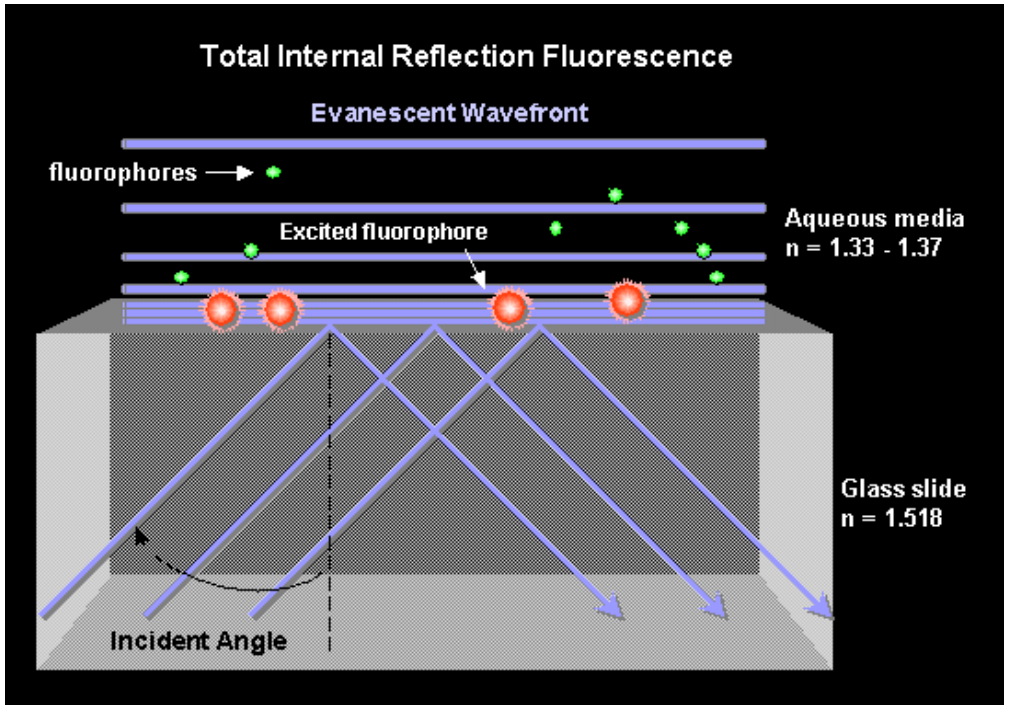
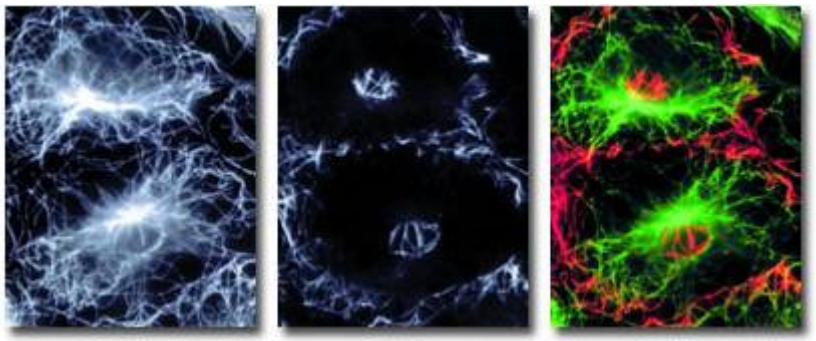
Biomedical Sensors
appendix 2:
SPR Biosensor

Total Internal Reflection Fluorescent (TIRF) Microscope

- Real-time, rapid, in situ, non-destructive, low volume technique.
- Exceptional versatility - TIRF measurements give a lot of information about mechanisms of biomolecular interactions.
- But, TIRF need a fluorescence dye!

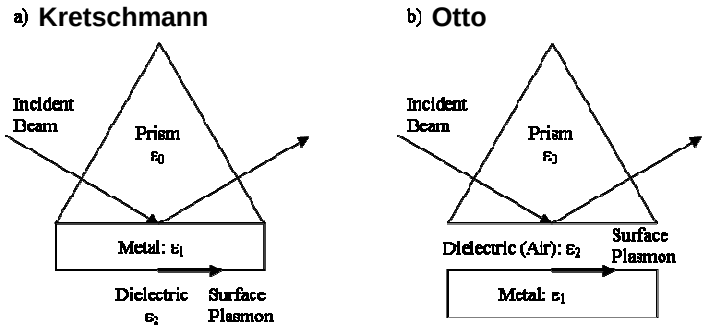




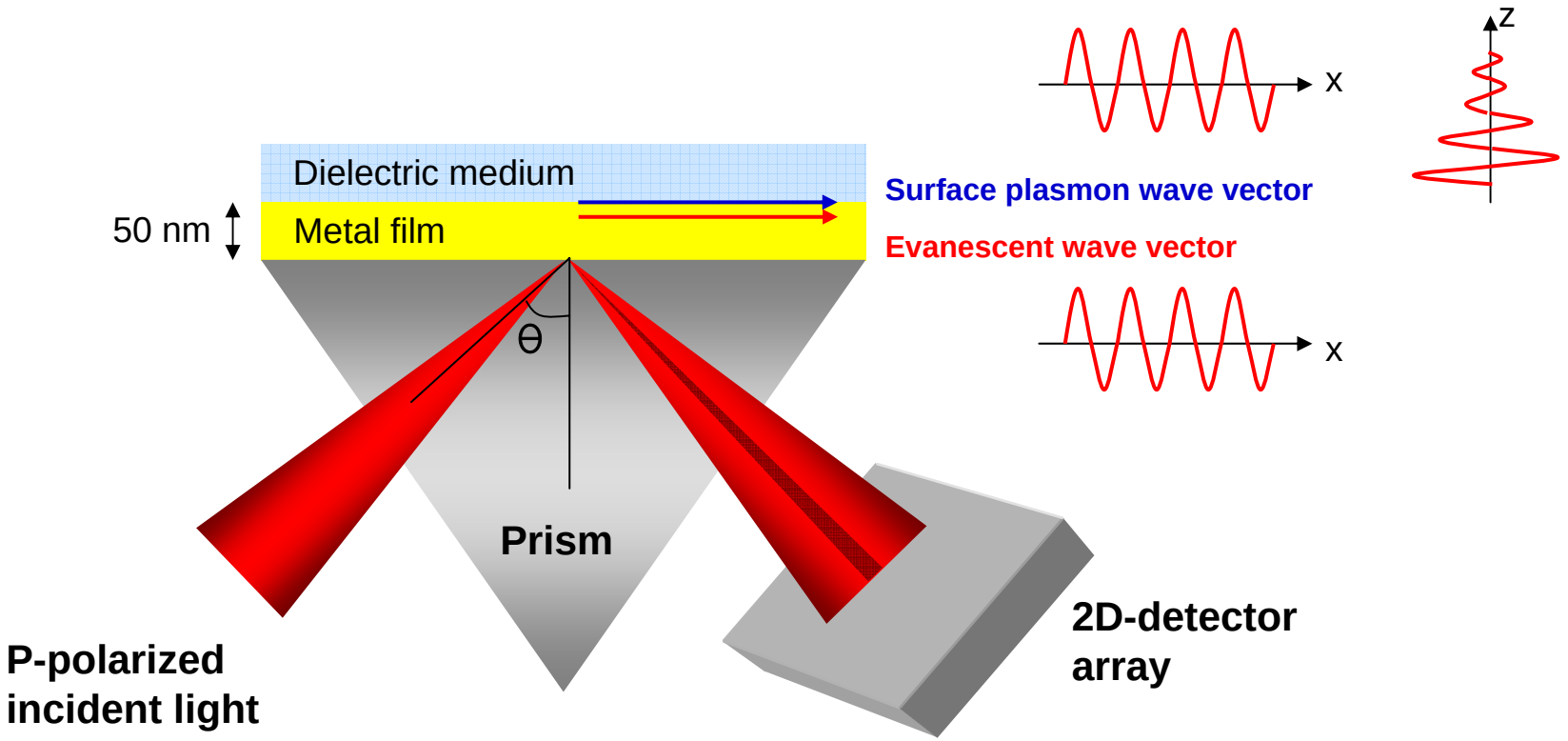
Cell structure investigated by TIRF microscope

Surface plasmon resonance (SPR): History

- 1939: Wood and Fano
  - Find a phenomenon of surface plasmon resonance in the continuous source diffraction spectra of metallic gratings.
- 1957-1958: Ritchie and Stern
  - Derived the dispersion relations for surface EM waves at metal surface.
- 1968: Kretschmann and Otto
  - Devised and modified the prism coupling geometry, which is now the most widely used geometry.
- 1989: Knoll
  - Introduced the technique of surface plasmon microscopy.
- 1990: Biacore (GE Healthcare)
  - Commercialized, for the first time.
- 1990 ~ now:
  - Many researchers from a wide variety of disciplines find surface plasmons useful as an analytical tool for surface analysis.
  - Continue to see a increase in the number of articles published each year utilizing SPR biosensor technology.



Surface plasmon resonance (SPR) : Concept



$$k_x = \frac{2\pi}{\lambda} n_p \sin\theta\,, \quad k_{sp} = \frac{2\pi}{\lambda}\sqrt{\frac{{n_m}^2 {n_d}^2}{{n_m}^2 + {n_d}^2}}, \quad k_x = k_{sp}$$

(n_p, n_m, and n_d: Refractive index of prism, metal, and dielectric medium)

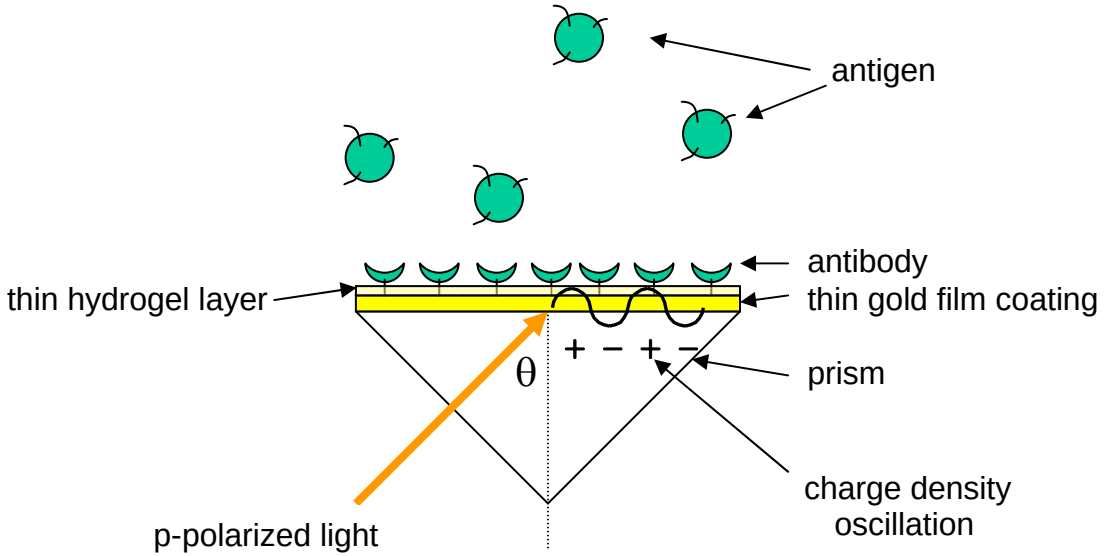
Surface plasmon resonance (SPR) : Concept

- Using surface plasmon resonance

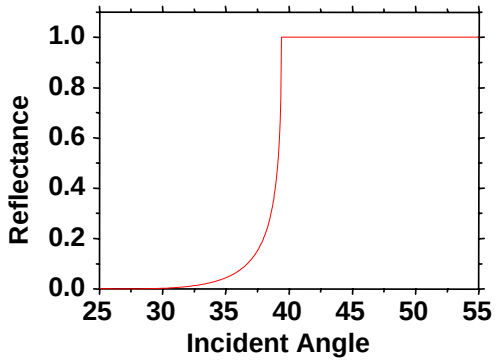
- Detecting interactions in real time

http://www.biacore.com

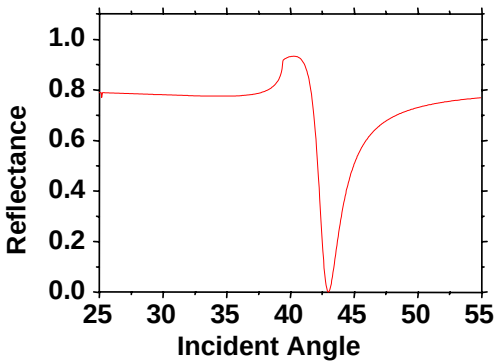
Surface plasmon resonance (SPR) : Concept



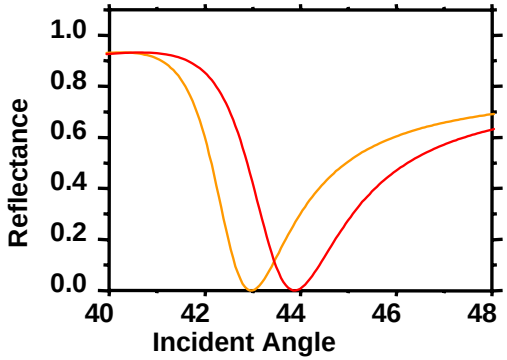
Normal TIR



Surface Plasmon Resonance



Binding causes the dip to shift.



Rothenhäusler *et al.,* Nature 1988
Wilson, Science 2002

Features of SPR biosensor

•No Labeling

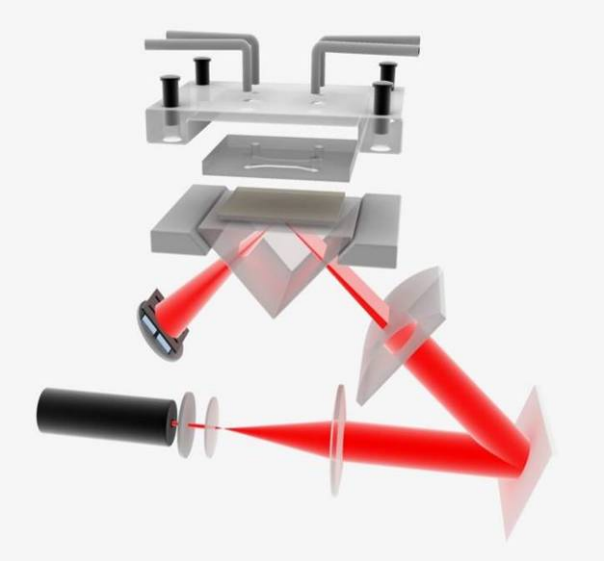
– No Fluorescence Dyes

• Real Time Measurement

– Insight to dynamic nature of binding system and layer formation

• Exceptional sensitivity within Localized Volume

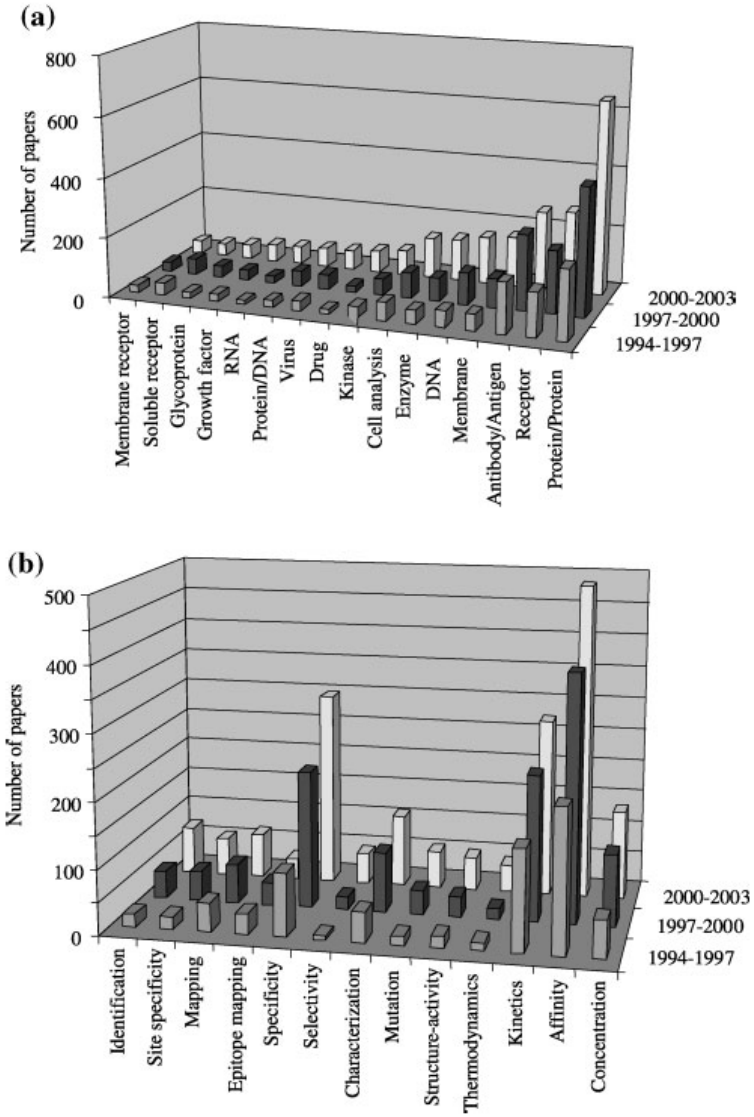
– Small quantities of purified reagents are required



SPR biosensor: Applications

Wide Range of Applications

- Peptide / Protein – Protein
- DNA / RNA – Protein
- Protein / Receptor – Cell
- Antibody – Antigen
- Protein – Virus / Phage
- Cell surface interactions



Revecca *et al.*, Journal of molecular recognition 2006

SPR biosensor: Recent research trend

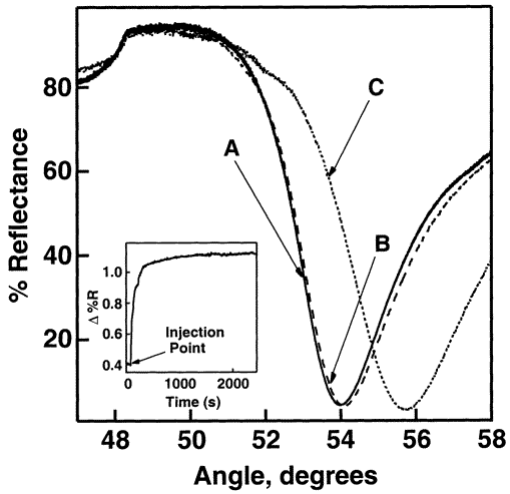
Most of SPR researches focus on the:

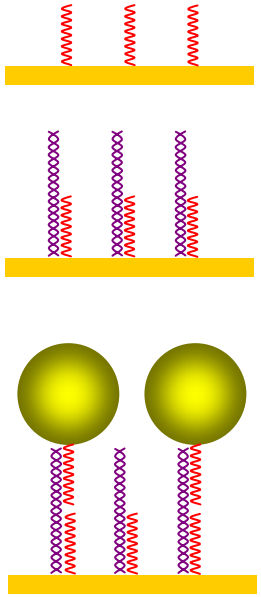
1. **Sensitivity**
2. **Portability**
3. **Imaging**
4. **and, Extension of application**

SPR biosensor: Recent research trend

1. Sensitivity enhancement using nano-particles

- Sensitivity=minimum detectable substance; need largest change of Angle.
- metallic nanostructures enhance the sensitivity by 1 - 2 orders of magnitude by localized surface plasmon effect





(A) 12-mer oligonucleotide

(B) Hybridized with the complementary 24-mer oligonucleotide

(C) Hybridized with the Au-particle tagged complementary 12-mer oligonucleotide

He *et al.* JACS 2000

Lyon *et al.* Anal. Chem. 1998

Mucic *et al.* JACS 1998

SPR biosensor: Recent research trend

1. Sensitivity enhancement using nano-wires

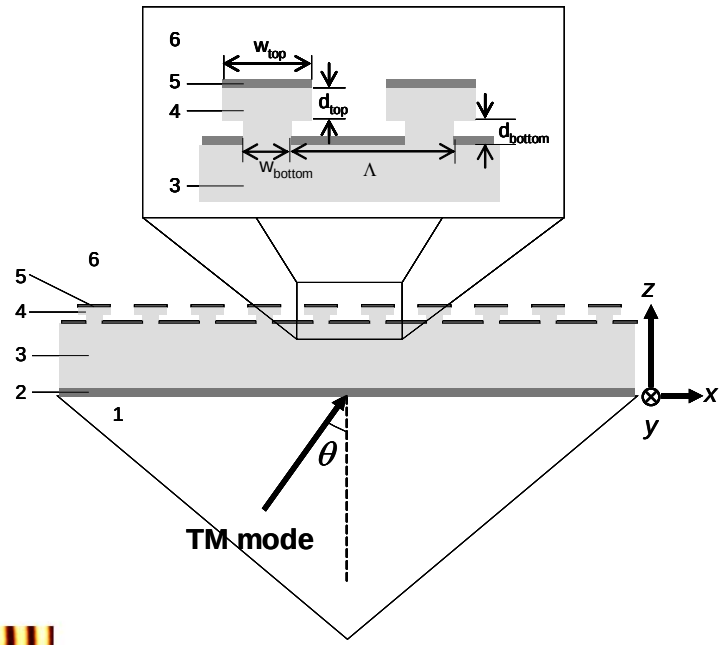
– Localized surface plasmon produced at nanowires also known to amplify sensitivity of SPR

Optimal nanowire geometry :

T-profile (w_{top} = 40 nm, w_{bottom} = 20 nm)

Geometrical factor (GF) :

0.8 (d_{top} = 16 nm, d_{bottom} = 4 nm)



1 - BK7 glass prism
2 - binding metal of chromium (2 nm)
3 - gold film (40 nm)
4 - gold nanowires (20 nm)
5 - target analytes (1 nm)
6 - air

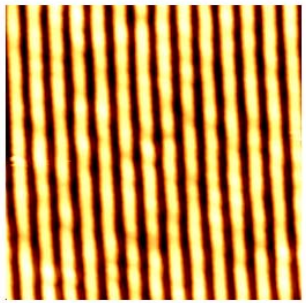
* Peak SEF = 40.91

→ the second highest among T-profiles

* Nanowire period at the peak SEF = 100 nm

→ relatively longer period over 100 nm

Byun *et al.* Opt. Express 2005

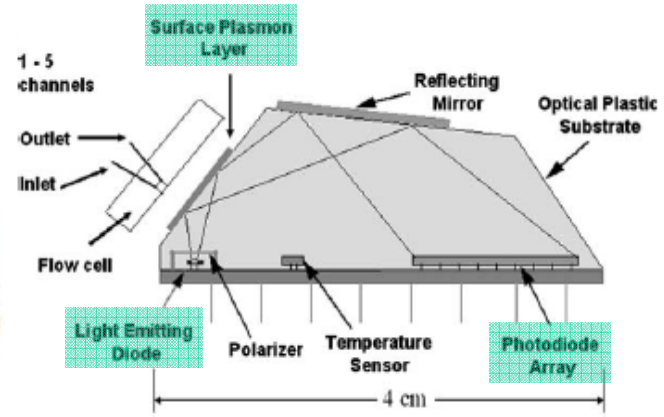


SPR biosensor: Recent research trend

2. Portability

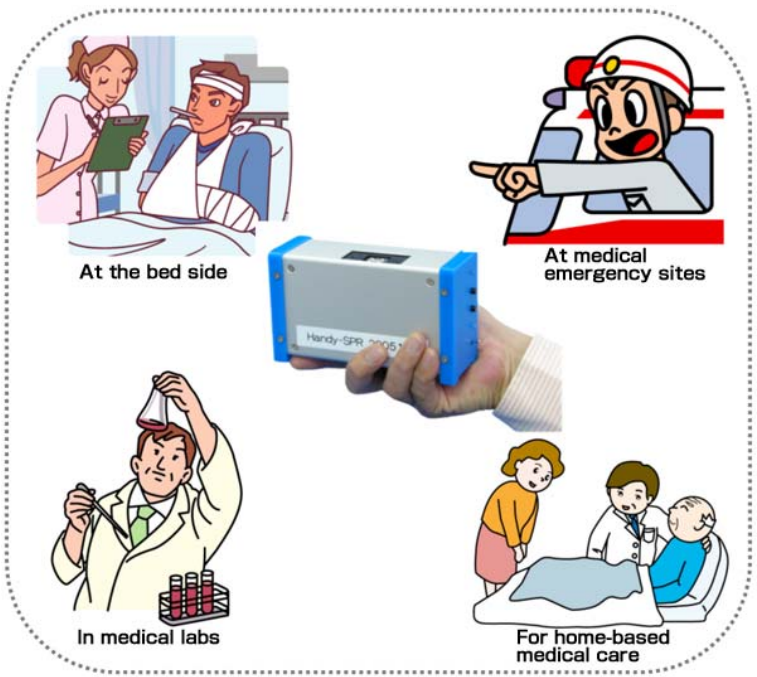
Texas Instrument: *Spreeta*

- Size : 40 x 15 x 7 mm
- Light source: LED (< 100 mA)
- Refractive index range: 1.33 to 1.4
- Drift: < $1x10^{-6}$ RIU/min
- Flow cell vol.: 20 – 100 nL



NTT-AT: *Handy-SPR PS 0109*

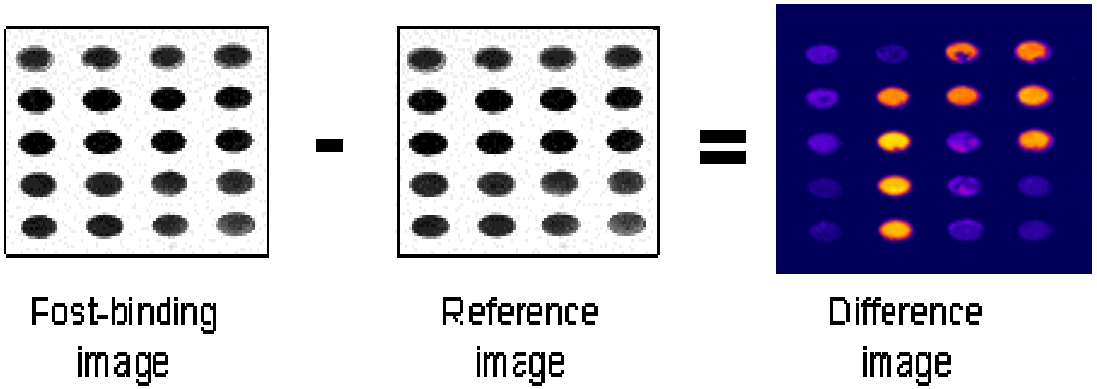
- Size : 170 x 100 x 50 mm
- Weight: 2 kg
- Measurement range: 65 ~ 75 °
- Light source: LED@770 nm
- Detector: 2048 pixel CCD line sensor



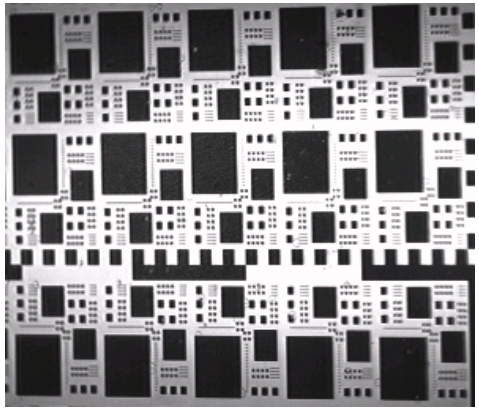
SPR biosensor: Recent research trend

3. Imaging

GWC Technologies
BioForce
KMAC
Plasmonic
Xantec
Etc.

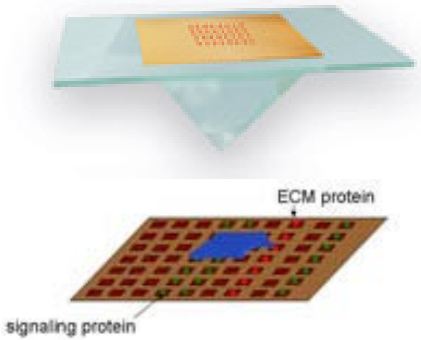


GWC Technologies



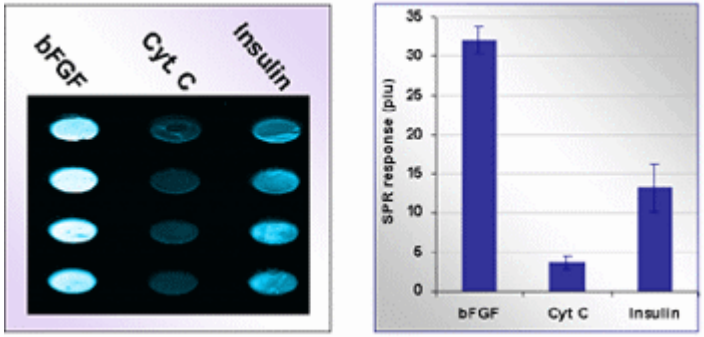
Microscope image of a patterned SPR gold surface.

Xantec



The Nano eNabler system provides a solution for a number of interesting experiments because it uses a patterned substrate.

BioForce



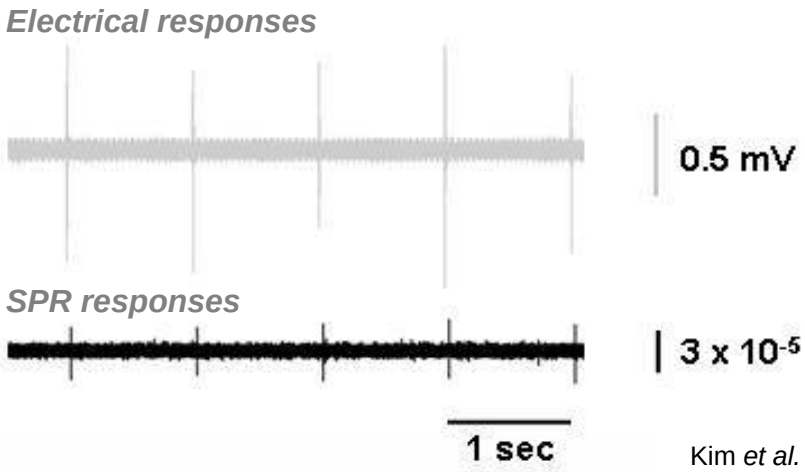
Array image and corresponding histogram quantifying BHK21 cell binding to a protein ligand array. Strongest signals are observed for bFGF probes, with minimal signal for cytochrome C controls.

GWC Technologies

SPR biosensor: Recent research trend

4. Extension of application

- Both the electrical (gray traces) and the SPR responses (black traces) increased in magnitude when the stimulation intensity was increased when supra-threshold stimulation currents were applied.
- The SPR responses were highly correlated with simultaneously recorded electrical responses.



Kim *et al.* Opt. Letters 2008