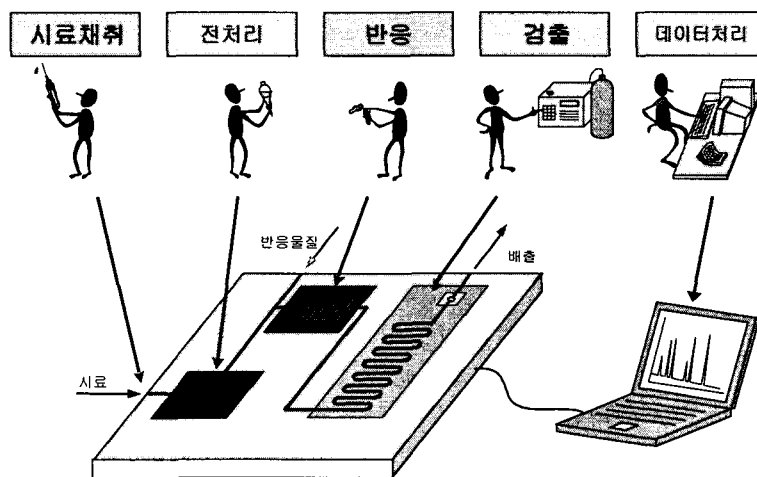

The Need for Visualizing Microflows in Lab-on-a-Chips

한 중 훈
포항공대 화학과

Lab-on-a-Chip: Bio/Chemical Microprocessor



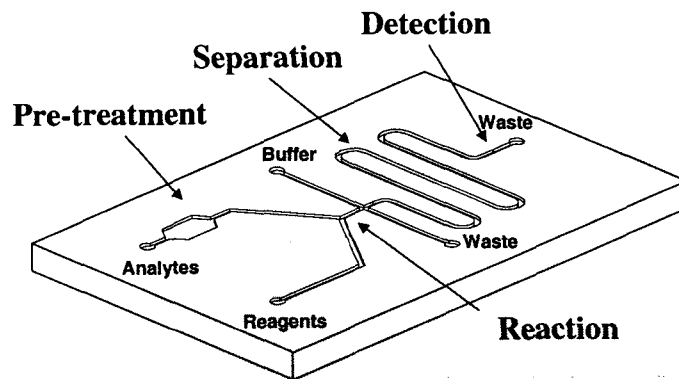
Lab-on-a-Chip의 장점

- 초고속 분석 (수초 ~ 수분)
- 시료 및 시약의 소모량 최소화 (~nL)
- 다종 시료의 동시 분석
- 자동화로 인한 높은 재현성
- 휴대 가능
- 저가, 대량생산 가능

Applications

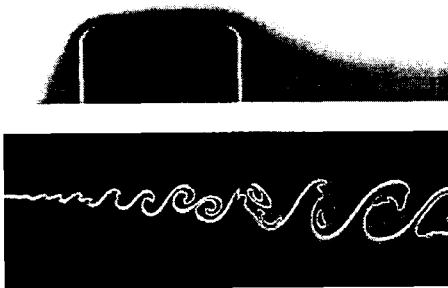
- 환경오염물질 분석 및 모니터링
- 화학, 생물공정 모니터링
- 의료진단, 건강검진
- 식품, 의약품 안정성 평가
- 화생방용 무인 화학/생물 작용제 탐지/식별
- 소형화학공장
- 고속신약탐색

Concept



Laminar Flows

Laminar flow : $Re < 2100$



$$Re = \frac{ud\rho}{\eta}$$

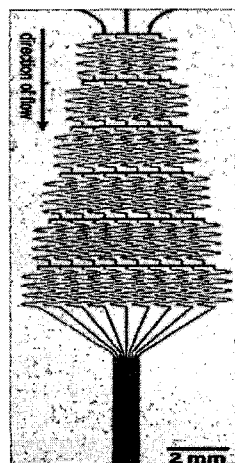
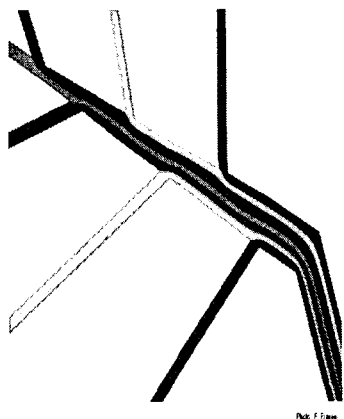
u : mean velocity of fluids [m/s]

d : diameter of the channel [m]

ρ : density of the fluids [kg/m^3]

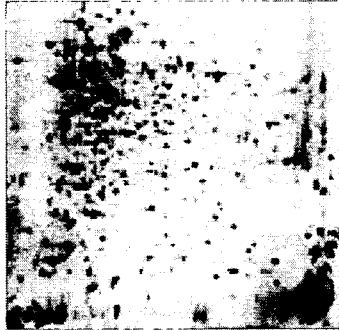
η : viscosity [$\text{kg}/\text{m}\cdot\text{s}$]

Laminar Flows in the Microchannel



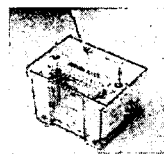
**Sample Clean-up Using
Multiphase Laminar Microfluidics
for ESI-MS**

Proteomics



"The study of proteins that are encoded by the genes of an organism"

Proteome Analysis



Two dimensional
gel electrophoresis



Gel staining

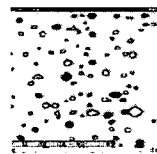


Image capture



Spot picking



Data base search



Mass analysis

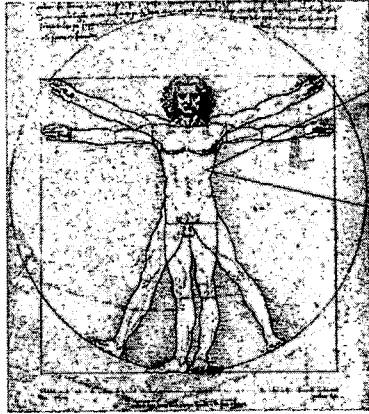


Peptide cleanup



Digestion

How Many Proteins?



0.5 ~ 1 million
different protein forms
expressed in the human!

Proteomics & Automation

Automation!

In order for proteome analysis to become a viable and widely used method, a reasonable degree of automation must be achieved to

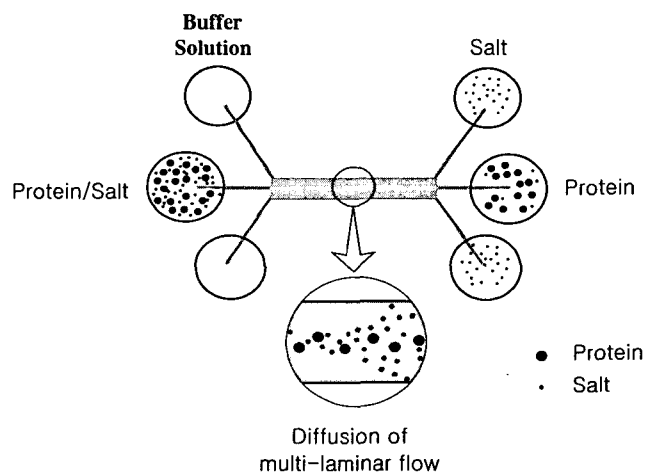
1. Increase reproducibility
2. Make the process less labor-intensive
3. Increase throughput.

Proteome Analysis

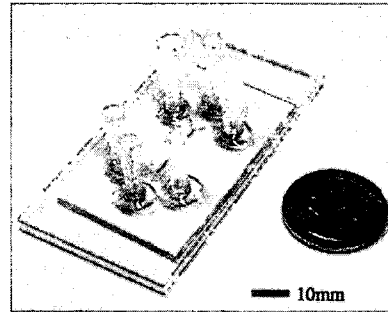
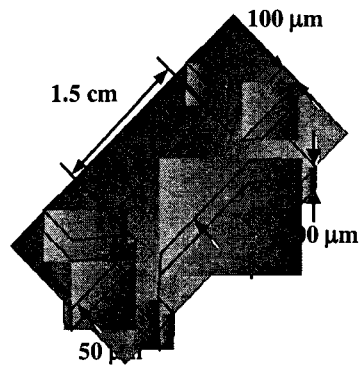
Process	Manual throughput per person	Automated/semi-automated throughput per instrument
2-D gels	10 gels/day ^{a)} 1500 spots/gel 15000 spots/day	Same
2-D gel staining (silver)	10 gels/day	10 gels/day
Image capture and analysis	5 gels/day	25 gels/day
Spot picking	200 spots/day	200 spots/h/robot 1600 spots/day
Digestion and peptide extraction	200 spots/day	200 spots/day/robot
Peptide clean-up and spotting	100 spots/day	200 spots/day/robot
MS analysis and database search	50 spots/day	200-500 spots/day

a) 8 h day

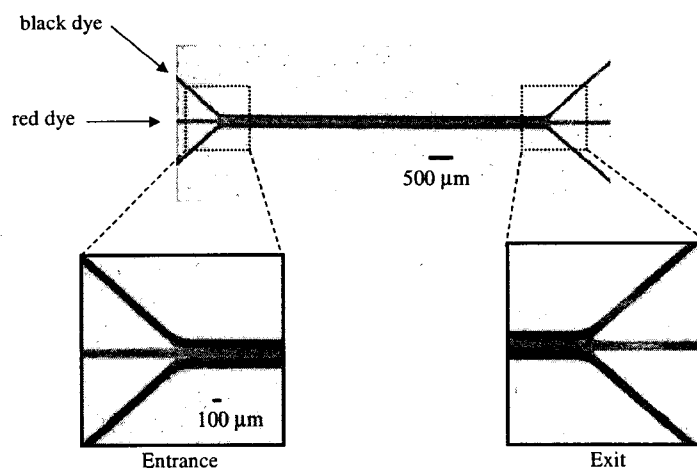
Concept of Clean-up Chip



Clean-up Chip

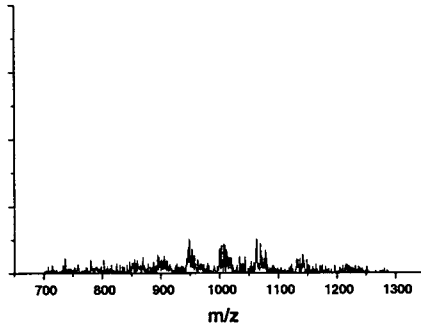


Multiphase Laminar Flows

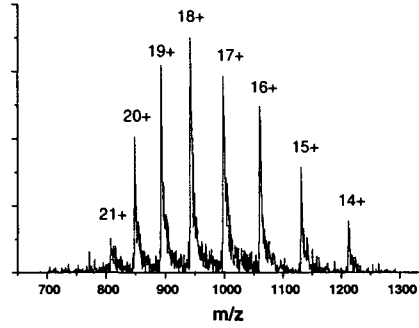


Desalting

Direct injection

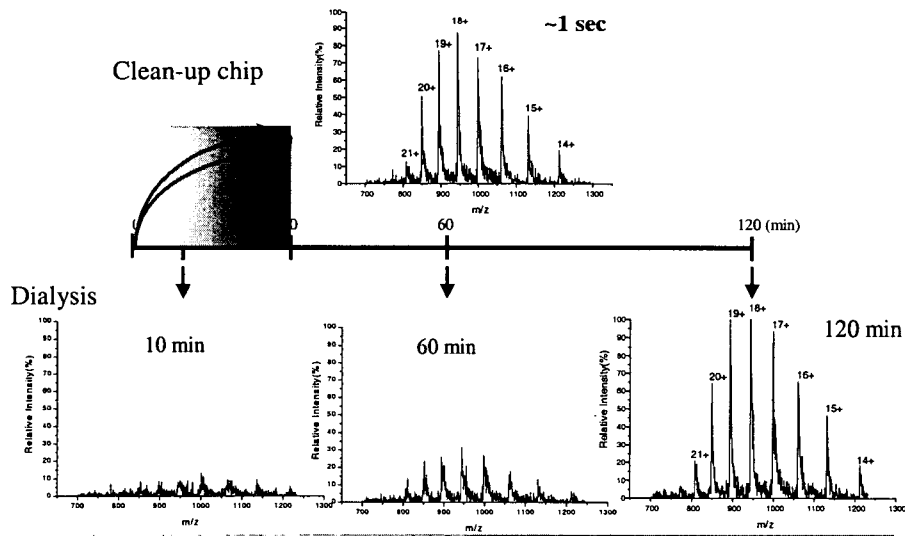


After clean-up

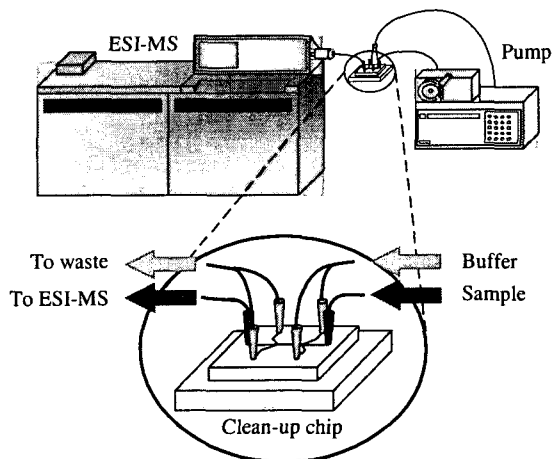


- Sample : Horse Heart Myoglobin (1mg/ml), NaCl (500mM), Tris (100mM), EDTA (10mM)
- Buffer : NH₄OAc (10mM), Acetic acid (1%)

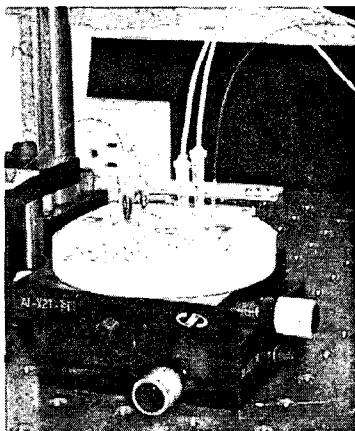
Dialysis vs. Clean-up Chip



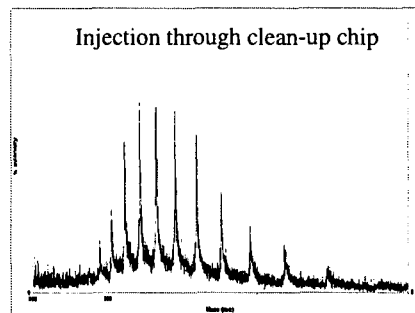
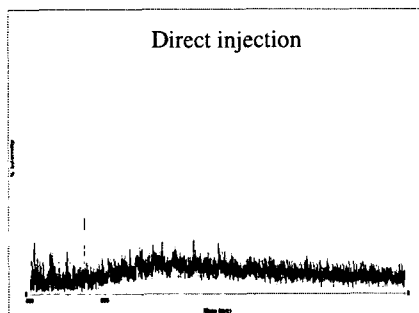
On-Line Clean-up System



On-Line System



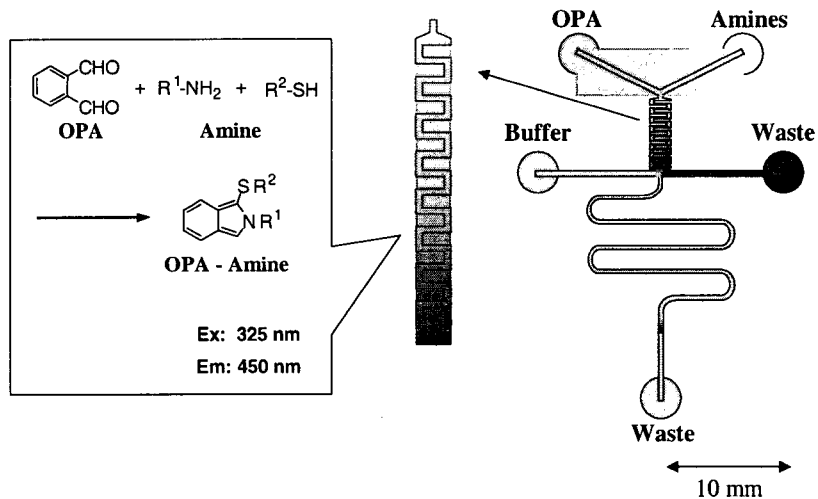
On-Line Clean-up



- Sample : Horse Heart Myoglobin (1mg/ml), NaCl (500mM)
- Buffer : NH₄OAc (10mM), Acetic acid (1%)

Precolumn Reaction and Separation Chip

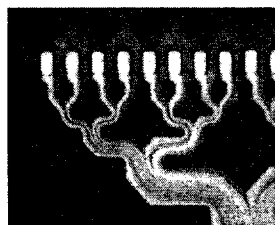
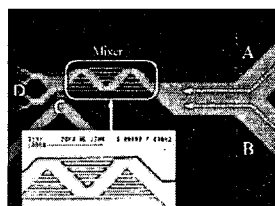
Precolumn Derivatization/Separation



Mixing Enhancement

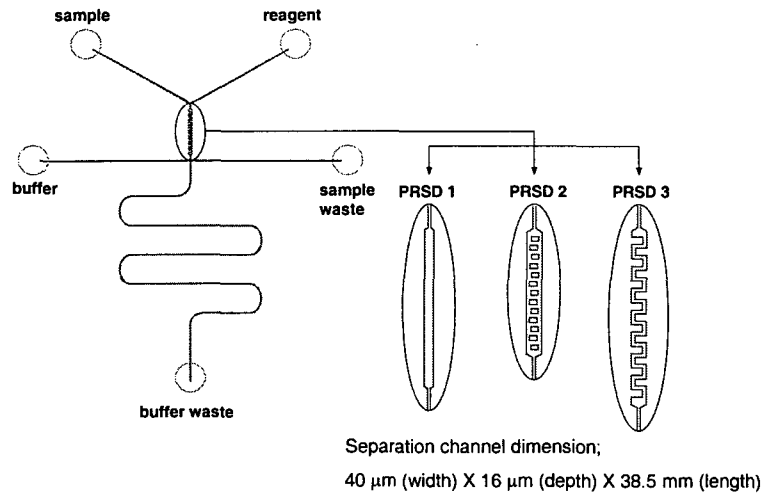


Active mixing

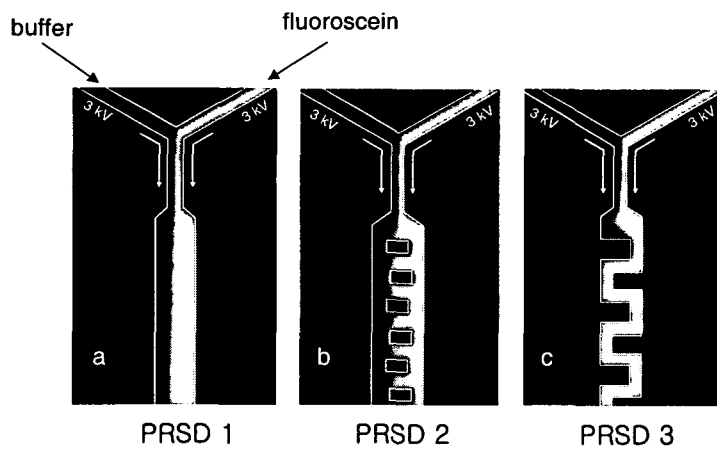


Passive mixing

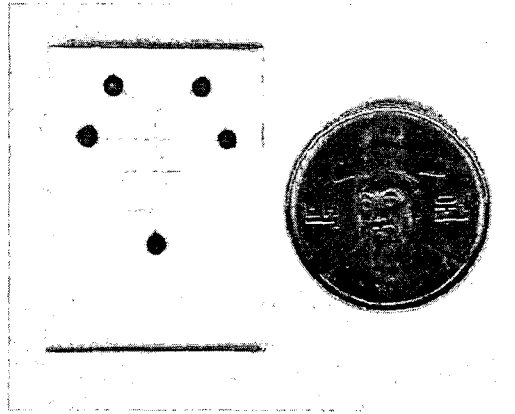
Reaction Chamber Design



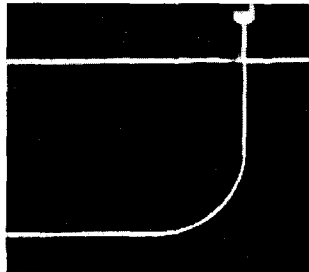
Mixing Efficiency



Precolumn Derivatization & Separation Chip

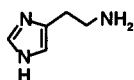


Gated Injection and Separation

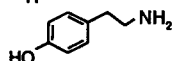


OPA-Biogenic Amines

1. Histamine



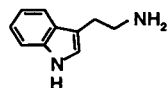
2. Tyramine



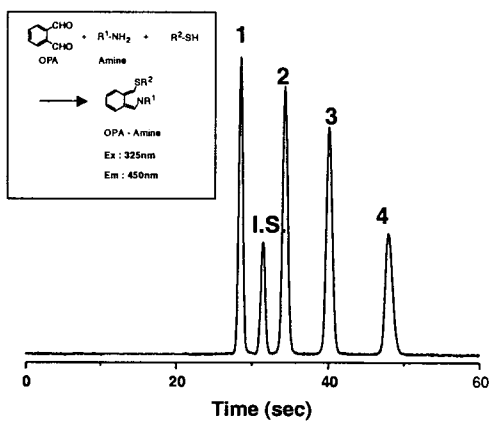
3. Putrescine



4. Tryptamine

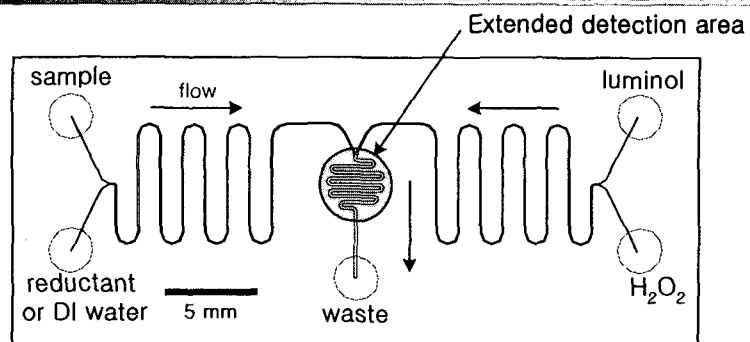


I.S.: Dansyl-OH



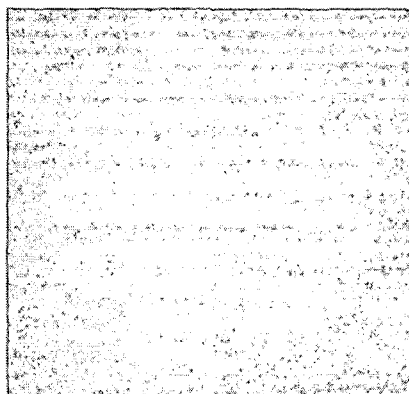
Simultaneous Monitoring of Cr(III) and Cr(VI)

Chemiluminescence Chip



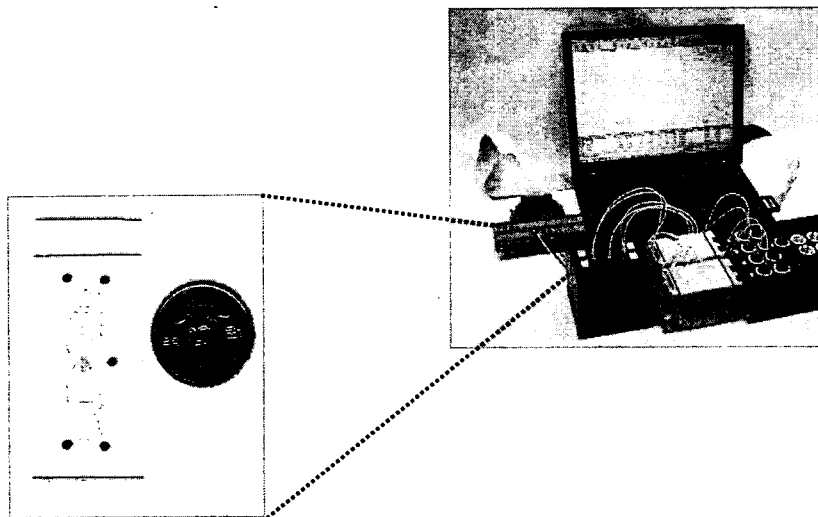
- **CL reaction**
 $\text{luminol} + 2\text{H}_2\text{O}_2 + 2\text{OH}^- + \text{Cr}^{3+}(\text{catalyst}) \rightarrow 3\text{-aminophthalate} + \text{N}_2 + 4\text{H}_2\text{O} + h\nu$
- **Reduction**
 $\text{Cr}_2\text{O}_7^{2-} + 3\text{K}_2\text{SO}_3 + 8\text{H}^+ \rightarrow 2\text{Cr}^{3+} + 6\text{K}^+ + 3\text{SO}_4^{2-} + 4\text{H}_2\text{O}$

Chemiluminescence Emission Image

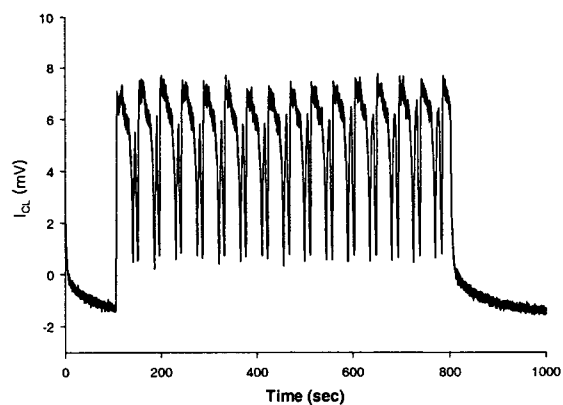


CL emission image by Cooled CCD
1 ppm Cr(III), Exposure time is 1 minute.

Compact System

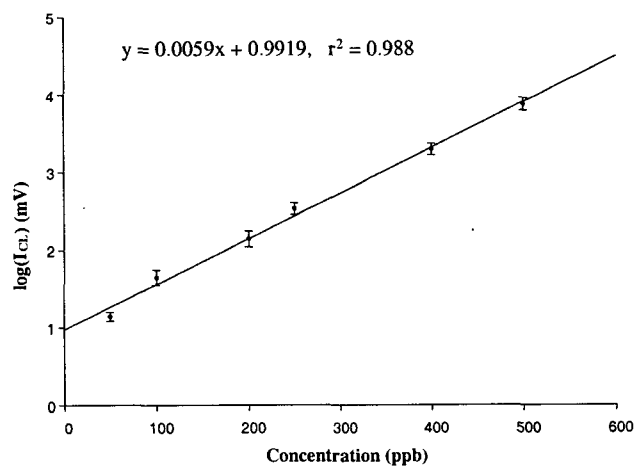


Signal pulsation



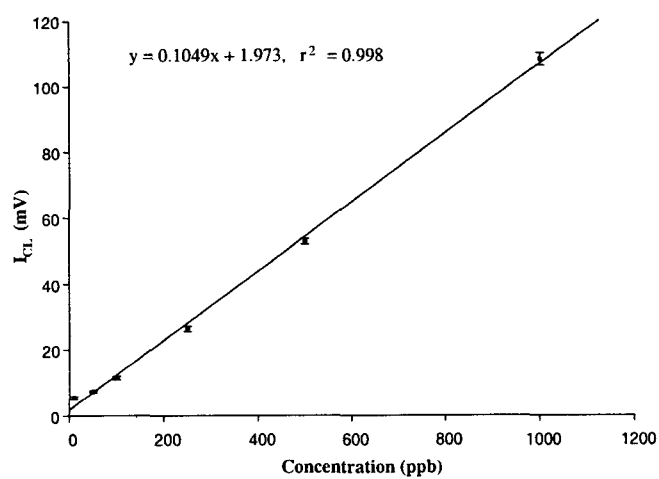
Consistent emission peak shape of 50 ppb Cr(III)
6.8 mM luminol in 20 mM boric acid (pH 11.5)
20 mM hydrogen peroxide in 20 mM boric acid (pH 11.5)

Cr(III)



Detection limit = 10 ppb

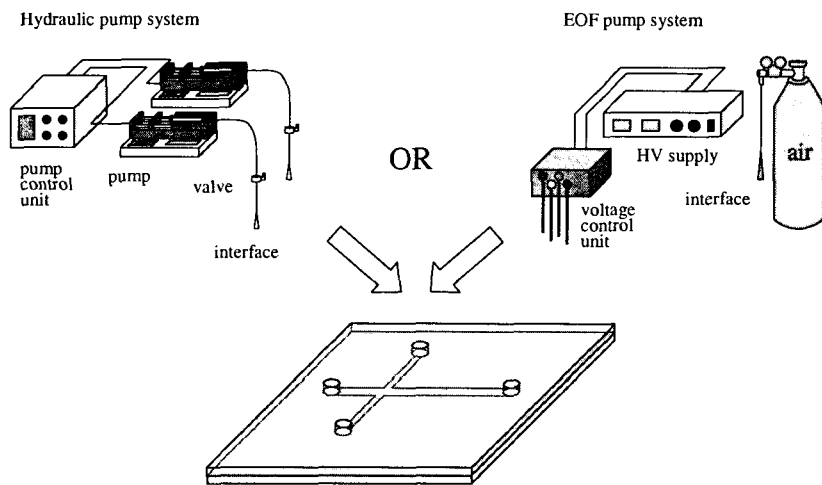
Cr(VI)



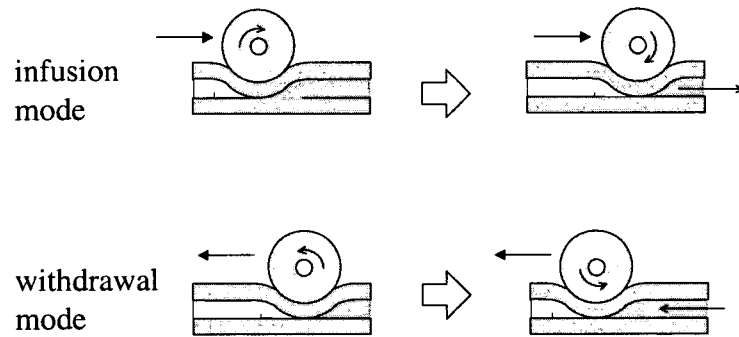
Detection limit = 1.3 ppb

Squeezing Micropumps

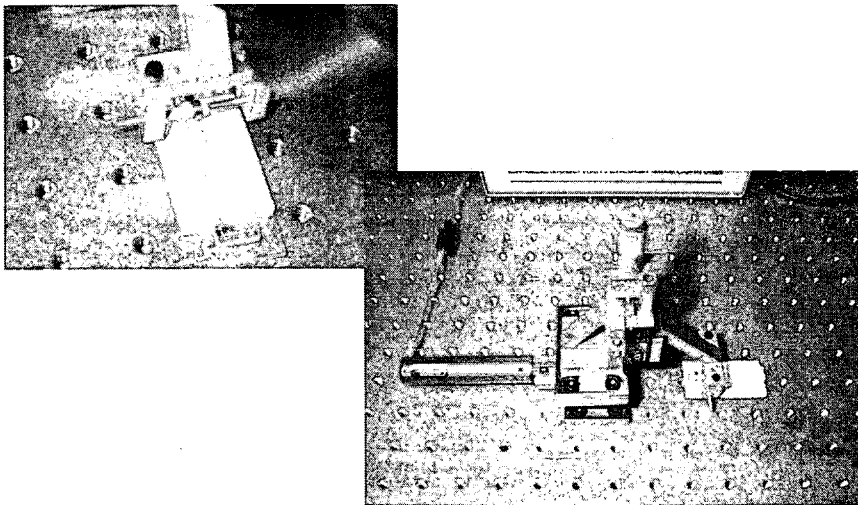
Controlling Microfluidics



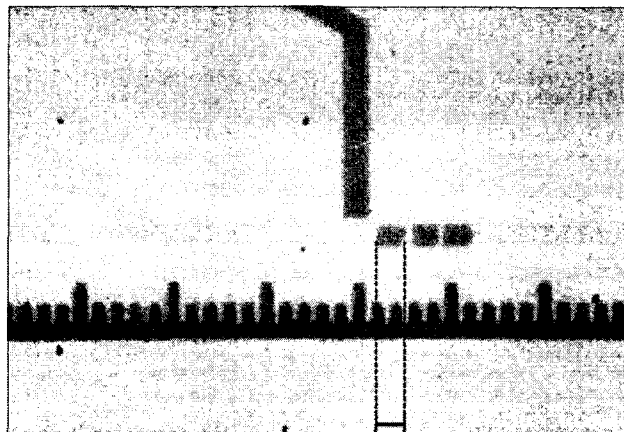
Pumping by Squeezing



Squeezing Micropump



50 pL handling



50 μm (50 pL)

Consistent Flow Rate

