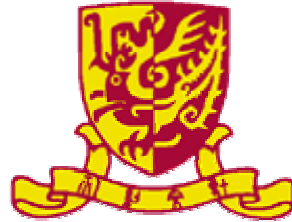


Shun Hing Institute of Advanced Engineering



Photonic biosensor micro-arrays for
molecular diagnostics applications

Principal Investigator

Aaron H.P. Ho, Department of Electronic Engineering

About the Project

- Project Investigators
- Project Objectives
- Surface Plasmon Resonance (SPR)
- SPR Phase Detection
- Our Work on Phase-sensitive SPR Biosensors
- Deliverables

Project Investigators

Principal Investigator:

- Aaron H.P. Ho, Associate Professor, Department of Electronic Engineering, CUHK

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Collaborators:

- Dennis Lo, Associate Dean, Faculty of Medicine, CUHK
- S.K. Kong, Professor, Department of Biochemistry, CUHK
- Paul K.S. Chan, Professor, Department of Microbiology, Faculty of Medicine, CUHK

Project Objectives

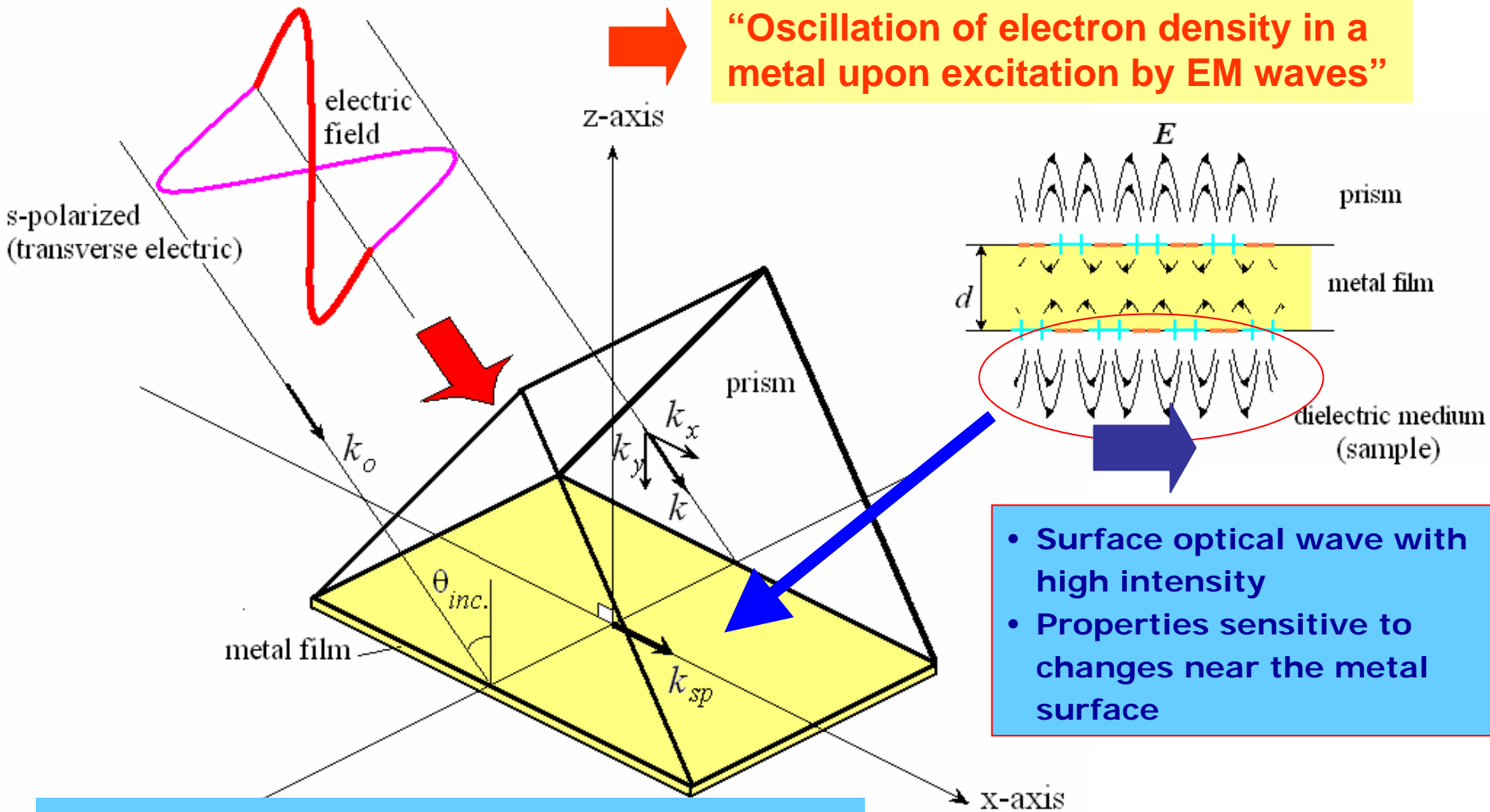
- To develop a photonic biosensor platform in which micro-arrays of sensor sites can provide parallel identification for a range of molecular species that are of relevance to diagnostics applications.
- To establish this micro-array platform as an enabling technology for other photon-based or molecular techniques, through which important multi-lateral information on the immobilized target biomolecules may be collected.

SURFACE PLASMON RESONANCE

p-polarized
(transverse magnetic)

s-polarized
(transverse electric)

“Oscillation of electron density in a metal upon excitation by EM waves”



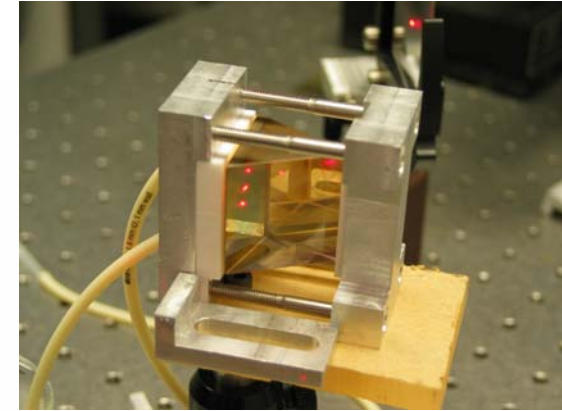
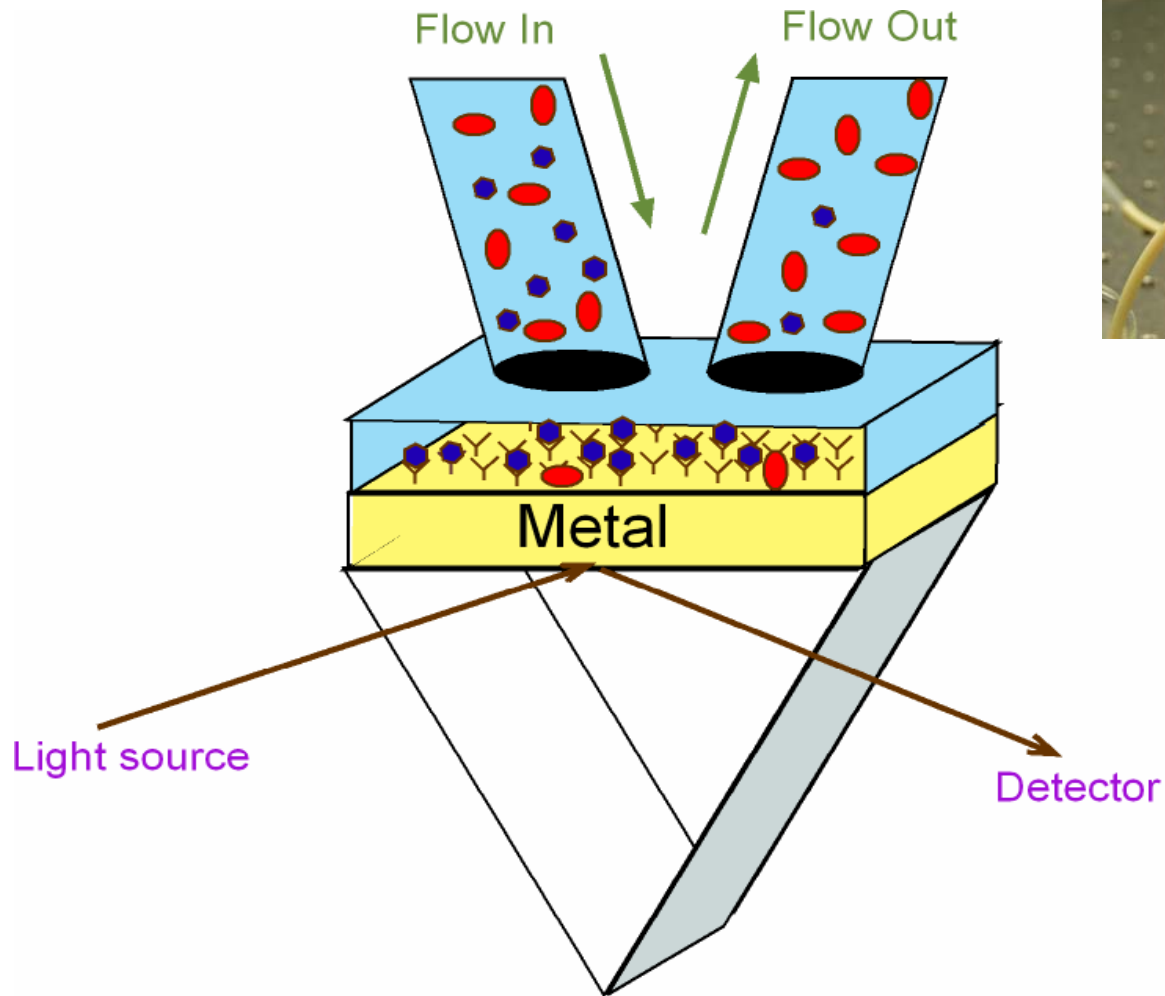
Requires momentum matching, $k_x = k_{sp}$

$$k_x = \frac{2\pi}{\lambda} \sin \theta_i \cdot \epsilon_{glass}^{1/2}$$

$$k_{sp} = k_o \sqrt{\frac{\epsilon_{metal} \epsilon_{sample}}{\epsilon_{metal} + \epsilon_{sample}}}$$

$$n_{glass} \sin(\theta_i) = \sqrt{\frac{\epsilon_{metal} \epsilon_{sample}}{\epsilon_{metal} + \epsilon_{sample}}}$$

Surface Plasmon Resonance Biosensing

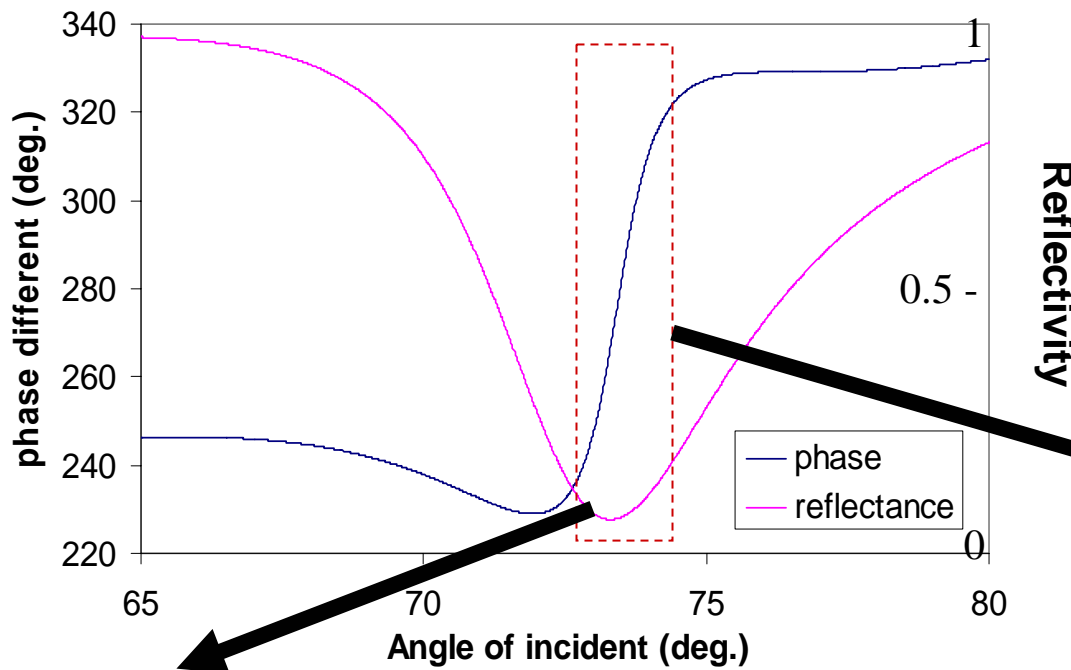


- Y Receptor
- Target Bio-molecule
- Unrelated Bio-molecule

Why SPR Phase?

Sensitivity - SPR Phase Vs Intensity measurement

Simulation results (Sensor configuration: BK7-gold (47nm)-water)



50 deg phase
jump for $n =$
1.3384 - 1.3388
($\Delta n = 0.0004$ RIU)

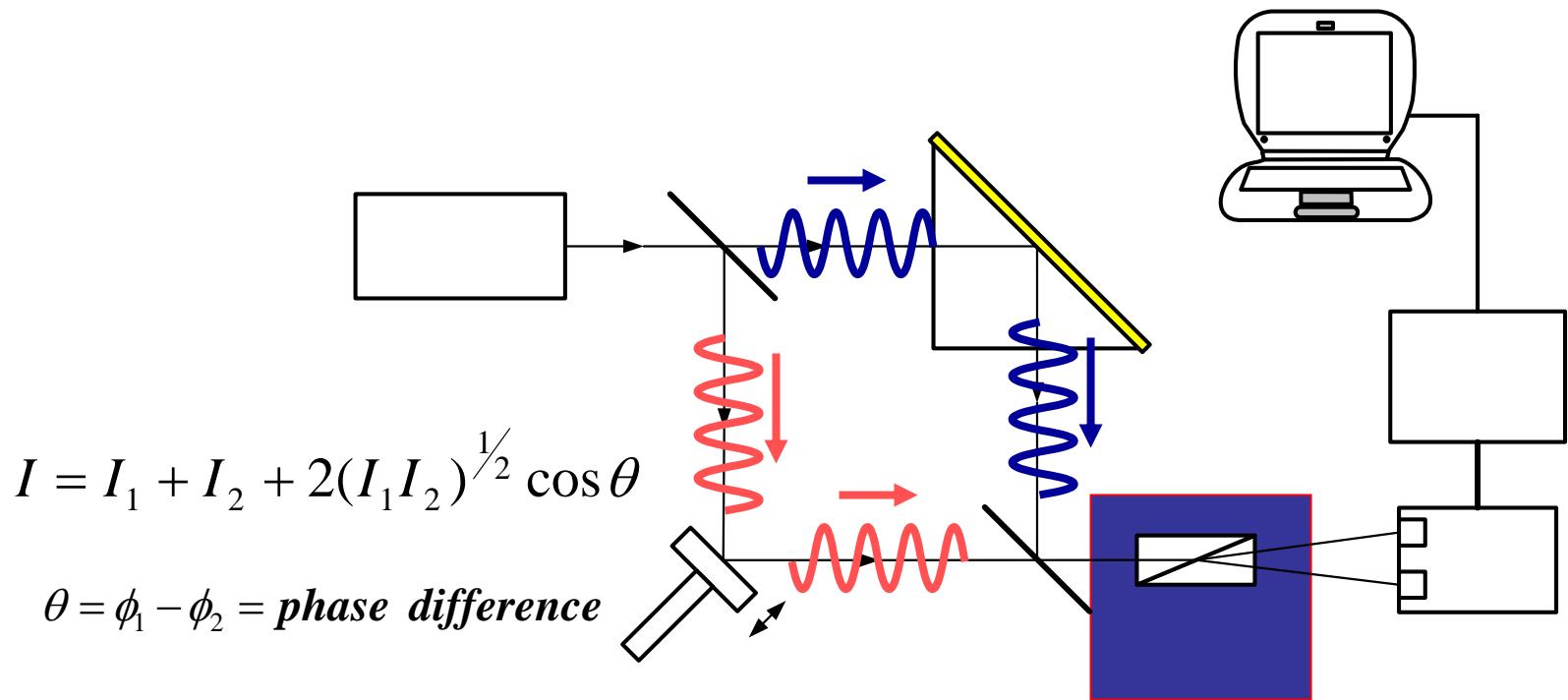
Assume 0.01°
phase resolution
 \Rightarrow sensitivity
factor

8×10^{-8} RIU

Angle measurement \Rightarrow **1.7×10^{-7} RIU**

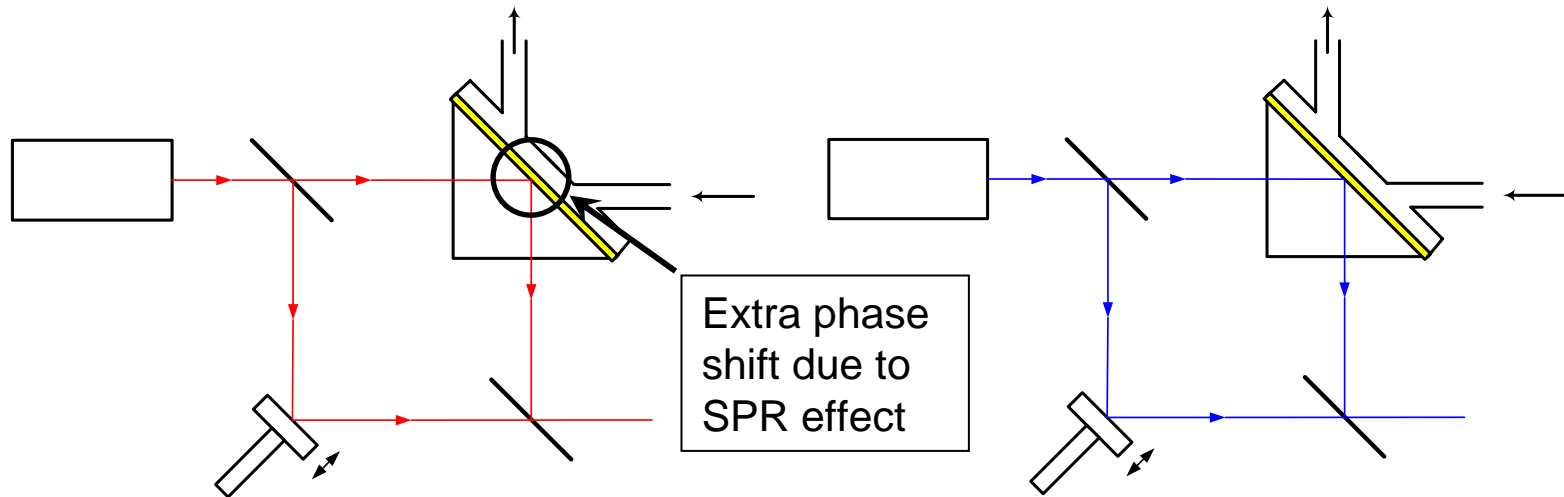
**More sensitive
SPR devices**

Differential phase surface plasmon resonance biosensor



Wu & Ho *et al*, Optics Letters, 29(2004), 2378 – 2381

Two Mach-Zehnder interferometers working in parallel



P-polarization

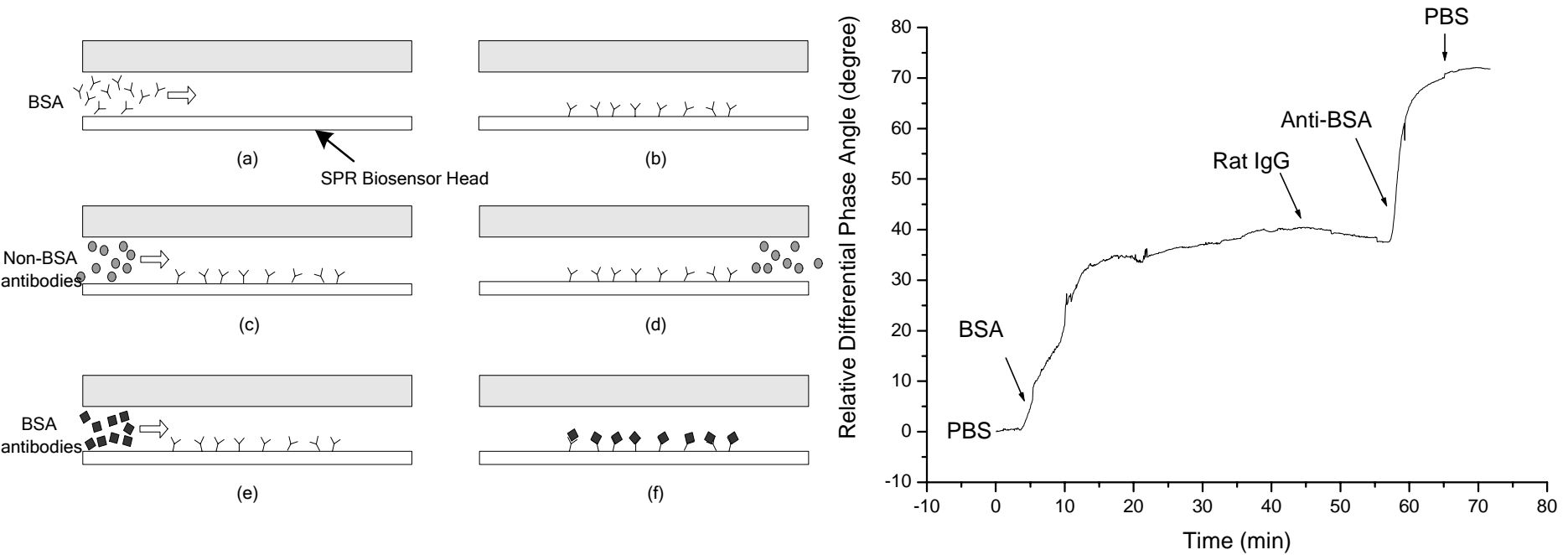
S-polarization

Differential phase \Rightarrow Much improved stability



Differential SPR phase measurement set-up

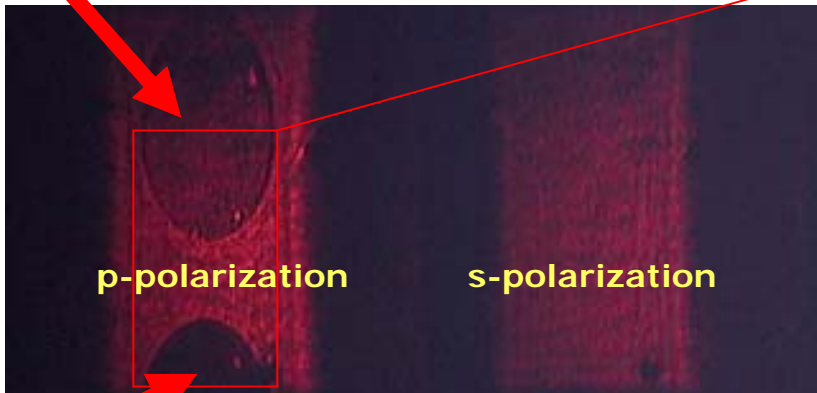
Biosensing of Anti-BSA/BSA binding



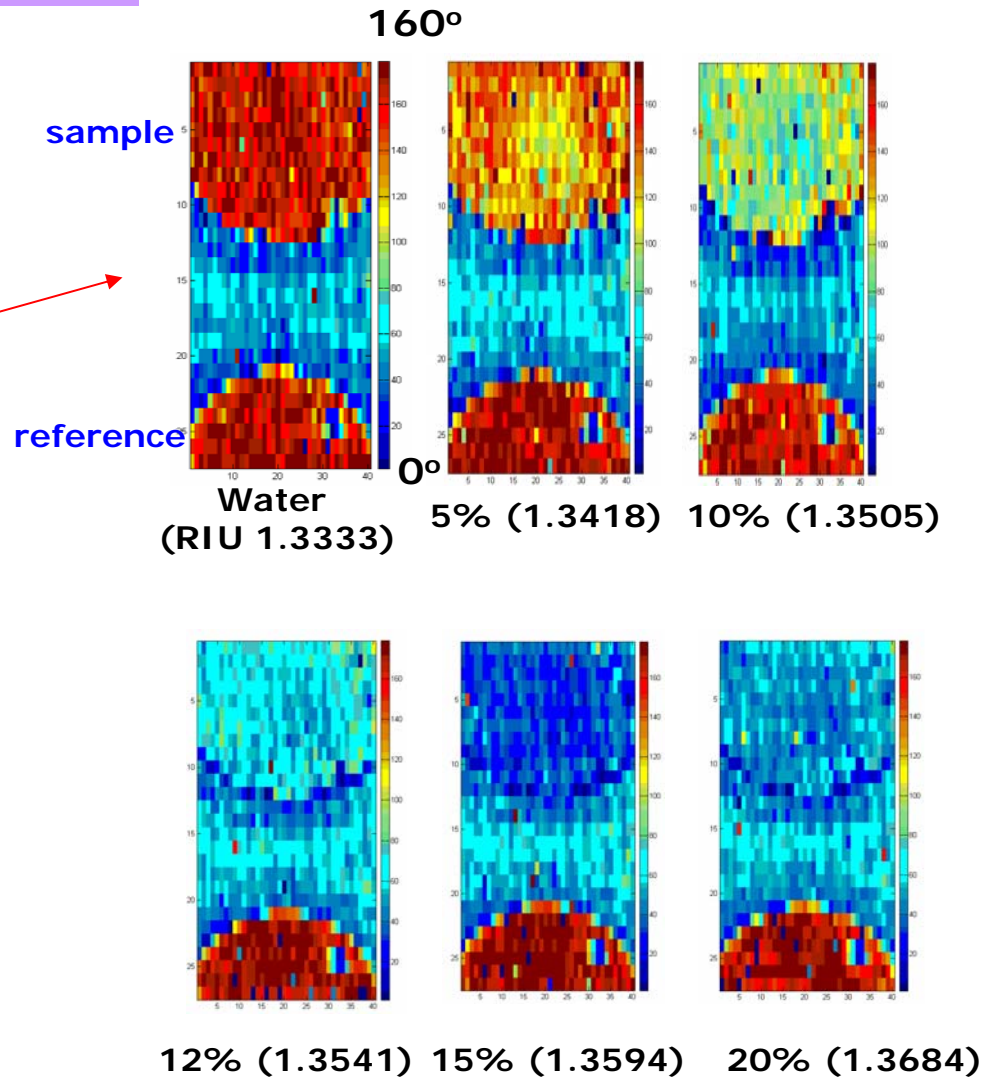
Sensitivity: 10.76ng/ml

SPR phase imaging

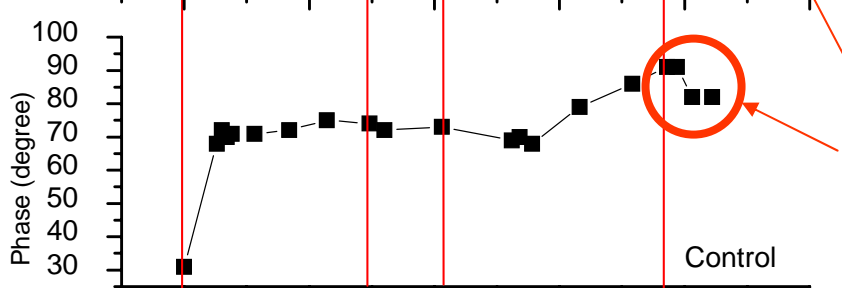
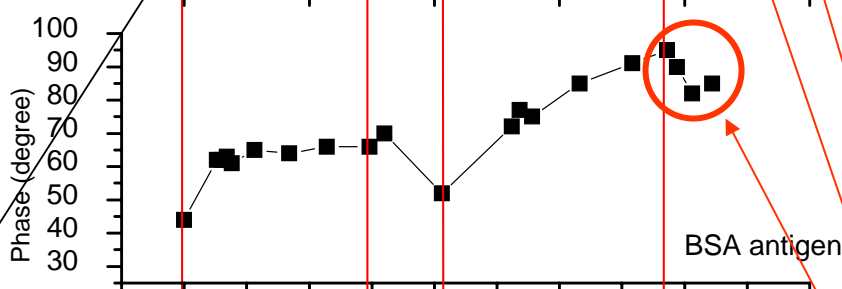
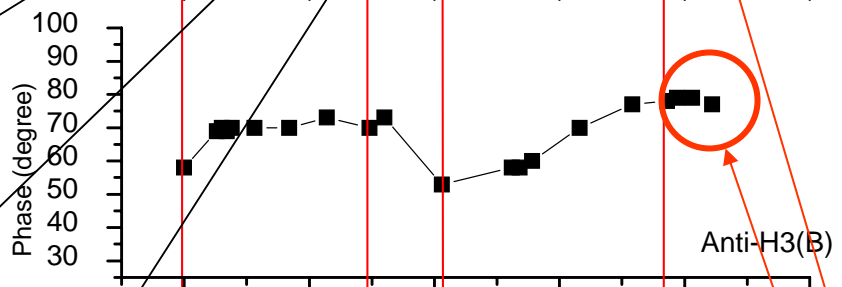
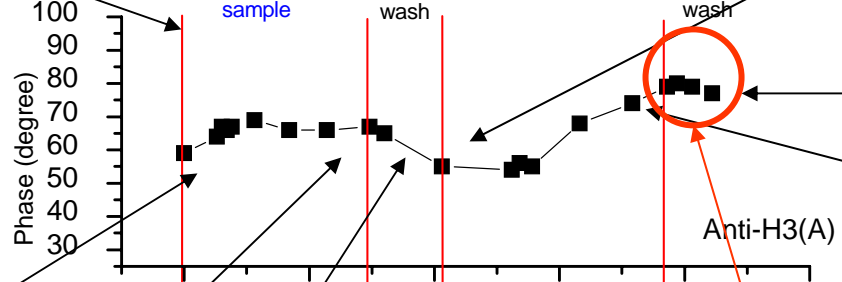
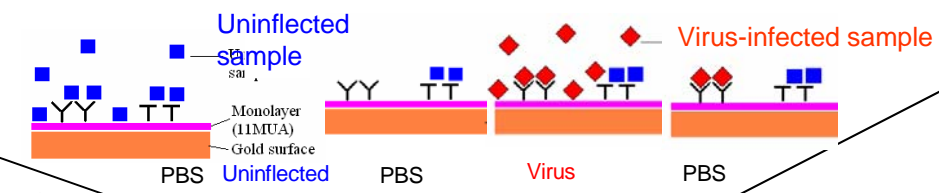
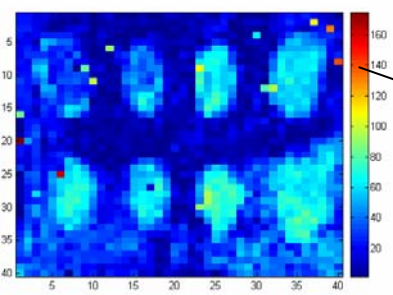
Salt solution (sample)



Water (reference)

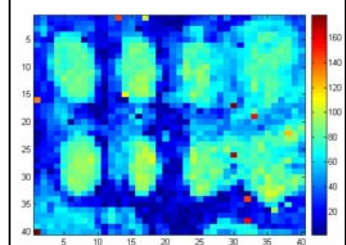
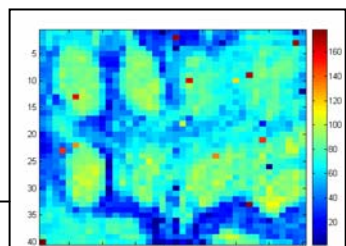
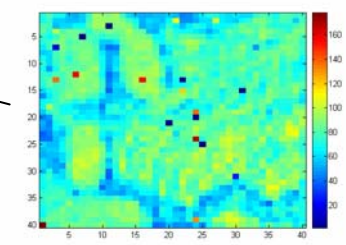
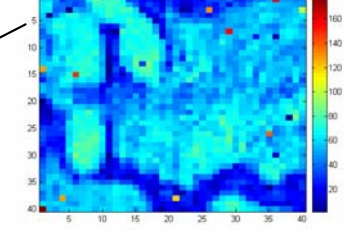
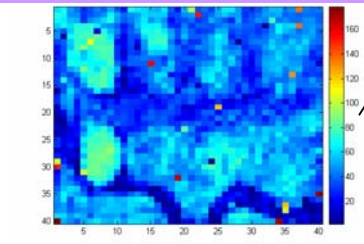
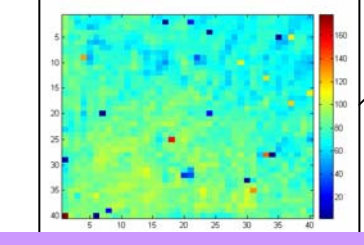
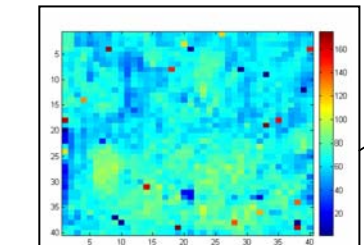


Control BSA Anti-H3

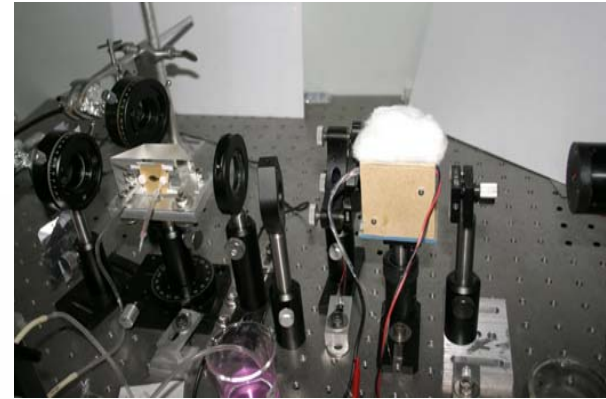
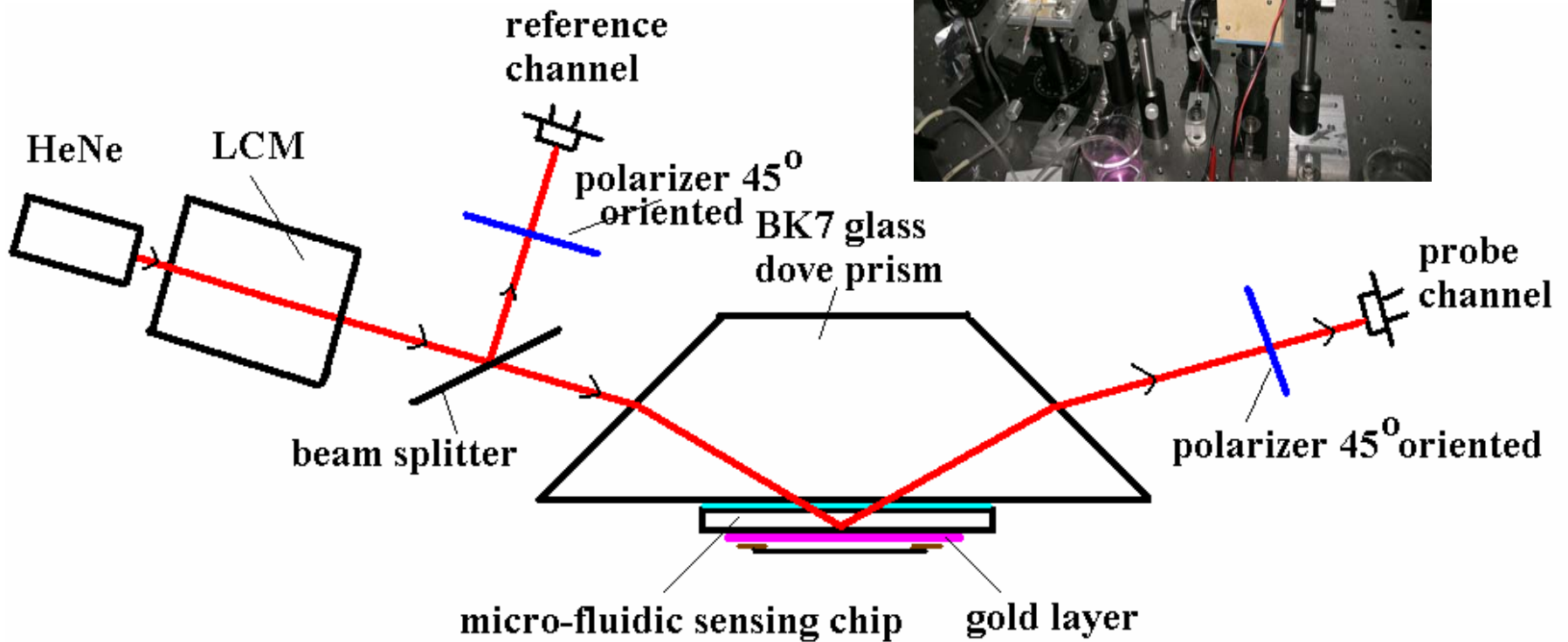


Selective sensing of H3 Influenza

Only H3 antibodies bind specifically to Anti-H3 sites

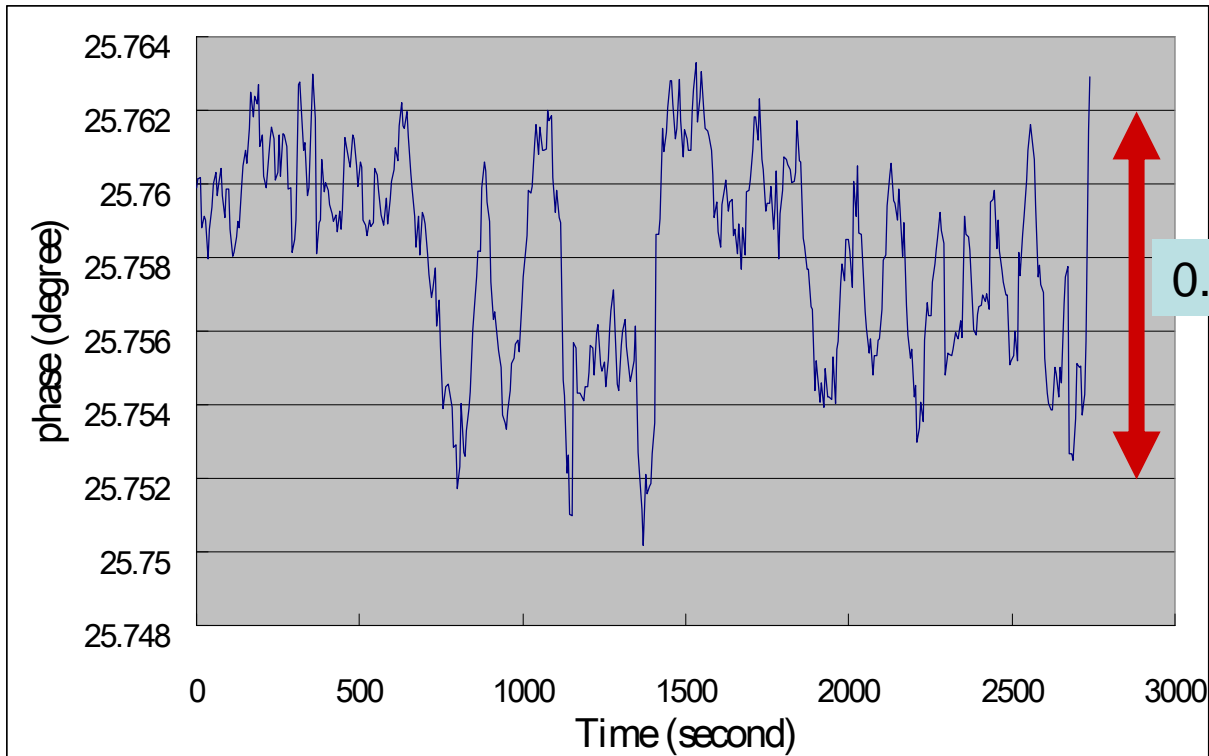


Single beam interferometer using liquid crystal phase modulator



Experimental stability results

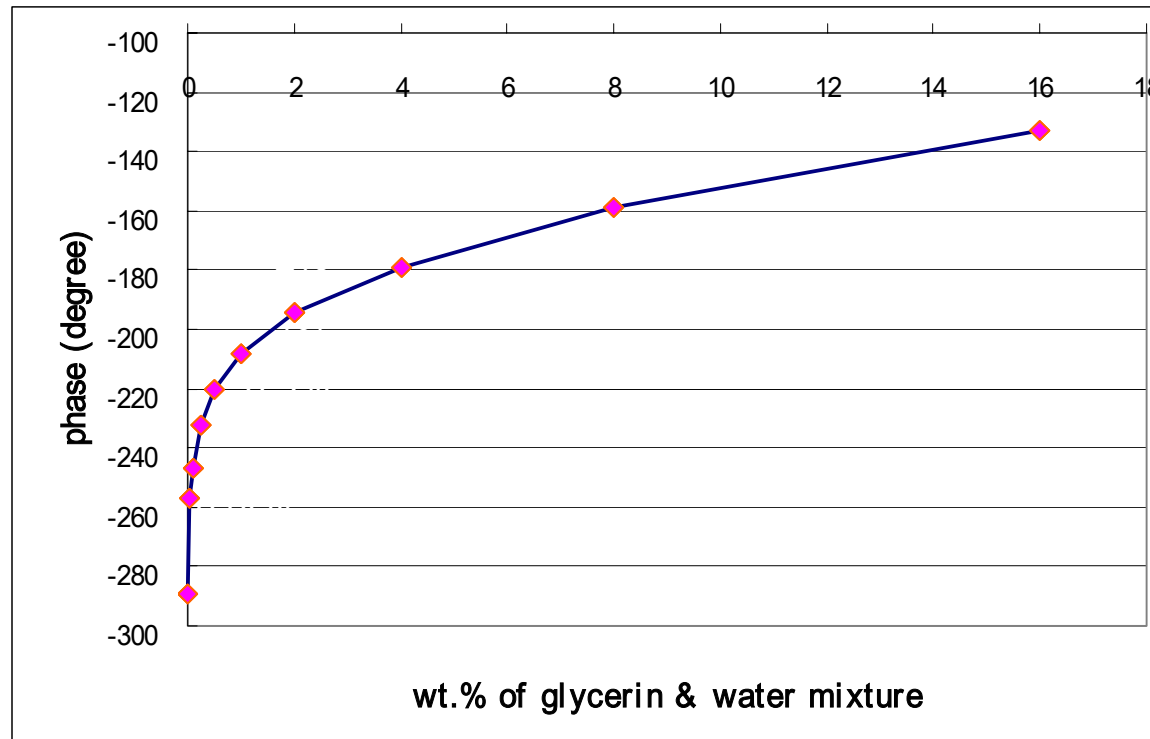
0.01° phase error over 45 minutes



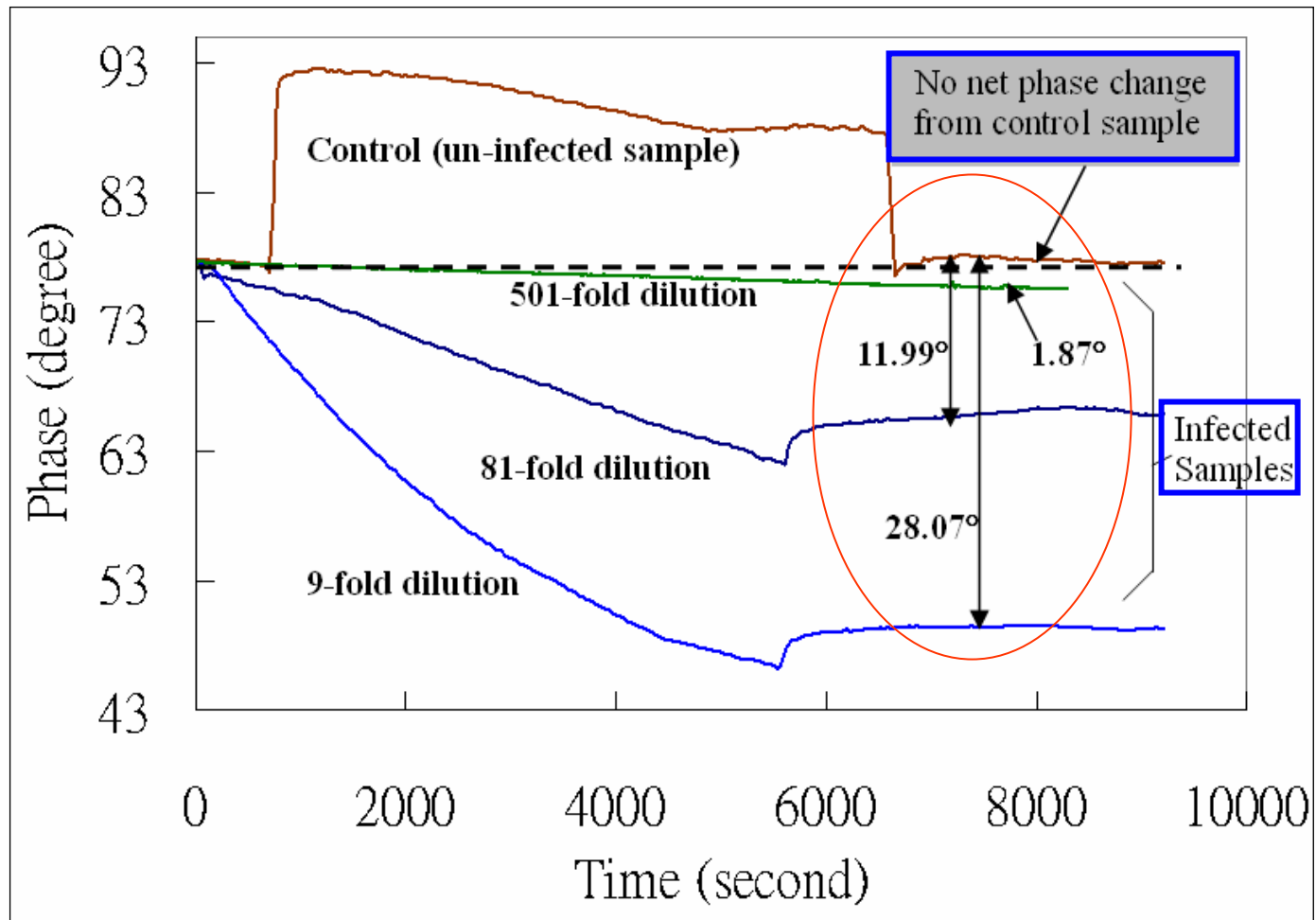
Experimental sensitivity

Phase shift of $32^\circ \Rightarrow$ RI change of 6×10^{-5} RIU (0% \rightarrow 0.05%)

Sensitivity limit **1.9×10^{-8} RIU** based on 0.01° resolution (March 2006)



Experimental detection of H3 influenza antibody



Deliverables

- Photonic platform for performing multiple analytic measurements on a 2-D array scale

SPR phase imaging offers real-time monitoring of molecular adsorption in the sensor surface.

SPR also provides highly localized optical energy near the sensor surface. This enables physical effects, including RAMAN (molecular diagnostics), non-linearity (high resolution microscopy), enhanced fluorescence.

Deliverables

- SPR + DNA amplification (PCR) in the same chamber

Integration between SPR and PCR for parallel detection of many DNA species – this is not possible with present PCR equipments

This will completely remove the requirement of fluorescence labeling, which can significantly simplify the synthesis of reporter molecules.

END