기 배열 정보를 가지고 있는 DNA Chip에, 분석하고자 하는 DNA 샘플을 주사한 다음, 어떤 염기의 결합이 이루어지는 지를 확인하면 샘플 DNA의 염기배열을 알 수 있다.

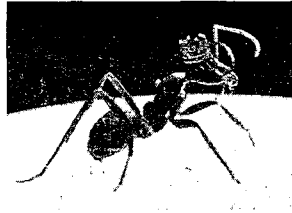


DNA Structure

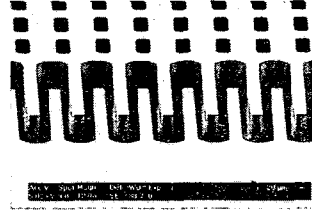




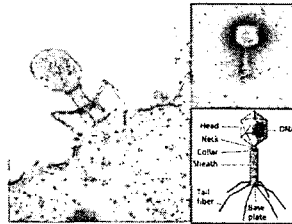
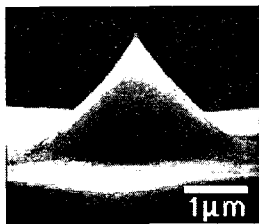
5mm



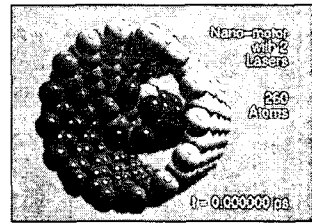
0.5mm



20µm



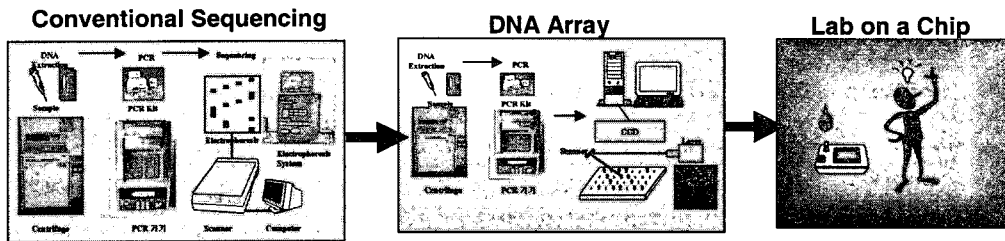
200nm



Benefits of Miniaturization

Properties	Benefits
Heat Transfer	Higher cooling and heating rates
Separation efficiency	Improved separation speed
Reagent Consumption	Reduced reagent consumption
Flow	Generally laminar
Material Transport	Less external pumping and valving required
Portability	Improved
Parallelization	Readily achieved
Disposability	Improved

Technology Tread (DNA 분석기의 발전방향)



DNA Pocket Lab (Michigan 대학, David Burke)

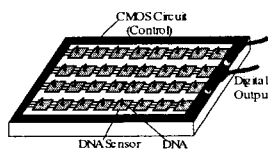
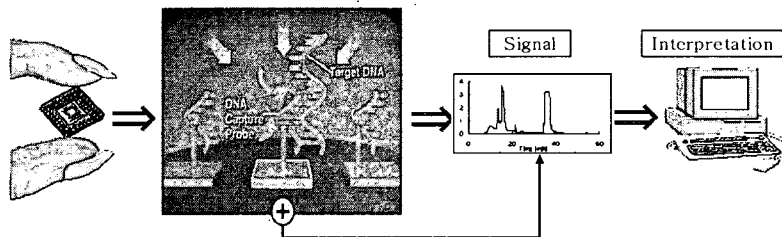
“Lab on a chip”은 현재의 DNA기술을 간단하고 저렴하며 이동성 기구로 가능하게 하는 기술이다. 약 15년 안에 연구나 실험실은 물론이고 일반 가정용으로도 시장이 형성될 것

Future Manufacturing and Products in BioMEMS

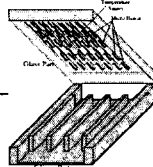
(John West, Marketing Director for Microfluidics, Microcosm Technologies)

- Seamless Microsystem
- BIOMEMS : Beyond Batch Fabrication
- Living Chip Technology

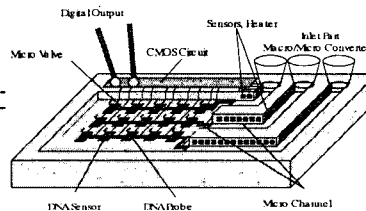
Lab on a Chip 개념도



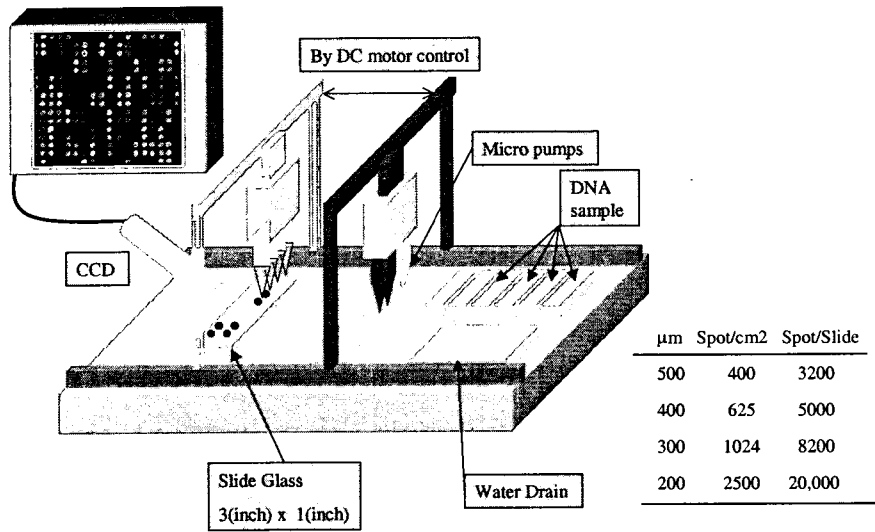
DNA to Electrical Transducer



Micro Fluidics



Spotting

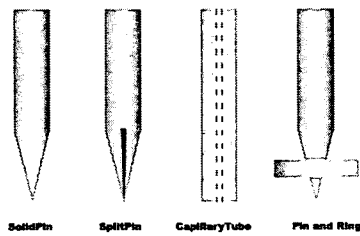


S&C Sector

MEMS Lab

Spotting

Contact Pin Type



- 종류
1. Non-Contact Printing ==> Inkjet
 2. Contact Printing ==> Pin
 - Genetic Microsystems (GMS)(Takara)
 - Cartesian Technologies
 - Beecher Instruments
 - Genome Solutions
 - BioRobotics

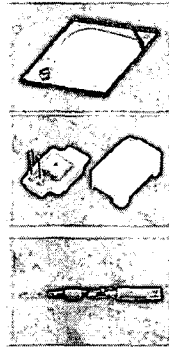
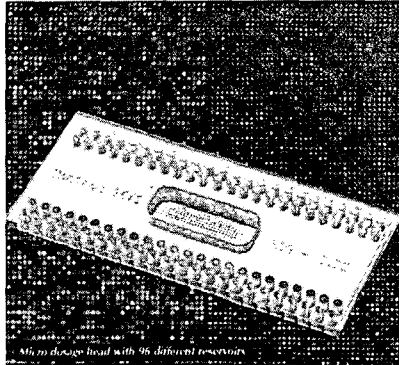
문제점
Spot량의 재현성 이 일정치 못함
=> 다른 Sample간의 정량적 비교가 곤란

S&C Sector

MEMS Lab

Microarray

TopSpot technique developed by HSG-IMIT is the first spotting procedure for serial manufacturing of biochips (~1000 different analyzing substances on a chip)



Microvalves

Microdosing

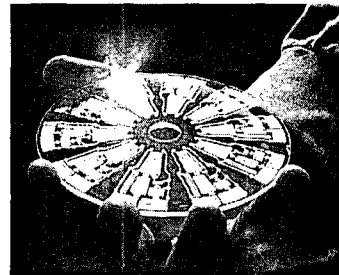
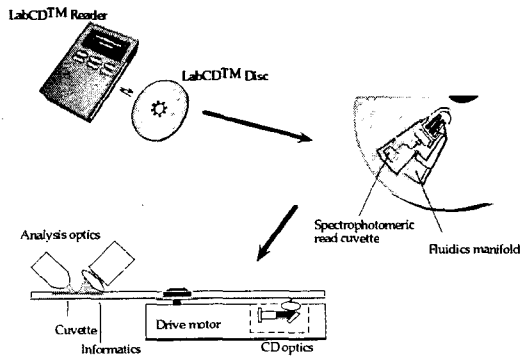
Nanojet dispenser(5nL)

S&C Sector

MEMS Lab


❑ Plastic CD (Centrifugal Device) on a CD (Compact Disc)


- ◆ Centrifugal device on a compact disc-like
- ◆ Optical detection using conventional CD player
- ◆ Polycarbonate (PC)



S&C Sector


MEMS Lab


 Injection moulded microstructures

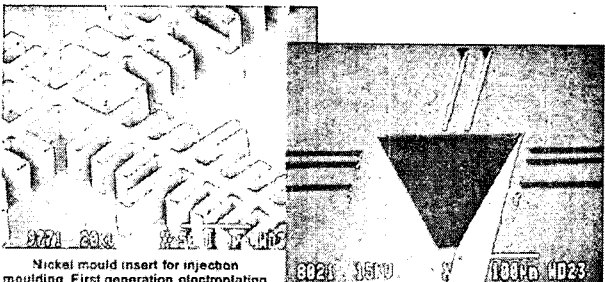


Dual depths
Microfluidic structure with 100/35 µm depth in injection moulded polycarbonate (PC)

Ornic AG, Burgländeplatz 15, D-713 23 Nürting-Geislingen, Germany, Phone +49 7141 432220, Fax +49 714 432226, info@ornic.de




 Electroplated microstructures



Nickel mould insert for injection moulding. First generation electroplating from Silicon DRIE-master.

Nickel replica of silicon master structure. Second generation electroplating from Silicon KOH-master.

Ornic AG, Burgländeplatz 15, D-713 23 Nürting-Geislingen, Germany, Phone +49 7141 432220, Fax +49 714 432226, info@ornic.de



PDMS (PolyDiMethylSiloxane)

Silicone rubber (Sylgard, Dow Corning)

Biomedical grade silicones are popularly used in breast implants and the medical world to carry gases and solutions.

PC (PolyCarbonate)

For optical devices such as compact disks and eye lenses

PMMA (PolyMethylMethAcrylate)

Well known from the generation of micro-optical devices

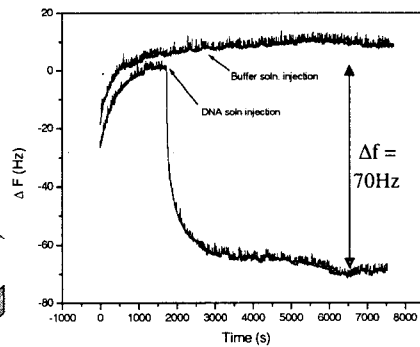
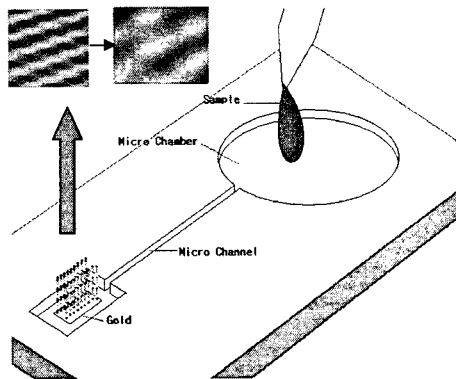
Favorite polymer for the fabrication of microfluidic structures

Implantable grade PMMA is used in intraocular lenses and orthopaedic cement

Polymers / Plastics

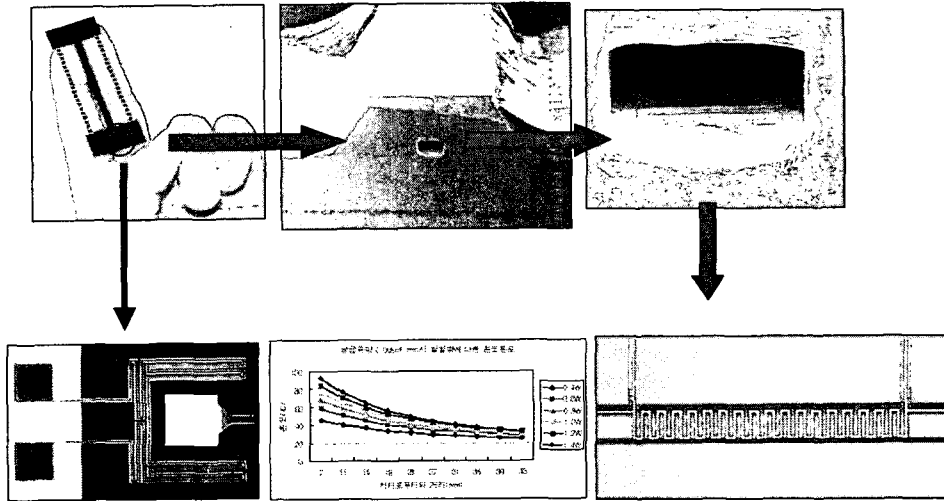
MEMS (Micro-Electro-Mechanical Systems) does not always mean silicon, it could be polymers / plastics

Sample Delivery



(Multi Channel)
 Sample Delivery + Micro Pump & Valve
 ↓
 (Micro Reactor?)

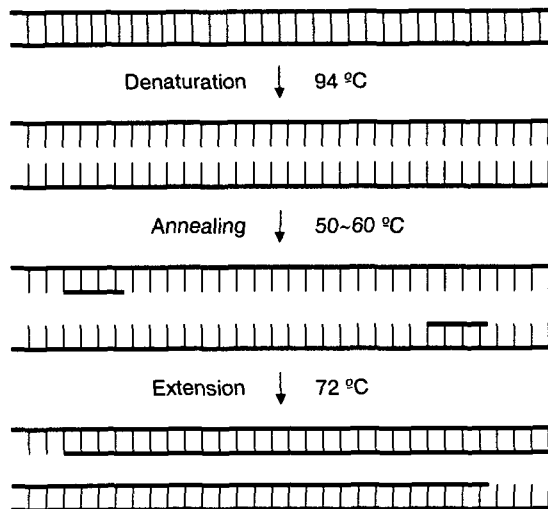
Micro Fluidics -PCR-



S&C Sector

MEMS Lab

The Schematic flow of PCR reaction



S&C Sector

MEMS Lab

Some factors which affect PCR reaction

Critical factors

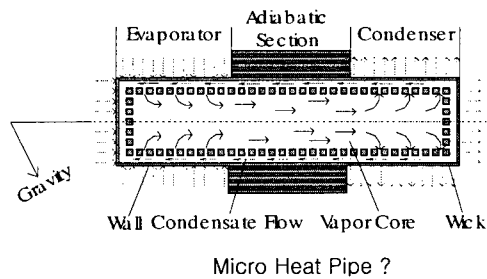
- Designing primer and its concentration
- Annealing time and temperature

Some other factors

- Extension time and temperature
- KCl concentration
- Cycles number

Micro PCR 문제점

Cooling ?



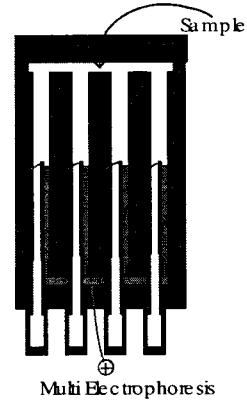
Micro Electrophoresis

Market:

1. 연간 \$400M 정도의 시장이 지속되고 있다.
Small Size의 Kit 화가 되면서 시장이 급격히 늘어남
2. CE(Capillary Electrophoresis) 가 차지하는 비율: 약 1/4

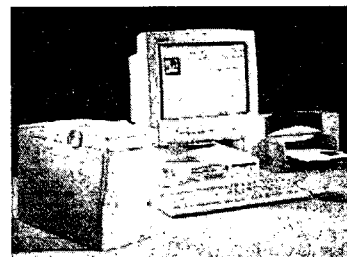
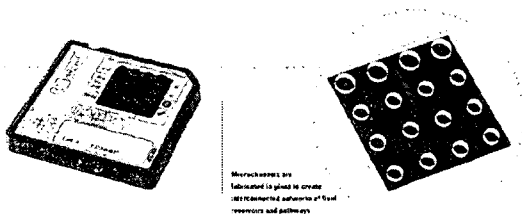
High Voltage = 빠른 분석
Band Brodening 방지
Post PCR 가능

상품명: LabChip

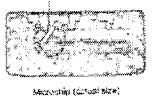


HP Bioanalyzer "Labchip"

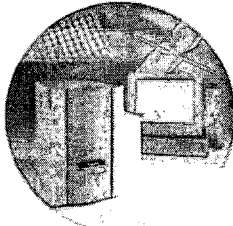
- Hewlett Packard : '99 Sep. Labchip 판매 시작
- Caliper Lab. chip technology. 전기영동법을 이용한 DNA 분석
" The future of your lab is on a chip "



Microchip Electrophoresis System



A New Era in Separation Analysis, Encapsulating the Essence of Technology ***



MCE-2010

Shimadzu Microchip Electrophoresis System

S&C Sector

MCE-2010 Main Unit

Sample rack	Maximum capacity: 96 samples
Microchip	Quick replacement (change within 30 secs). 80 chips (chip type 2048) for DNA, 2048 chips (chip type 2048) for protein analysis (chip type 2048). Chip type 2048 is supported with a single computer.
Usable solvent	CAA, separation gel, Type B, or HPLC grade water
High-voltage power source	A highly individualized isolation transformer
Electrophoresis voltage	0 to 3000V
Separation time	10 to 600 min (step 20 min). Step 10 min. (power on for 10 min. before starting the operation)
Detection method	UV absorbance, fluorescence, laser induced fluorescence (LIF)
Wavelength	254 nm (UV absorbance), 366 nm (LIF), 690 nm (fluorescence)
Detector	UV detector (photo diode), LIF detector (photomultiplier tube), fluorescence detector (PMT)
Sensitivities	1 ng (DNA), 10 pg (protein), 10 ng (fluorescence)
Light source	Gas discharge lamp
External dimensions	Width: 318 mm, Height: 410 mm
Weight (mass)	Approx. 20 kg
Power supply	AC100 V, 220 V, 240 V, 50/60 Hz
Used software	
Main unit control	Windows-based (Windows 95, Windows NT, Windows 2000, Windows XP)
Electrophoresis control	File program software
Data processing	Identification software (peak search, etc.)
Cell image display	Real-time image display software (real-time image display software)
Electrophoresis display	Electrophoresis image display software (electrophoresis image display software)
Operating system	Microsoft Windows NT, 4.0 for English, Microsoft Windows NT, 4.0 for Japanese
Configuration	
MCE 2010 for DNA analysis	
Name	MCE-2010
Microchip electrophoresis system MCE-2010	2010-0010-01
PC printer interface (SCSI cable), etc.	2010-0010-02
Microchip Type D (2048 x 500 C)	2010-0010-03
Separation running gel Type D	2010-0010-04
Area ruler (10µm)	2010-0010-05
DNA size marker	2010-0010-06
General MCE 2010 analysis other than DNA	
Name	MCE-2010
Microchip electrophoresis system MCE-2010	2010-0010-01
PC printer interface, etc.	2010-0010-02
Microchip Type D (2048 x 500 C)	2010-0010-03

MEMS Lab

DESIGNING CORNER COMPENSATION FOR ELECTROPHORESIS IN COMPACT GEOMETRIES

Joshua I. Molho, etc. Stanford University
Read A. Brennen, etc. Agilent Laboratories



Figure 3: Diagrams to the left show corner designs examined using two dimensional field solutions. The skew normalized by the channel width is shown below each design.

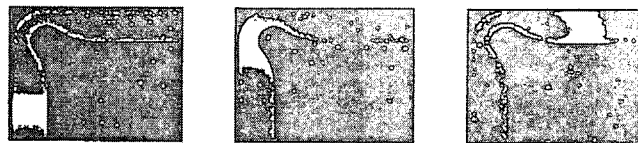
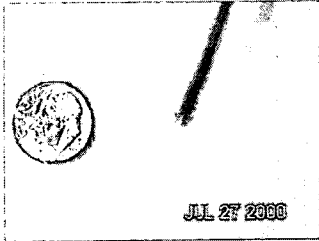


Figure 4: Simulation of an optimized corner design. The skew is reduced by almost an order of magnitude as compared to the skew seen in the constant radius turn.

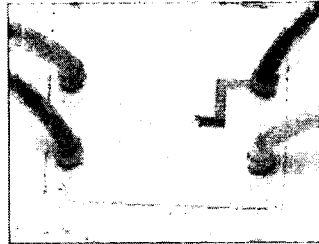
S&C Sector

MEMS Lab

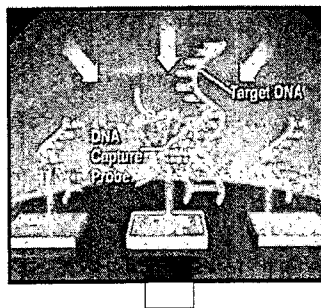
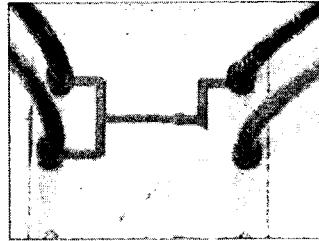


64-way splitter

Mixer



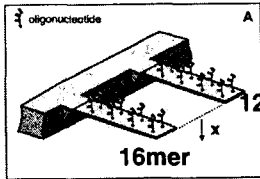
Non-Mixer



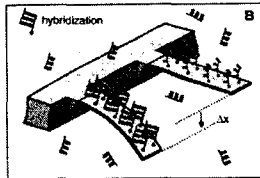
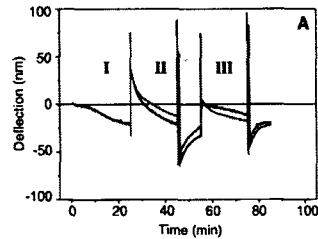
- QCM(Quartz Crystal Microbalance)
- MALDI-TOF 질량분석기
- SPR(Surface Plasmon Resonance)
- Fluorescence
- Electrochemical
- Ion Sensor

Translating Biomolecular Recognition into Nanomechanics

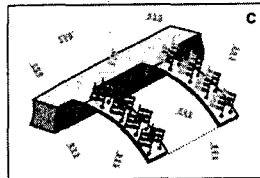
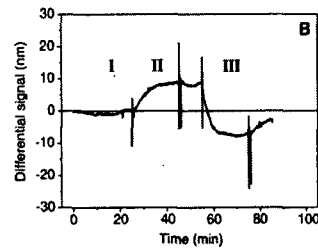
Science, 288, 316-318, 2000 (IBM Zurich research lab.)



I. Equilibrated in buffer
: difference set to zero



II. 16mer injection
: 10 nm
: purge 20 min later with 3ml HB

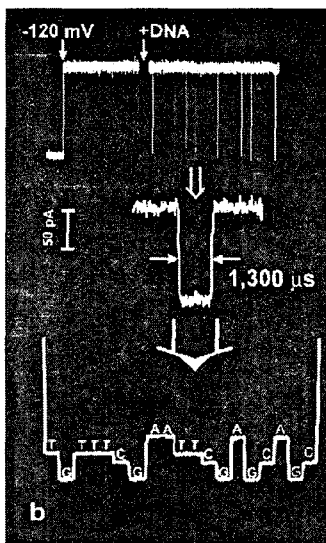
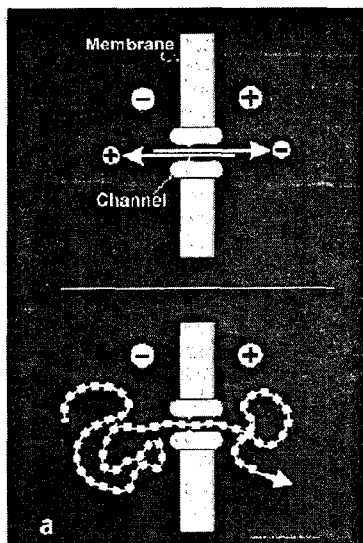


III. 12mer injection
: 16 nm
: why positive & negative?
: surface stress 5mN/m
(actuation force 300pN)

S&C Sector

MEMS Lab

NEMS? (Nano Sequencing)



<http://mcb.harvard.edu/branton/nanopore.html>

S&C Sector

MEMS Lab

SAMSUNG Advanced Institutes of Technology **Breakthrough**

Canada
Biomedical Photometrics
Osterio, Canada
Insigning Research
Osterio, Canada
Virtix Vision
ONTARIO, Canada

West Coast
Affymetric
Santa Clara, CA
Agilent Technology
Palo Alto, CA
Alpha Innotech
San Leandro, CA
Applied Precision
Ipswich, MA
Applied Biosystems
Foster City, CA
AVIVA Biosciences
San Diego, CA
Axon Instruments
Foster City, CA
BioDiscovery
Los Angeles, CA
Carnegie Technologies
Irvine, CA
Ciphergen Biosystems
Fremont, CA
Clinical Micro Sensors
Pasadena, CA
Clontech Laboratories (BD)
Palo Alto, CA
CombiMatrix
Mackinaw, WA
Digital Gene Technologies
La Jolla, CA
Display Systems Biotech
Vista, CA
GeneEd
San Francisco, CA
Genoscreen
Menlo Park, CA
Chromed Biosciences
San Francisco, CA

Midwest
Midwest Ambion
Austin, TX
BioForce Laboratory
Ames, IA
Genematrix
The Woodlands, TX
Genomic Solution
Ann Arbor, MI
Gene Technology
Maplewood, MO
HTS Biosystems
Eagan, MN

East Coast
AlphaGene
Woburn, MA
Boehringer Instruments
Silver Spring, MD
BioArray Solutions
Piscataway, NJ
bioDevsie Partners
Cohasset, MA
Gene Logic
Baltimore, MD
GENPAK
Stony Brook, NY
Mingant Bio-Instruments
Cape Cod, MA
Media Cybernetics
Silver Spring, MD
Mosaic Technologies
Waltham, MA
MWG Biotech
High Point, NC
NEN Life Science
Boston, MA
Origene Technology
Rockville, MD
Packard Bioscience
Meriden, CT
PerkinElmer Life Sciences
Boston, MA
Phytec
Lexington, MA
Radius Biosciences
Medfield, MA
Scanalytix
Irvine, CA
Matrix
Durham, NC
Spotfire
Cambridge, MA
Super Array
Bethesda, MD
Xeno
Research Triangle Park, NC

European
Advanced Array Technology
Belgium
Amersham Pharmacia Biotech
Sweden
Applied Maths
Belgium
Asper Biotech
Estoril
Biacore
Sweden
BioMérieux
France
BioRobotics
United Kingdom
Ceva
France
Cruschem
Scotland
Eurogentech
Belgium
Gene Data
United Kingdom

Genetix
United Kingdom
GeneScan Europe
Germany
GENSET
France
BioRobotics
United Kingdom
Germany
Interactive
Germany
Labman Automation
United Kingdom
LION Bioscience
Germany
Oxford Gene
Technology
United Kingdom

Asia
Capital Biochip
Beijing, China
SuperBiochips
laboratories
Seoul, S.Korea
Hitachi
Japan
takara Shuzo
Japan
Takeda
Japan
Toyobo
Japan

DNA LAB ON A CHIP

SAMSUNG Advanced Institutes of Technology **Breakthrough**

Core Competencies

- Microfluidics & MEMS
- Surface Modification Processes
- Polymer Chemistry
- Manufacturing in Plastics

S&C Sector **MEMS Lab**

DNA chip : Multidisciplinary Project.

Micro Fluidics : Micro Heat Transfer

Understanding Molecular interaction on the chip surfaces is a crucial factor.

Biomolecules (DNA, Proteins, Cells etc.) on Surfaces

: Structure & Dynamics of Polymers depending on surface & solution condition

(surface materials, surface chemistry, solution condition(pH, [I], T, concentration, etc.)