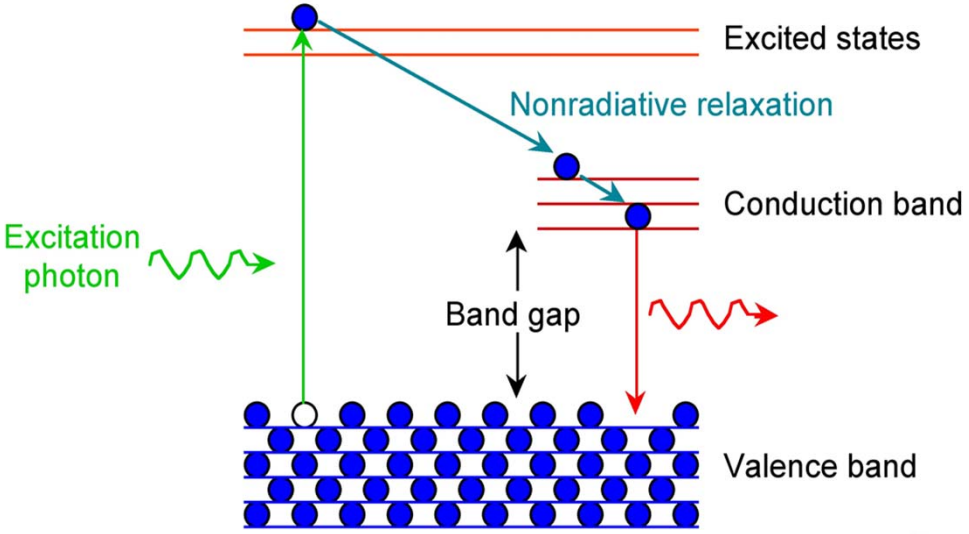
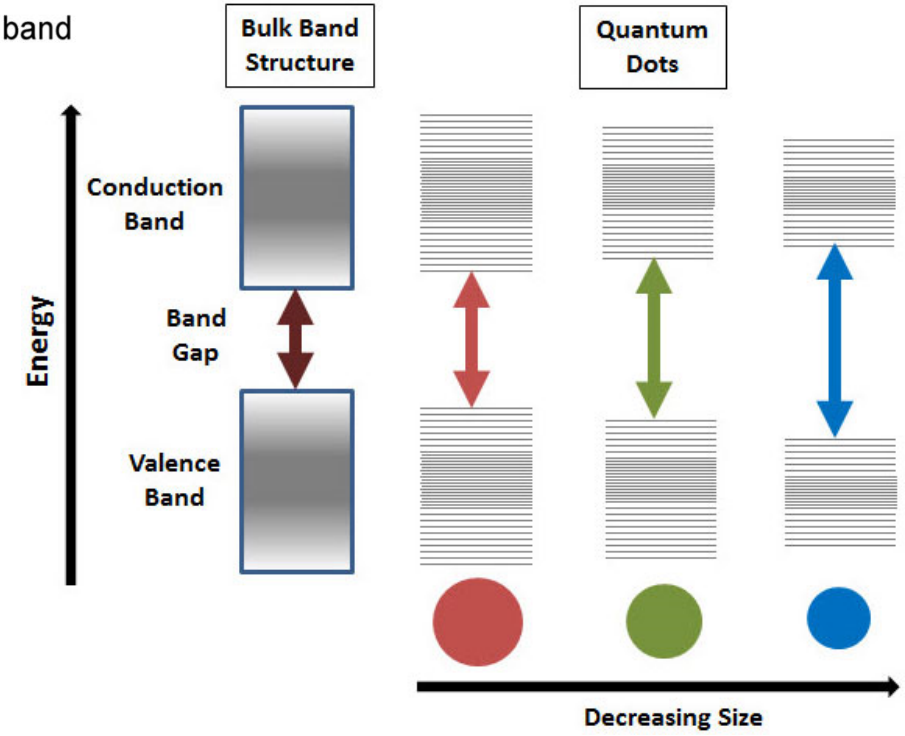
Soft Matter in Nanobiotechnology : Liposomes

Summarized by
Prof. Dong June Ahn
Korea University

https://www.youtube.com/watch?v=vGz-qDE3Go4

Band Theory on Quantum Confinement Effect





Photoluminescence

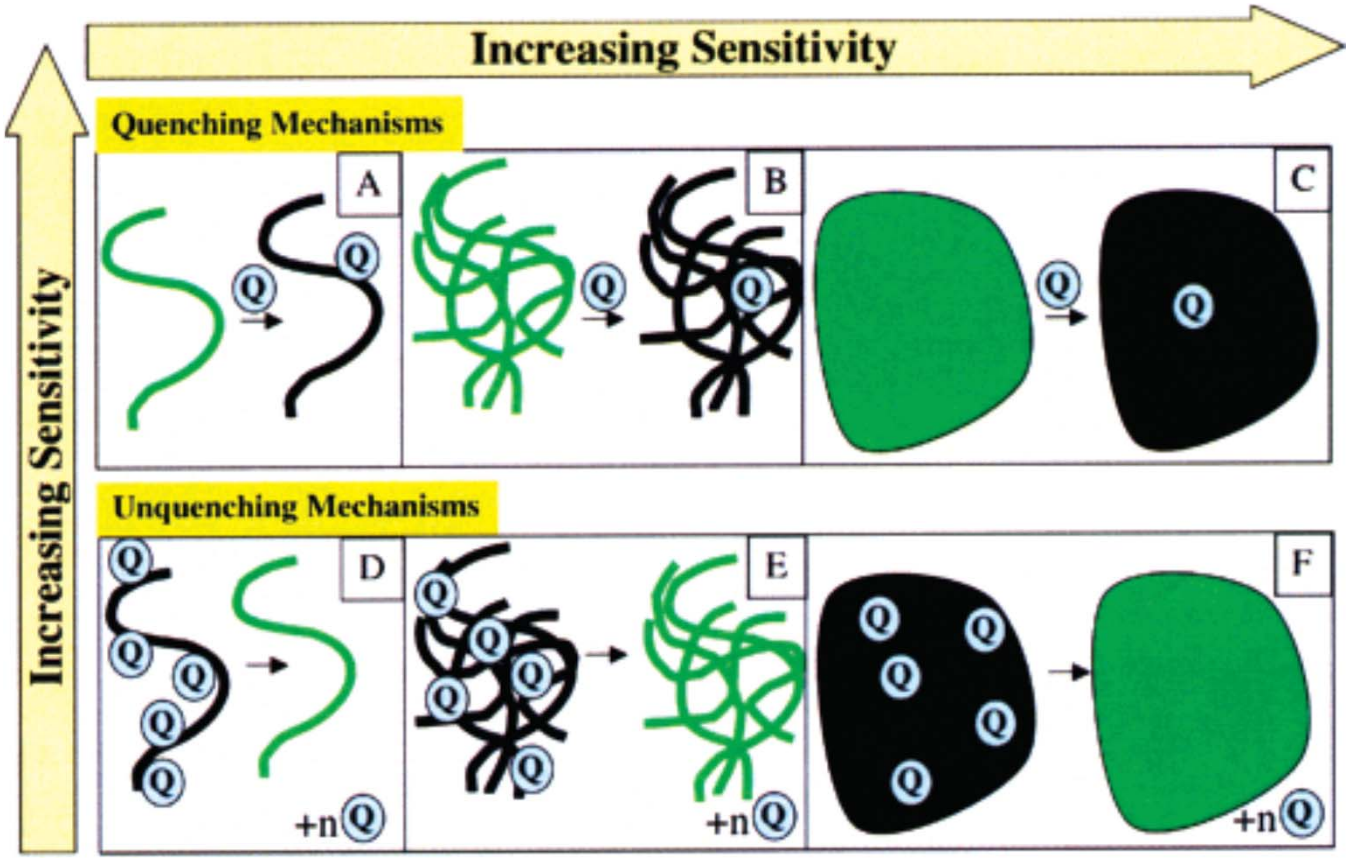
Photoluminescence is the emission of light from any material due to the loss of energy from excited state to ground state. There are two main types of luminescence – fluorescence and phosphorescence.

Fluorescence is a fast decay process, where the emission rate is around 10^8 s^{-1} and the lifetime is around 10^{-9} - 10^{-7} s. Fluorescence occurs when the excited state electron has an opposite spin compared to the ground state electrons. From the laws of quantum mechanics, this is an allowed transition, and occurs rapidly by emission of a photon. Fluorescence disappears as soon as the exciting light source is removed. Group 12-16 semiconductor quantum dots exhibit fluorescence properties when excited with ultraviolet light.

Phosphorescence is the emission of light, in which the excited state electron has the same spin orientation as the ground state electron. This transition is a forbidden one and hence the emission rates are slow (10^3 - 10^0 s^{-1}). So the phosphorescence lifetimes are longer, typically seconds to several minutes, while the excited phosphors slowly returned to the ground state. Phosphorescence is still seen, even after the exciting light source is removed.

Barron, A. Physical Methods in Chemistry and Nano Science, OpenStax_CNX Web site. http://cnx.org/content/col10699/1.18/, Jan 3, 2014.

Role of Mechanism and Dimensionality



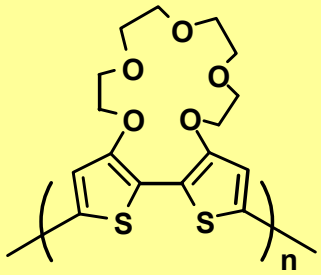
Turn-Off

Turn-On

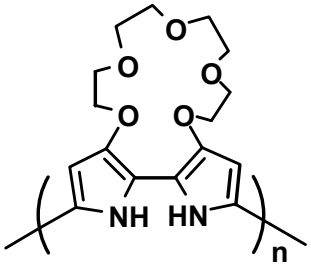
T. Swager et al., Chem. Rev. (2007)

π-Conjugated Polymers

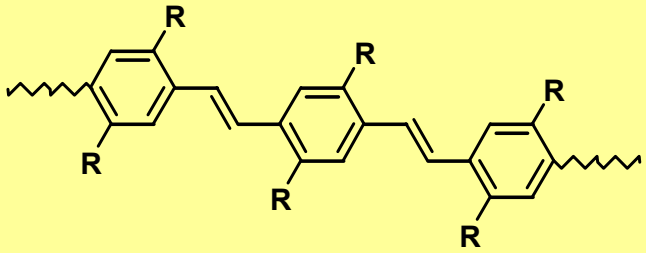
- **π-Conjugated Polymers**



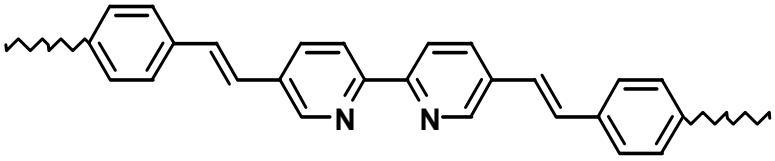
Polythiophene



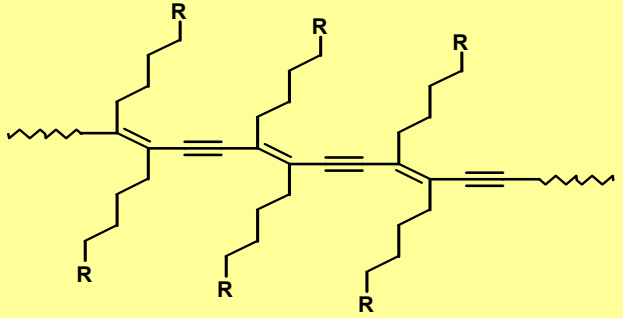
Polypyrrole



Poly(phenyleneethylene)



Combination (PPE + Bipyridil)

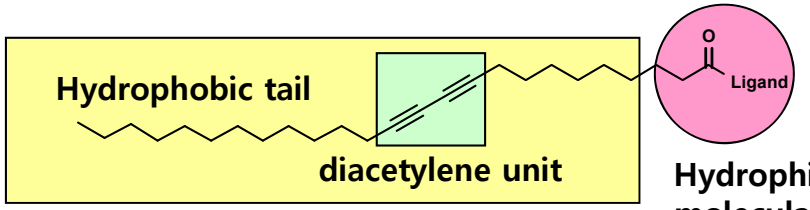


Polydiacetylene

- **Electrical and/or optical properties**

Easily dispersed into aqueous media !

Polydiacetylene Supramolecules

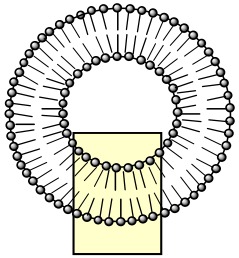


Hydrophilic head
molecular recognition

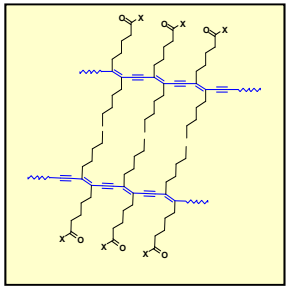
Colorless

Blue

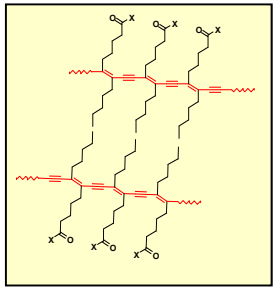
Red



hν



Stimuli



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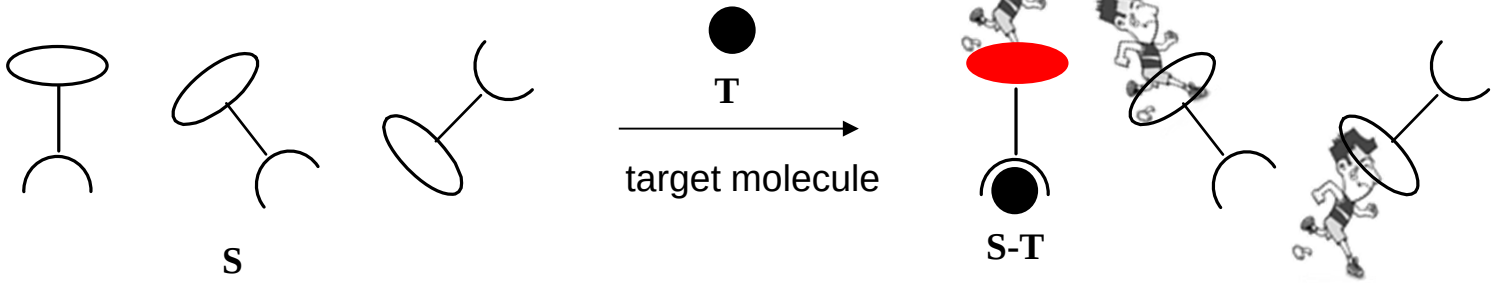
Conjugated Polymers

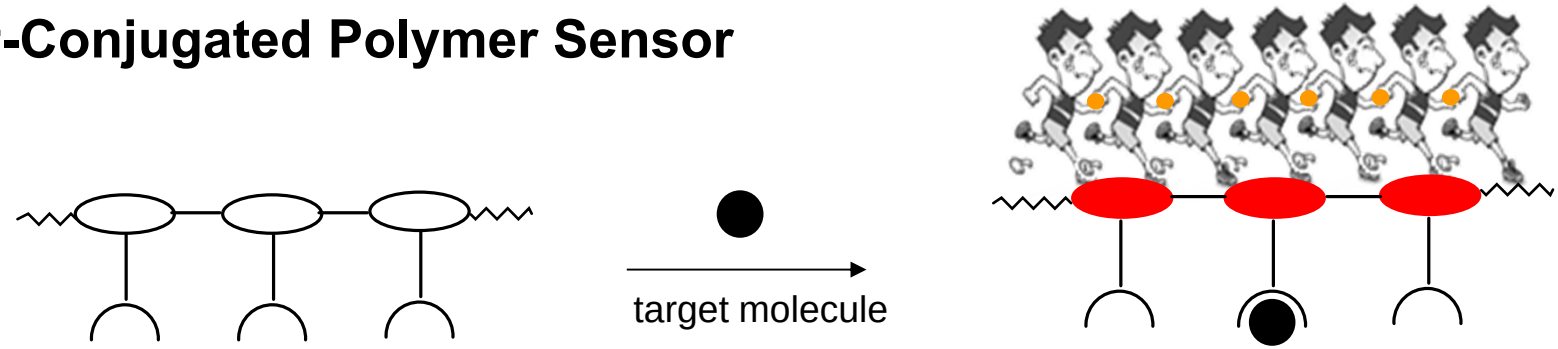
- **Conventional Chemosensor**



Sensitivity depends on the equilibrium constant.

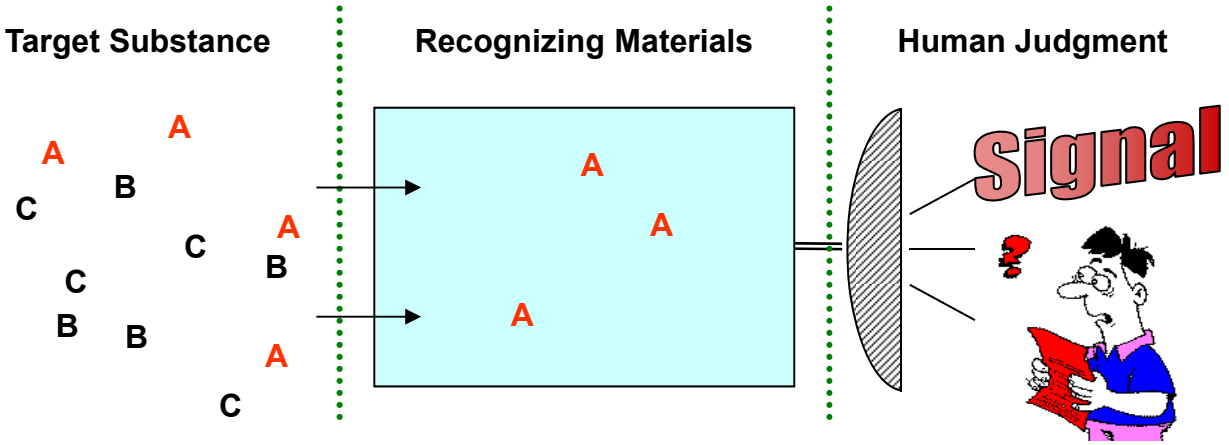
$$K_{eq} = [S\text{-}T] / [S]\,[T]$$

- **π-Conjugated Polymer Sensor**



Signal amplification can be achieved.

Sensor System



Interface I
Target / Sensor Matrix

Affinity
Shape
Size

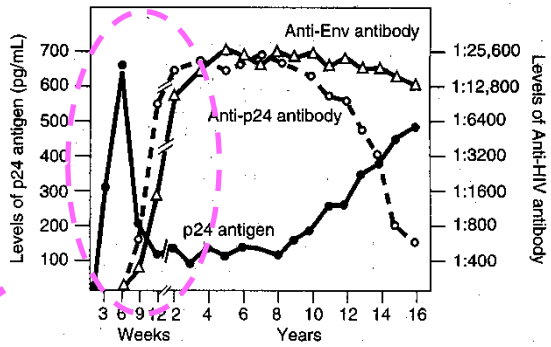
Interface II
Sensor Matrix / Human

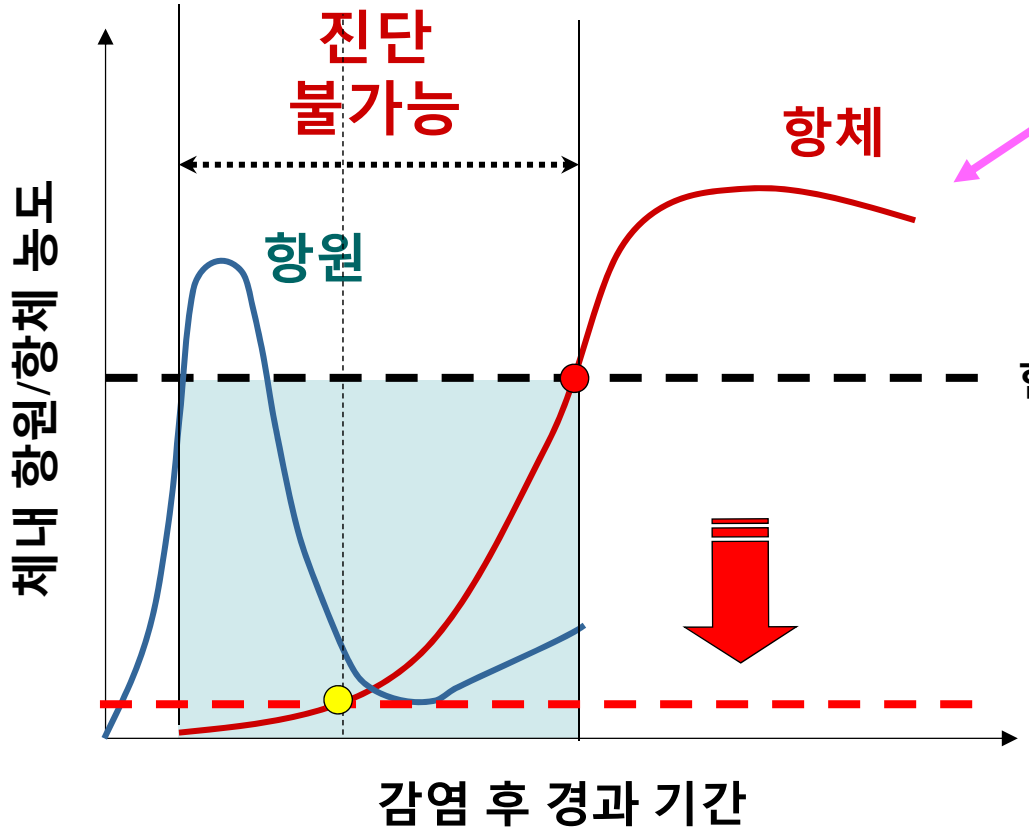
Signal Transducer
Transistors / Optics
Electrochemistry
Mechanics / Nanowires

Sensitivity, Specificity, Reliability

조기진단의 필요성

- 기존 감염진단의 **문제점** : 낮은 민감도
- 예: 수혈사고 (AIDS, 간염 등)





진단 가능

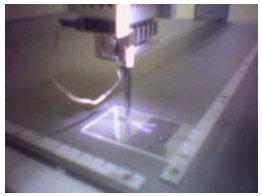
현 진단기술의 검출한계 (1-10 ng/mL)

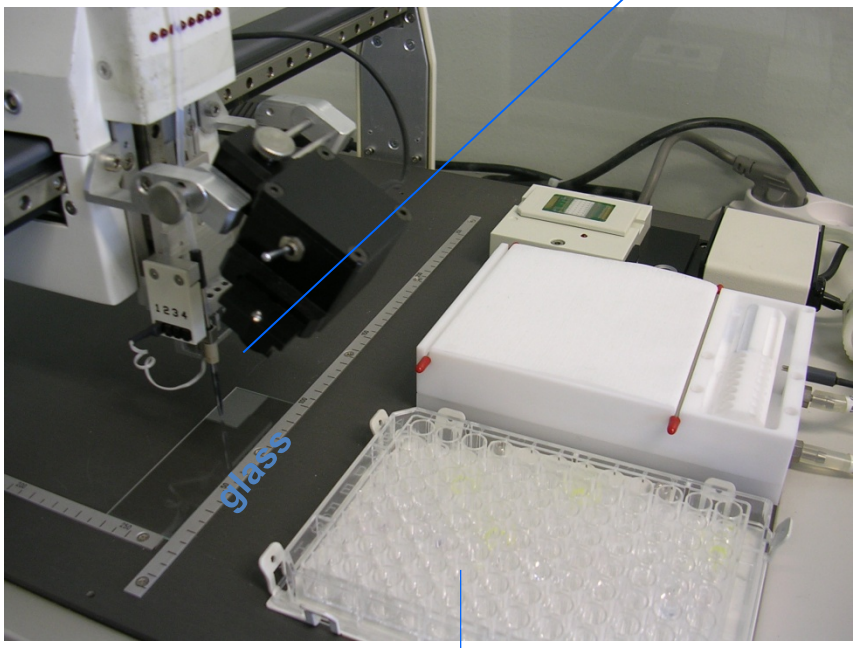
진단 불가능

나노기술 적용으로
초고감도 구현 !

Nanosome Array Chips

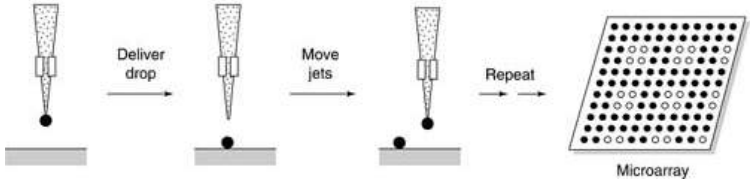
< Ink-jet Microarrayer >



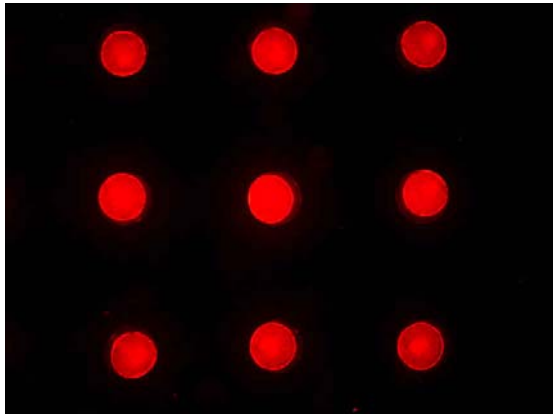


Pre-spot Nanosome Library
Solutions in 96 or 384 well plates

Inkjet (non-contact), single tip



< Microarray of Nanosomes >



1 spot (2 nL), width: 200 ㎛

- Conventional sol'n analysis: 0.1 mL
- 50,000-fold saving
- Tiny amount of analytes
- Simultaneous multiple screening

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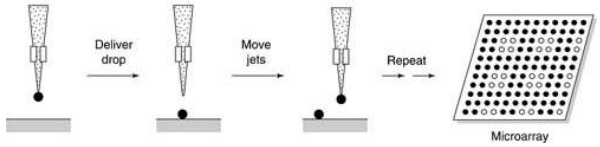
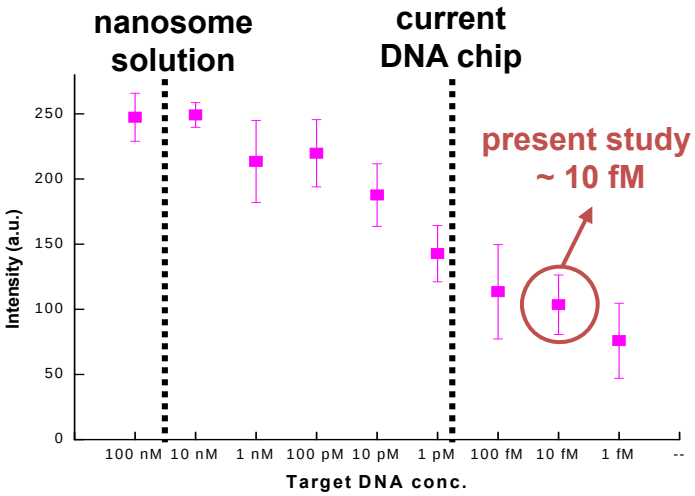
DNA Detection Sensitivity



3` - GAT GGA TGC CCA TTG - 5`-NH_2

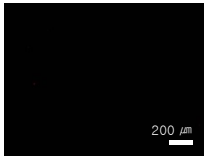
5` - CTA CCT ACG GGT AAC - 3`

E. coli lethal factor sequence 15 mer.

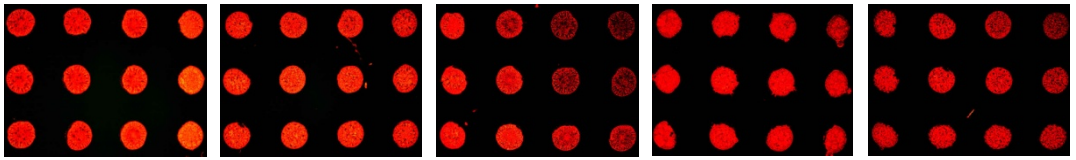


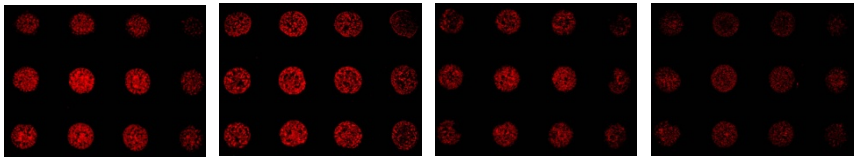
Spotting of nanosome-probe DNA complex

Polymerization



target DNA





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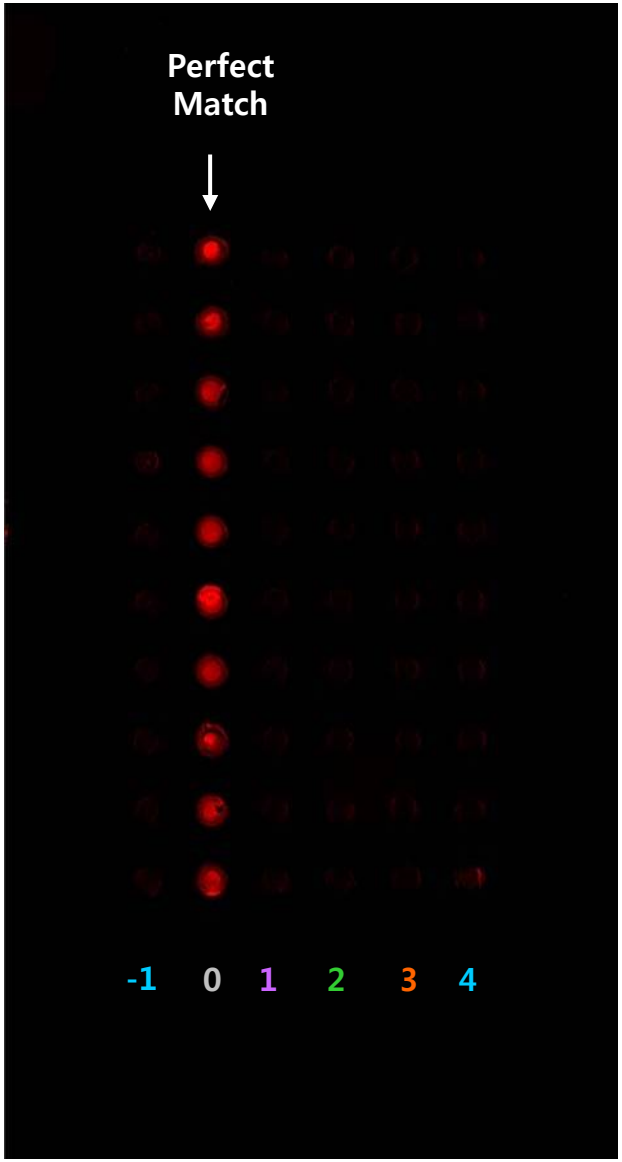
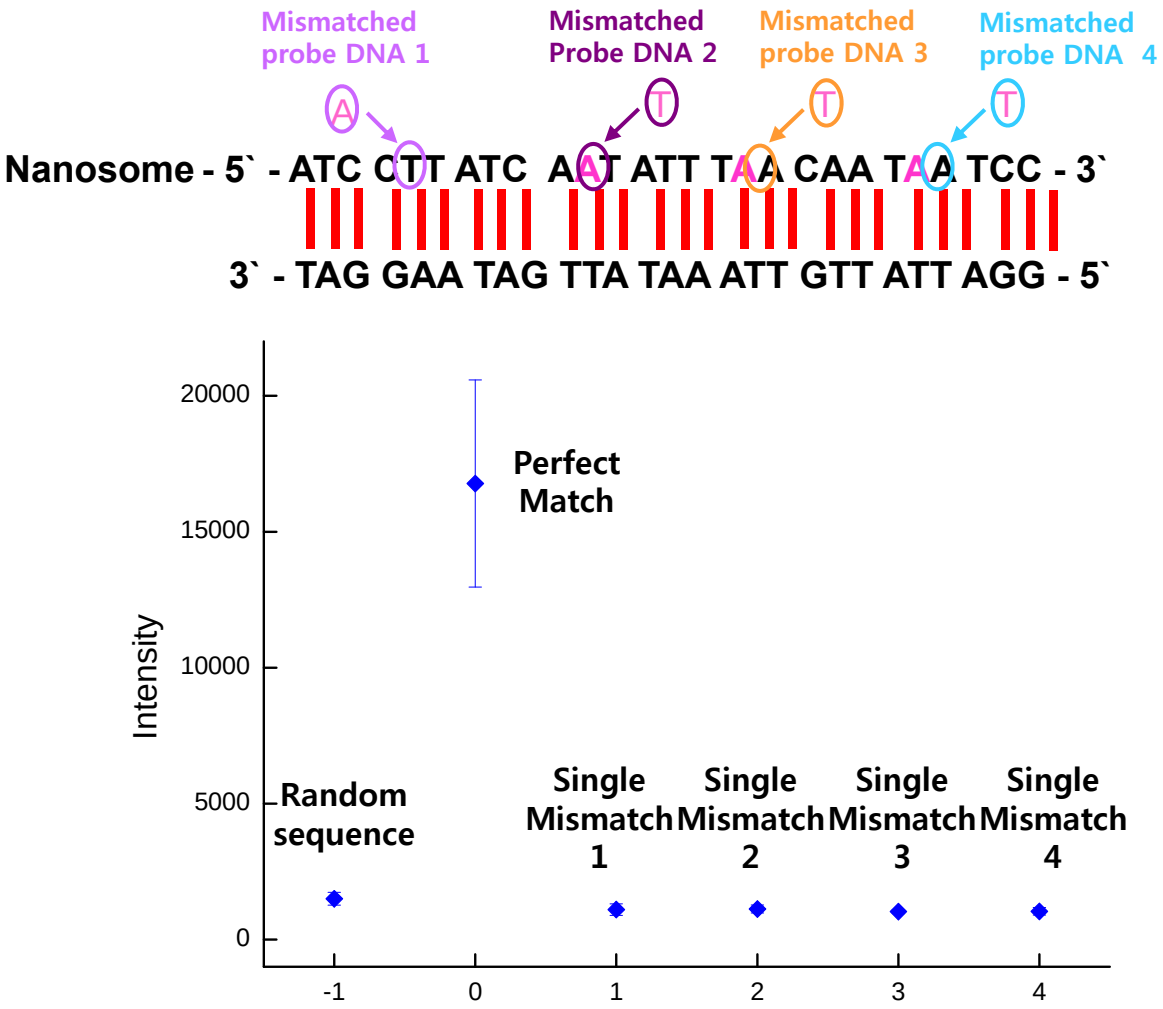
DNA Detection Selectivity





-1: Random, 0: Perfect, 1: Mis 1, 2: Mis 2, 3: Mis 3, 4: Mis 4

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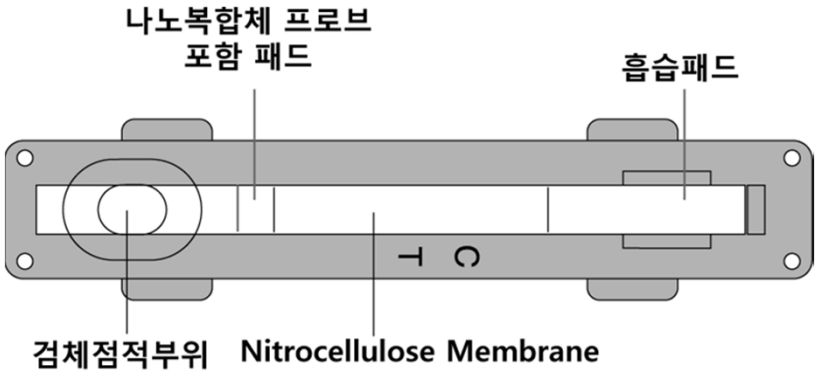
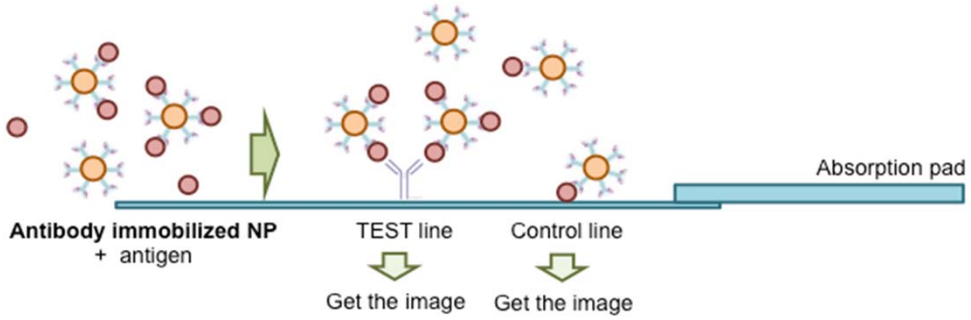
Assay Kit





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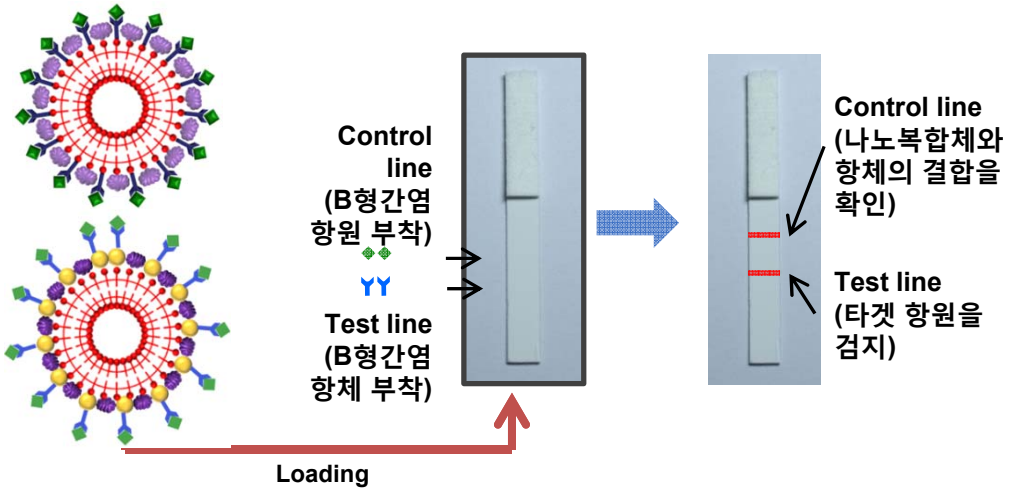
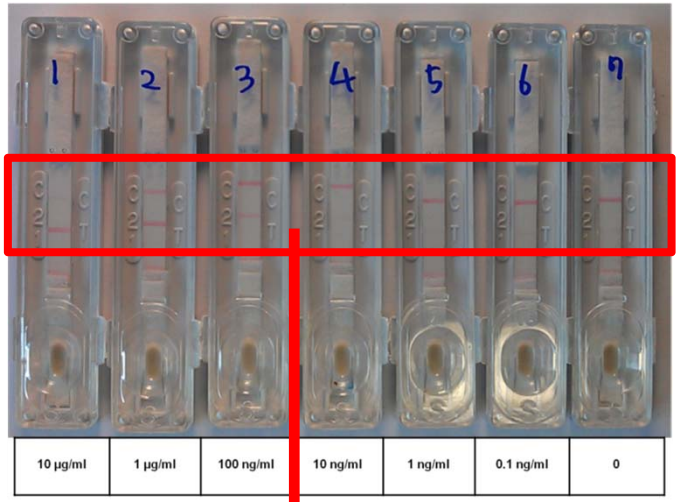
Diagnosis of Hepatitis B Antigen



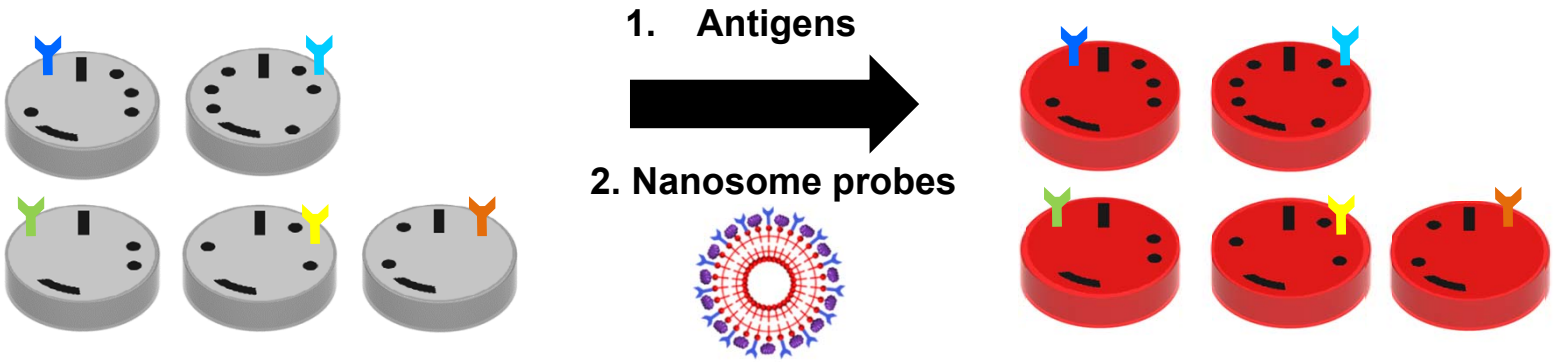
B형간염 진단 키트

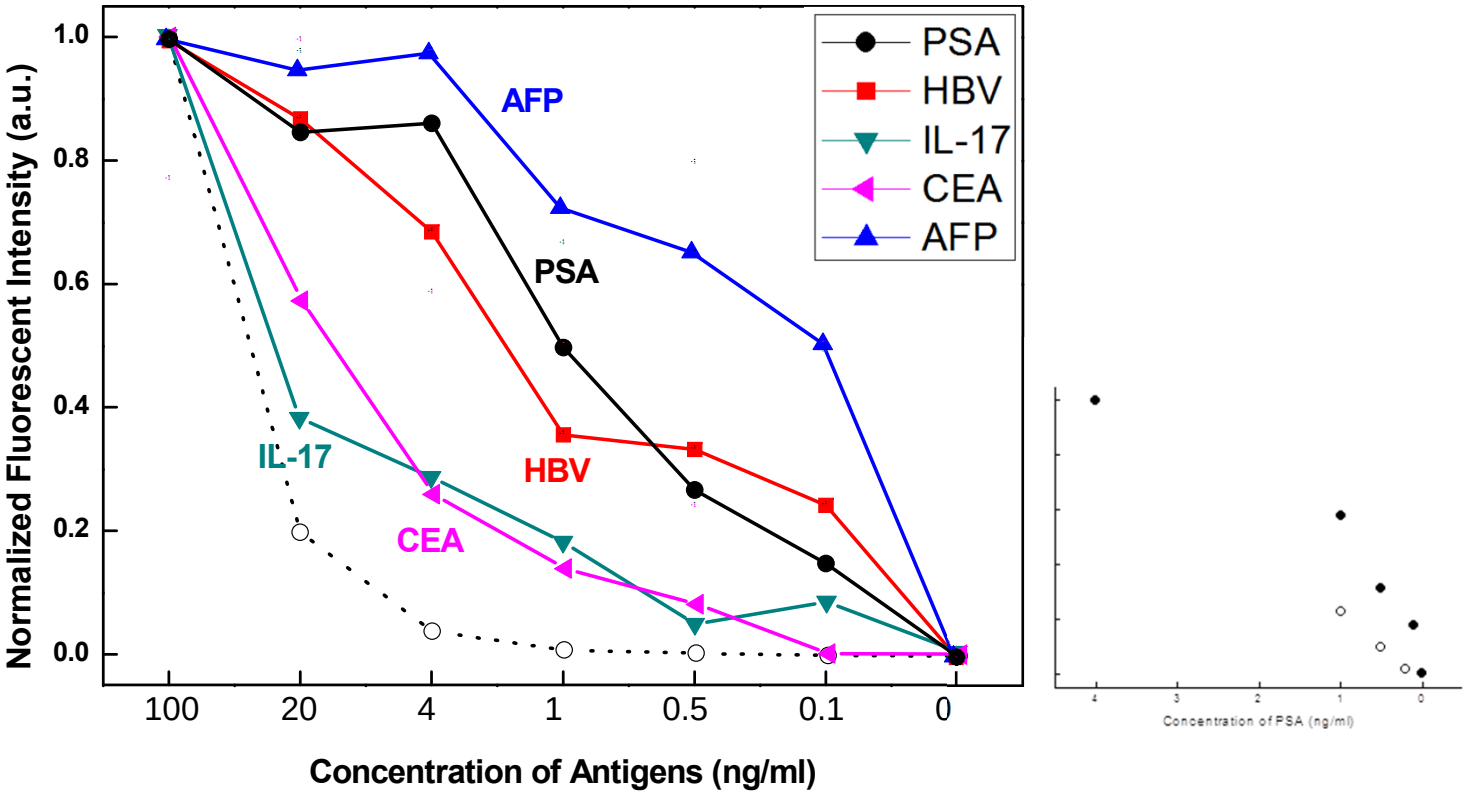


<Fluorescence images>

Conc. of HBsAg	10 μg/ml	1 μg/ml	100 ng/ml	10 ng/ml	1 ng/ml	0.1 ng/ml	0
Control line							
Test line							

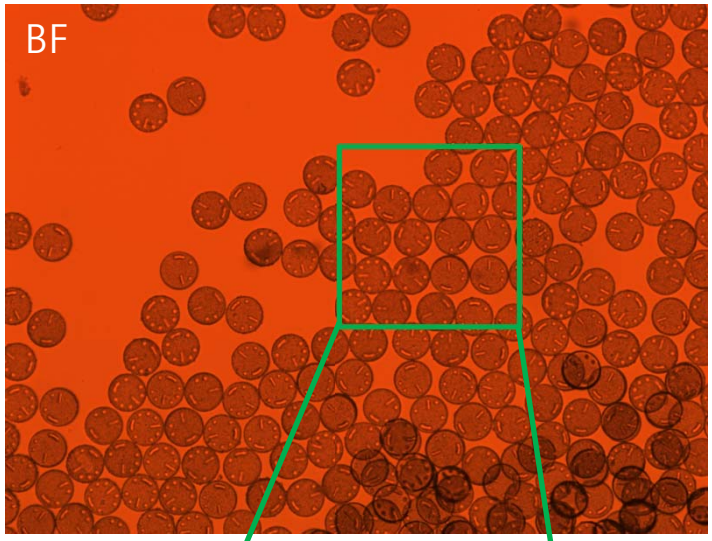
동시다중 검지결과: 타겟농도와의 상관성 (분석시간~30분)



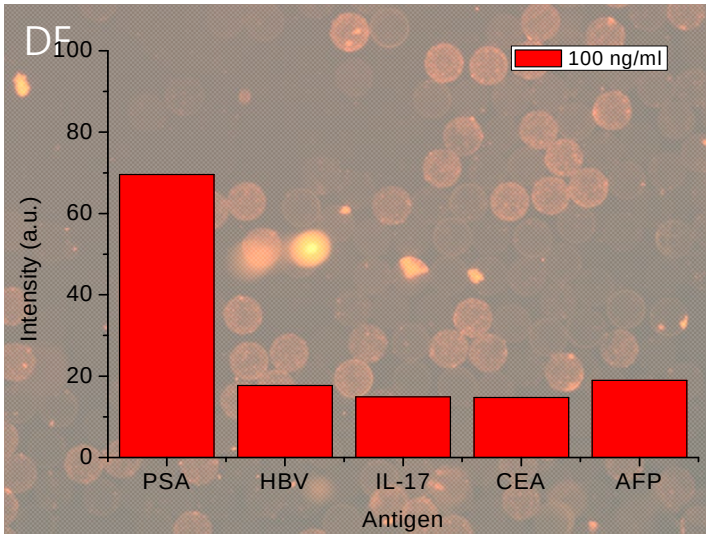


-o- : according to Invitrogen PSA ELISA Kit (~2hrs)

공명라만/형광 복합 진단기술에 의한 5종 동시다중 검지: 100~1ng/ml

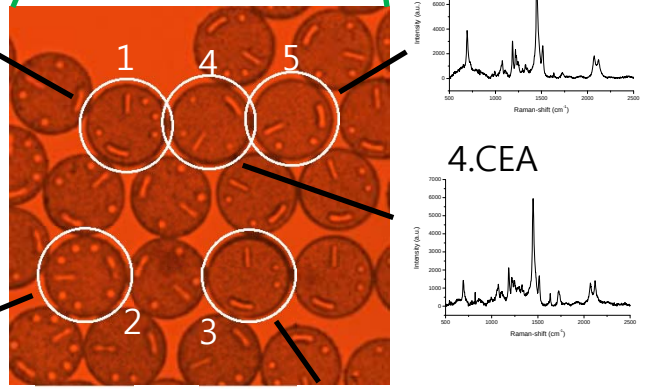


형광분석

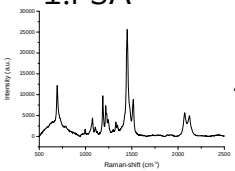


(Light source : 530 nm)

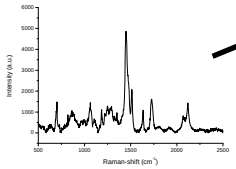
공명라만분석



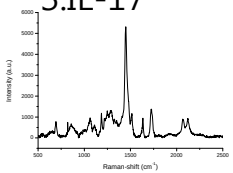
1.PSA



2.HBV

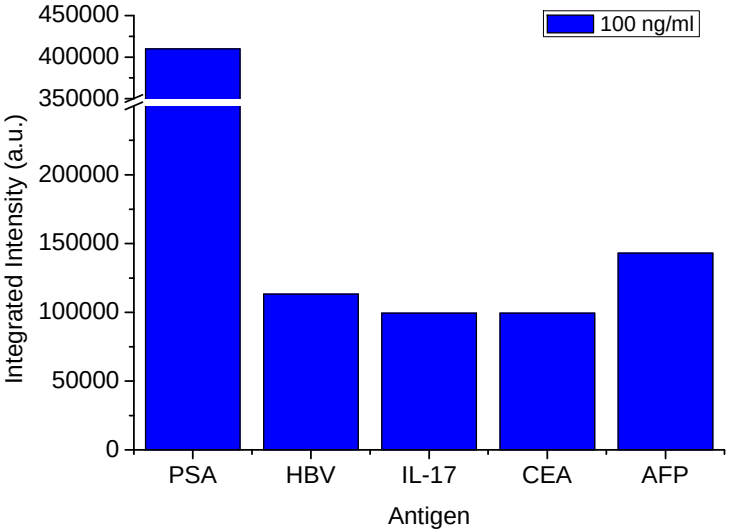


3.IL-17

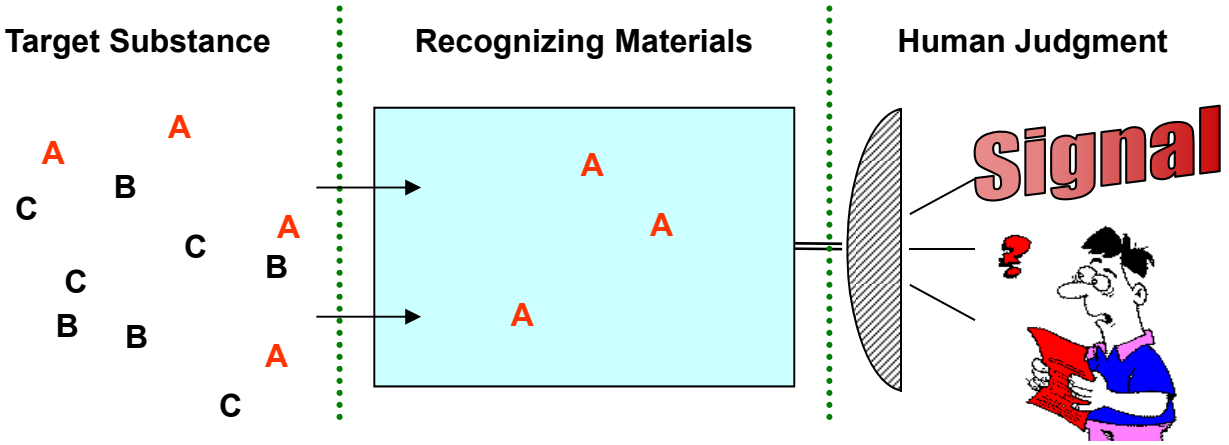


4.CEA

5.AFP



Sensor System



Interface I
Target / Sensor Matrix

Affinity
Shape
Size

Interface II
Sensor Matrix / Human

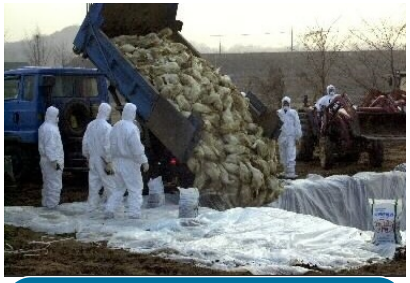
Signal Transducer
Transistors / Optics
Electrochemistry
Mechanics / Nanowires

Sensitivity, Specificity, Reliability

Speed

Global Hazard Transfer

글로벌 교역을 통한 유해물 확산에 따른 문제점 대두



2000년 이후 조류독감
(매몰가금류 1,829만 마리)

2010년 구제역
(매몰가축 수 347만 마리
한해 경제적 피해액 8조 추정

2011년 장출혈성 대장균

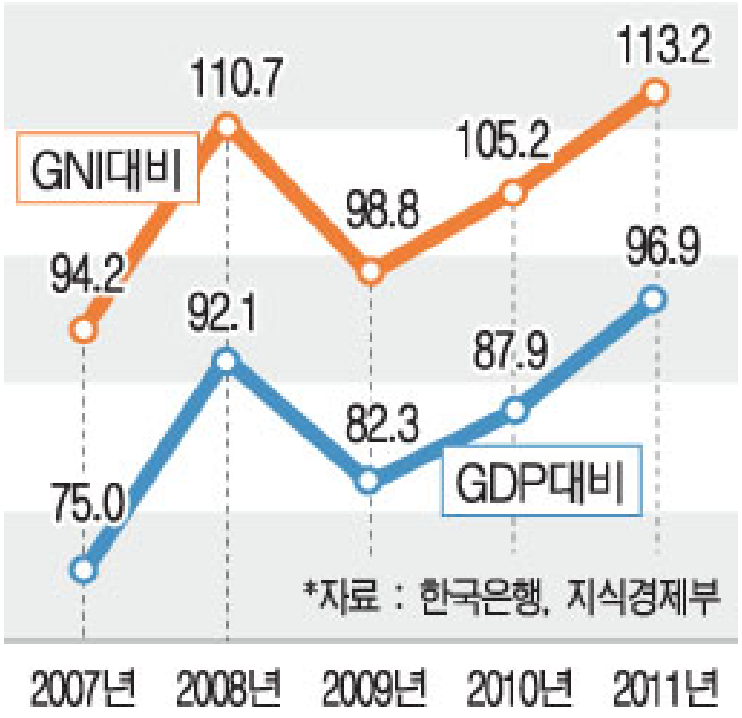
2011년 일본 방사능유출

기존 기술의 한계로 인해 충분한 검역을 하지 못하기 때문임

- 더 빠르고, 싸고, 간편하고, 신뢰도 높은 신개념 검사법 필요
- 표준화된 검역기술 필요

무역의존도 추이

(단위 : %)



G20 회원국 수출·수입 비중 순위 (GDP 대비 비중, 단위 : %)

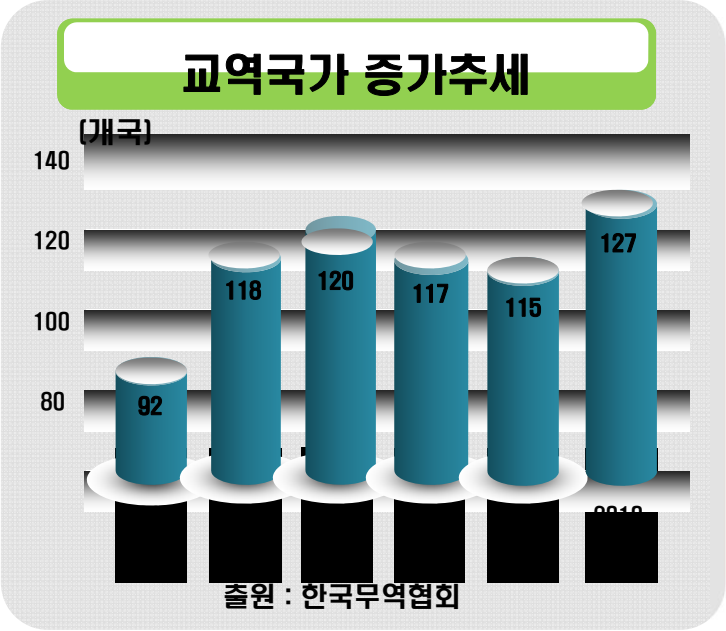
순위	수출		수입	
1	한국	(43.4)	한국	(38.8)
2	독일	(33.6)	멕시코	(28.1)
3	멕시코	(26.2)	독일	(28.0)
4	중국	(24.5)	남아공	(25.4)
5	러시아	(24.4)	캐나다	(24.6)
6	캐나다	(23.4)	사우디아라비아	(24.3)
7	인도네시아	(22.1)	터키	(22.9)
8	남아공	(21.7)	영국	(22.2)
9	이탈리아	(19.1)	프랑스	(20.9)
10	아르헨티나	(18.2)	중국	(20.5)
11	프랑스	(17.8)	인도	(19.8)
12	터키	(16.6)	이탈리아	(19.5)
13	영국	(16.3)	인도네시아	(17.2)
14	호주	(15.6)	호주	(16.6)
15	유로지역	(14.4)	유로지역	(14.0)
16	인도	(12.8)	아르헨티나	(13.5)
17	일본	(11.4)	미국	(11.4)
18	브라질	(9.7)	일본	(10.8)
19	미국	(7.5)	브라질	(8.5)

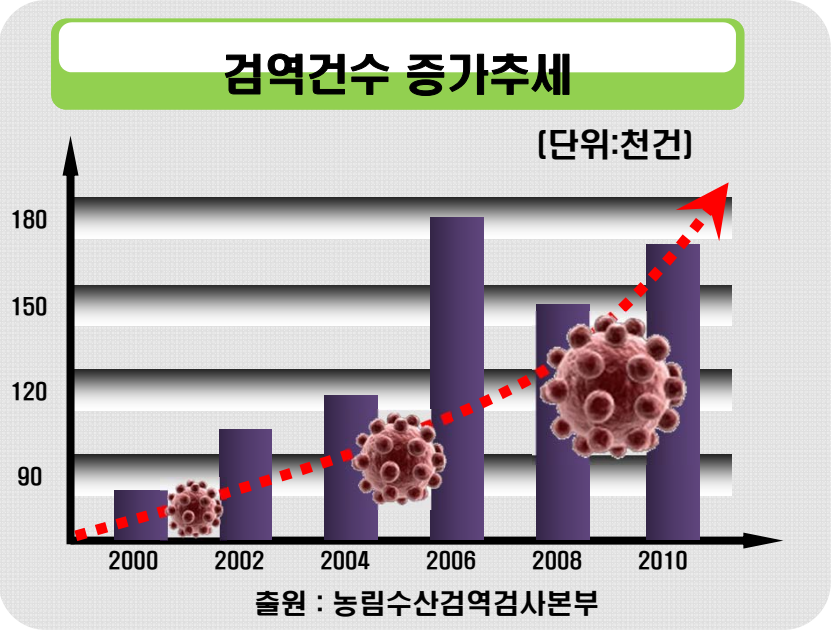
※ 2009년 기준. 수출에서 사우디아라비아 통계 제외, 수입에서 러시아 제외
자료 : 국제통화기금(IMF)·경제협력개발기구(OECD)

최근 교역/검역동향

1) 세계적으로 글로벌 교역이 크게 증가

- 한국 교역규모 세계 9위 (연간 ~1조 달러)
- GDP 중 97%가 수출입관련 생산활동
- 세계 최고 무역의존도



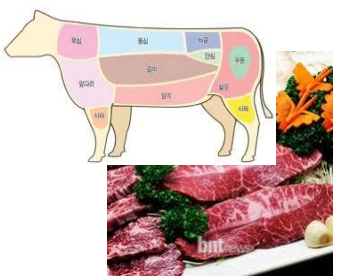


2) 검역관련 국가간 분쟁의 야기

- 다수의 FTA 체결 등 시장개방 확대의 시대를 맞아 국제무역분쟁도 증가
  (예, 한미 FTA, 쇠고기 수입, 등)
- 2010년 17만건중 무작위 6,359건 검사(3.7%). 이중 21건 불합격(0.33%)

기존 검역기술 문제점의 예

소고기 수입



서류검사

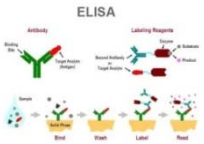
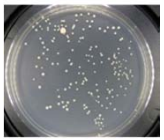
정밀검사 (18일)

- 잔류물질 180 항목
- 미생물 11종
- 중금속, 방사능 등

배양 등 생물학적 증폭에 장시간 소요
(극소수의 분석으로 제한)

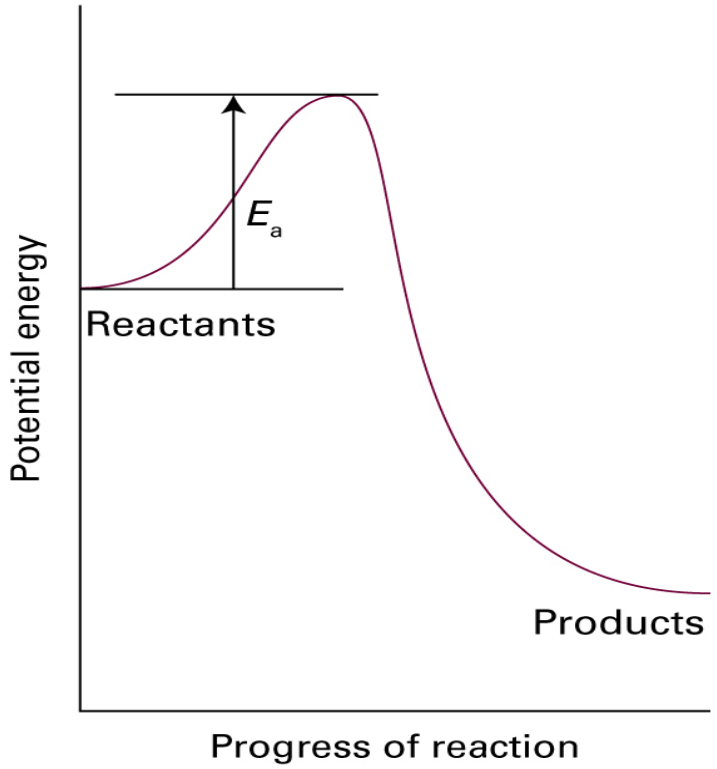
유통

주요이유는 기존 바이오 분석 기술의 한계 때문

검역대상물질	(단백질)	(DNA & RNA)	(박테리아, 바이러스)	(화학물질)
기존기술	ELISA 	PCR 	Colony Counting 	GC-MS & HPLC 
기술 한계	제한된 감도	고가, 느린 속도	복잡, 느린 속도	복잡한 전처리, 고가, 큰 장비

NBM Group

Basic Physical Chemistry of Recognition Kinetics



Receptor+Target ↔ Product

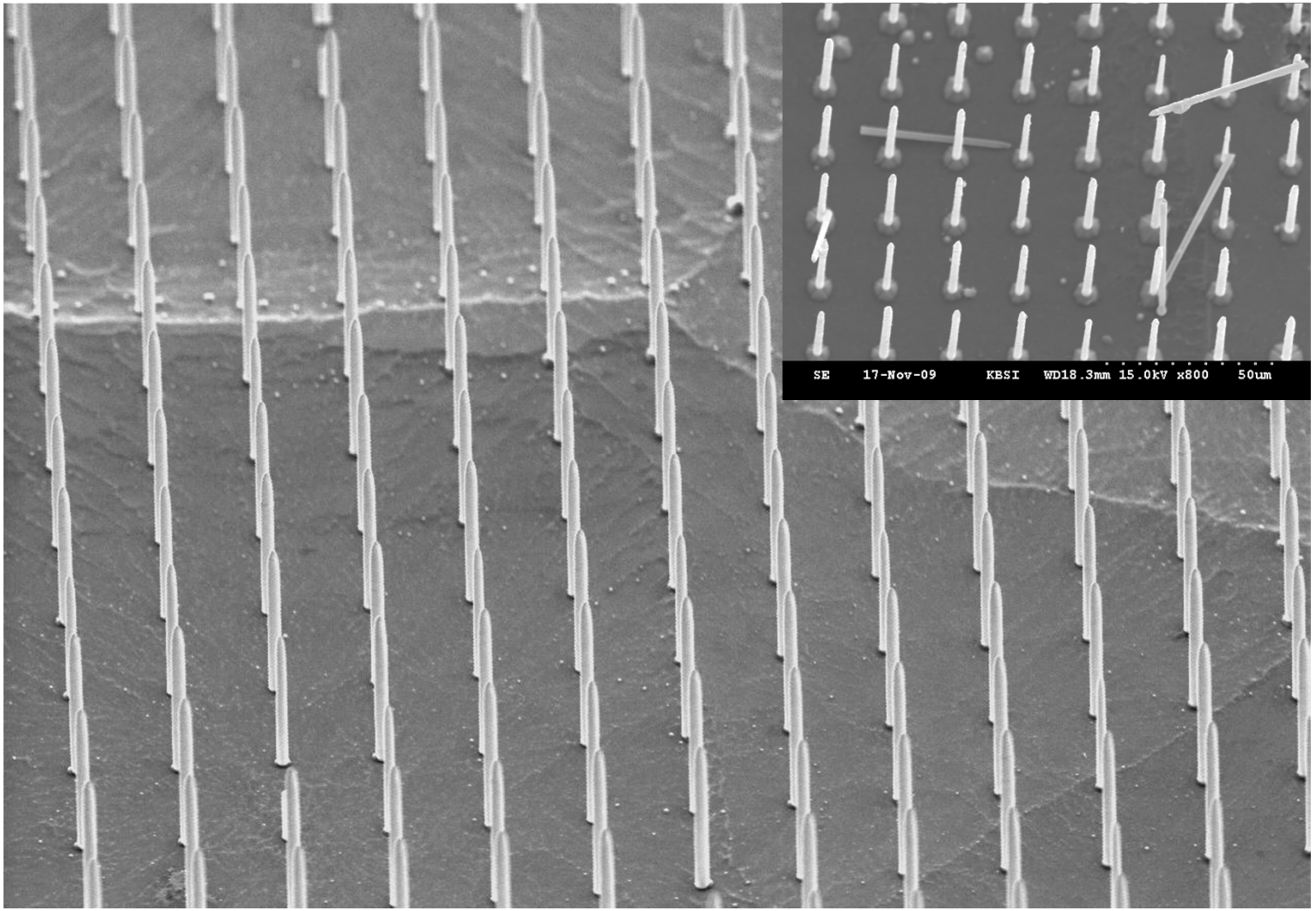
$$\frac{dP}{dt} = k \text{ x } function\ of\ activity\ (or, conc.)$$

$$k = A \exp\left(-\frac{Ea}{RT}\right)$$

(if Boltzmann distribution holds)

- Recognition process is exothermic:
  Low T favored
- Smaller Ea favored:
  Do we have catalyst? No
- *A* (collision) needs to be increased:
  High T or mechanical mobility

Silica Tube (“Obelisk”) Arrays



SEM image of exposed silica tube arrays

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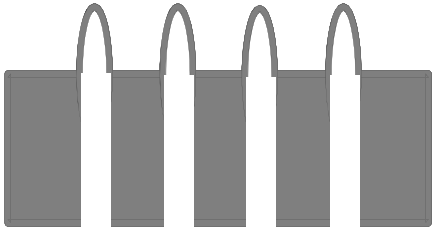
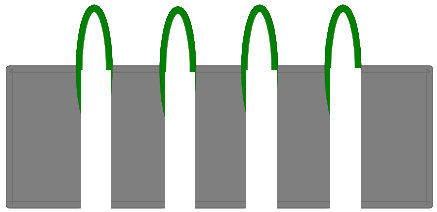
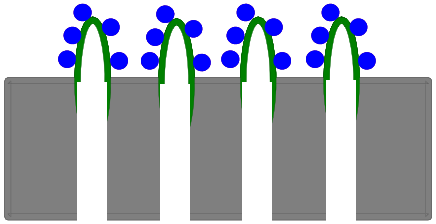
Nanosome Obelisk Arrays

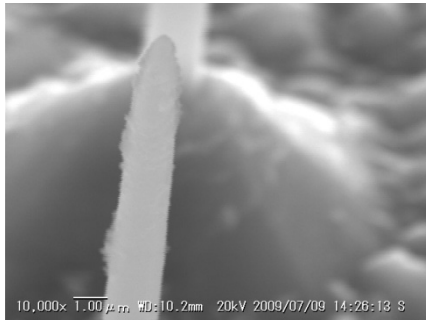
SAM
modification



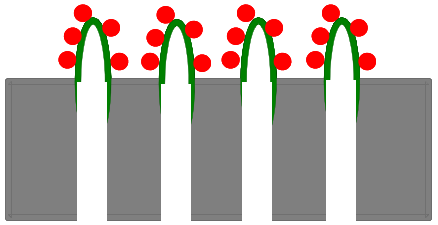


Nanosome
adsorption

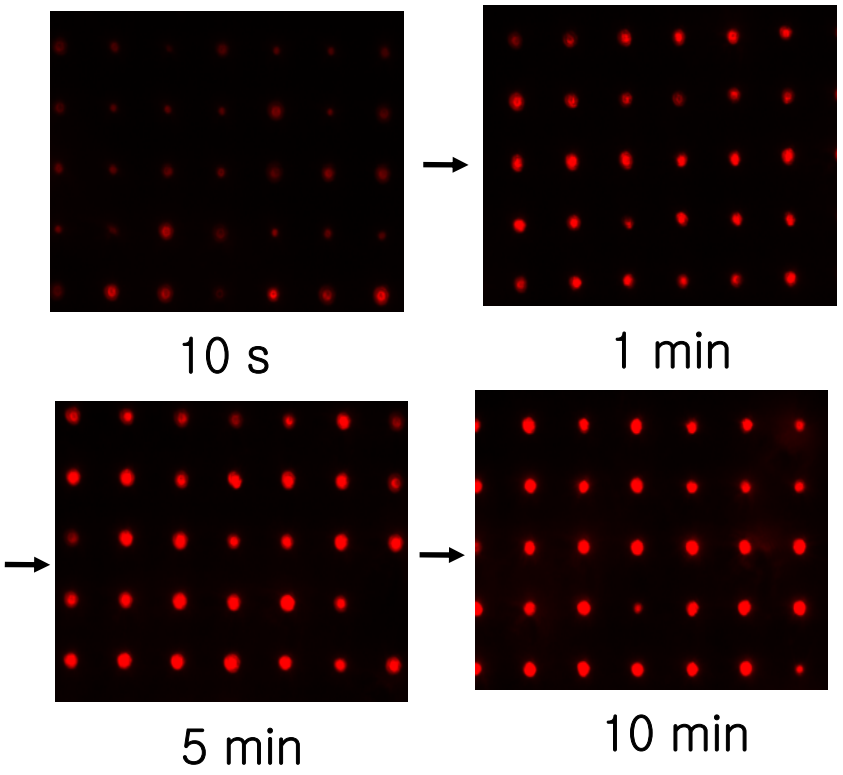


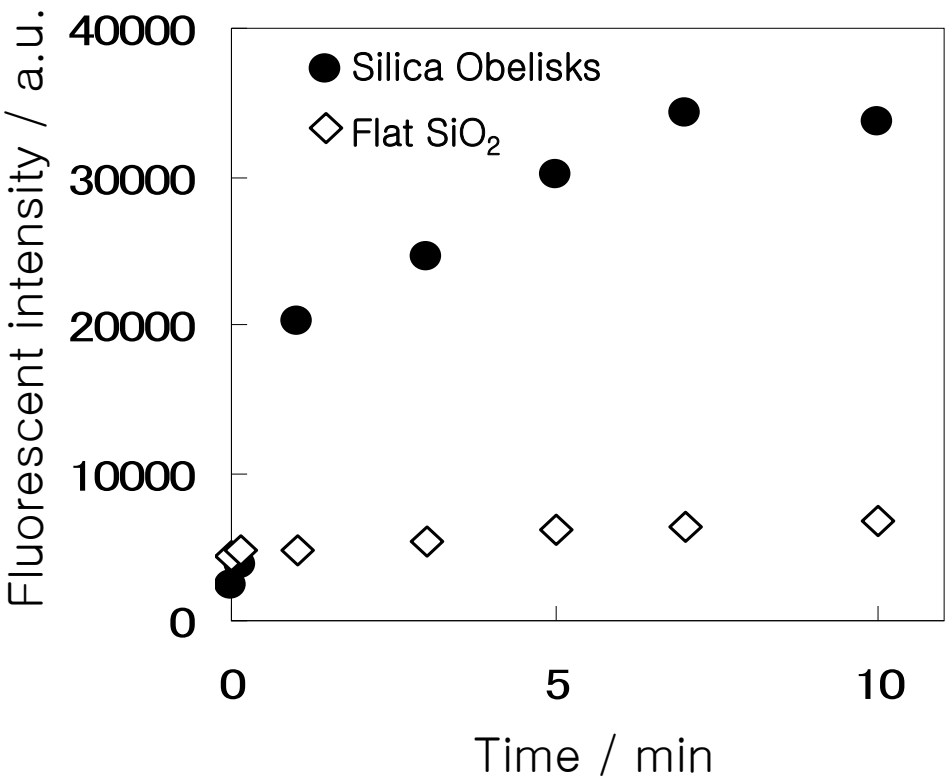


Sensing &
Fluorescence measurement



Proof-of-Concept: Ammonia Gas Detection

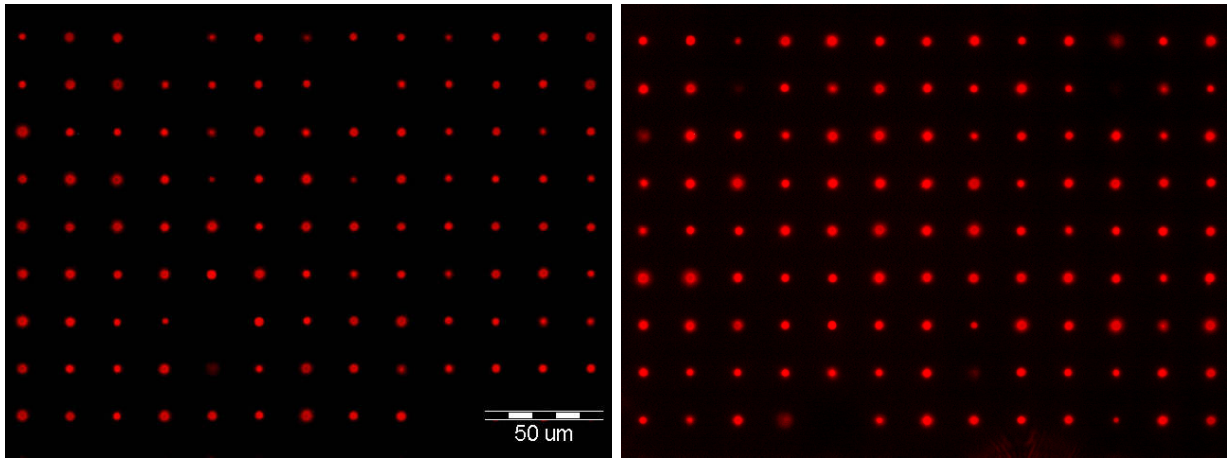




Label-Free DNA Detection in 10 min.

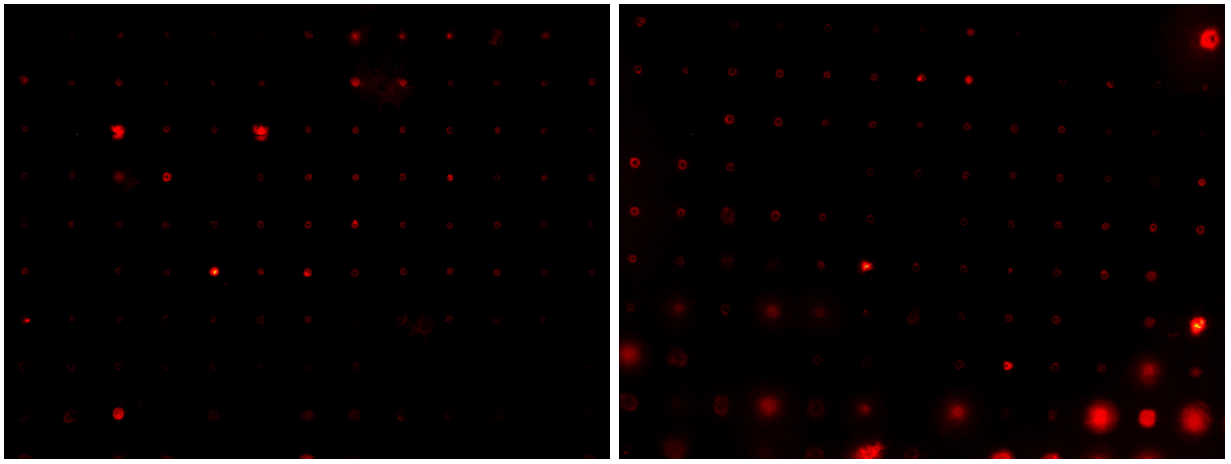
- *target* DNA

100nM *t*DNA **1μM *t*DNA**



- *random* DNA

100nM *random* DNA **1μM *random* DNA**



Exposure time: 0.5s

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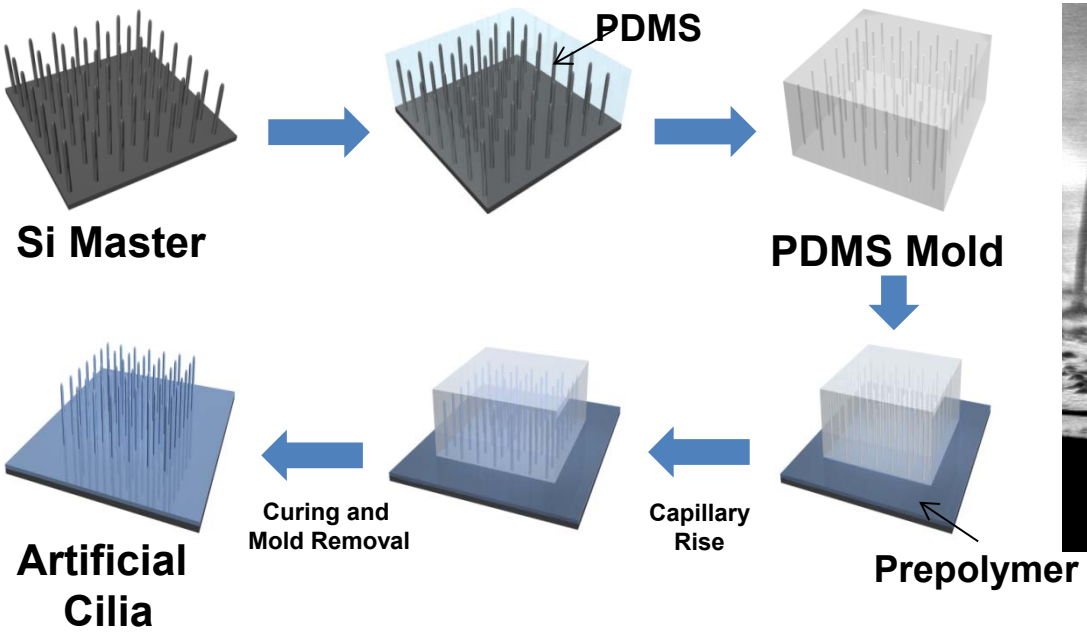
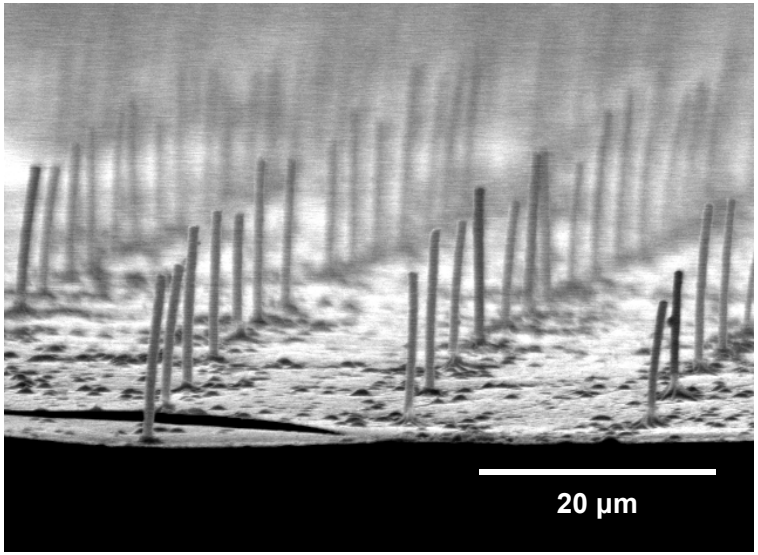
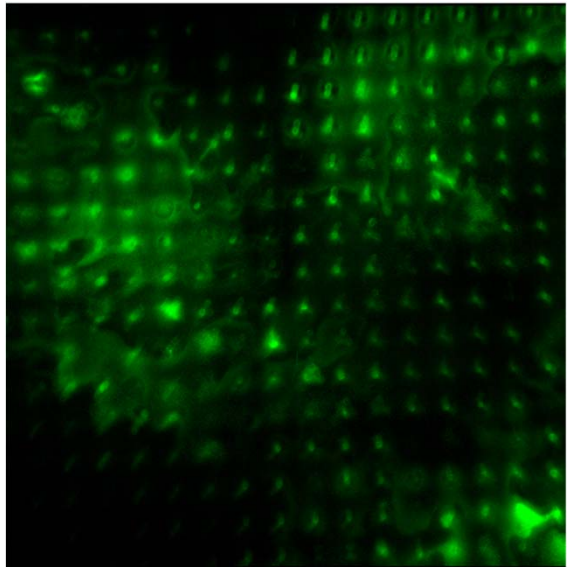
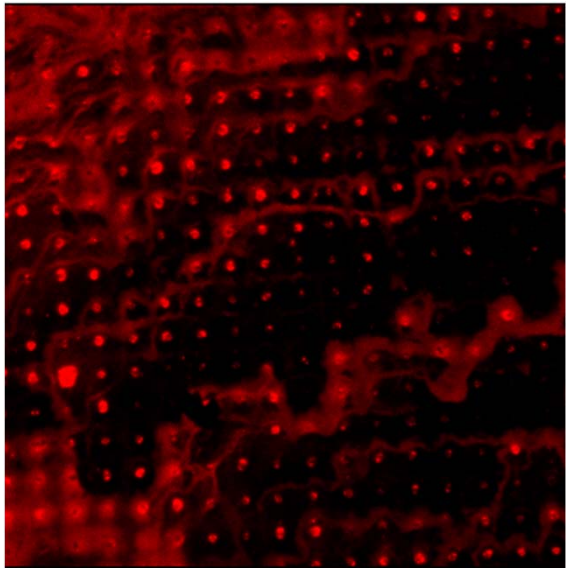
Artificial Cilia









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