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# An optical Fiber based Sensing System for Label-free Real-time Biomedical/Environmental Diagnosis by using Surface Plasmon Polaritons

2<sup>nd</sup> International Conference and Exhibition on Lasers, Optics & Photonics, Sep. 08–10, Philadelphia, USA

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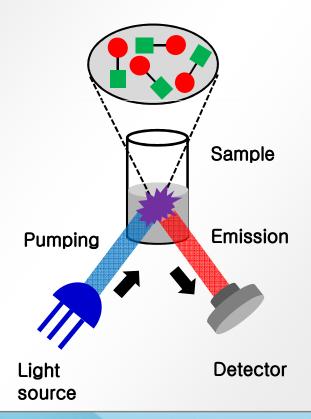
#### **Contents**

- Introduction1 Label-free bio/environmental Sensors
- Introduction2 Evanescent field sensing
- Introduction2 Surface Plasmon Resonance (SPR)
- The Working Principle of our Sensing Device
- Experimental Apparatus and Techniques
  - Sensing Device Optical Fibers with Bimetallic SPR Coating
  - ② Detection System
- Mathematical Description
- Results and Discussion
- The Sensing System Characteristics
- Conclusion
- Acknowledgement to Contributors

## Label-free Bio/Environmental Sensors - Introduction 1

#### **Sensors using labels**

- Label/Tag (QD, Dye, Radioactives)
- Analyte Molecule

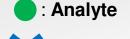


#### Sensors without using labels

- Avoid label-induced alteration of analyte molecular structure
- Continuous measurement possible (real-time monitoring)
- → Able to observe kinetic progress of binding interactions of biomolecules
- Avoid multi-step preparation for labeling
  - ① Cost-effectiveness
  - ② Time saving → real time monitoring
  - 3 Avoid contamination
  - Reproducibility (irrespective of user's hand skill)
- Remote sensing (e.g. using optical fibers carrying signals)
   for inaccessible (hazardous) sensing site
- Robustness to outer disturbance (e.g. to external EM wave)
- Relatively compact size
- Point-of-Care-Test (POCT) and portability
- Can be integrated into a small sized single chip for multiplexed bioassay
- Detection limit restricted
- Non-specific bonding induced noise

## Evanescent Field Sensing - Introduction2

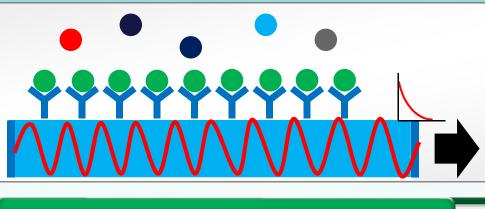
#### Concept





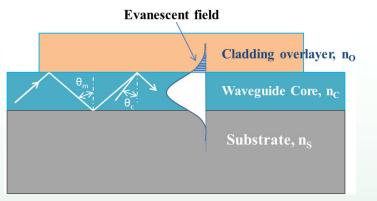
Light source





**Optical Properties Change** 

#### TIR based Evanescent Field



Characteristic penetration depth

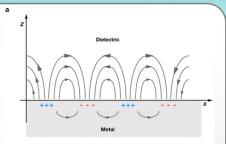
$$d = \frac{\lambda_m}{2\pi} / \sqrt{\frac{\sin^2 \theta_m}{n^2} - 1}$$

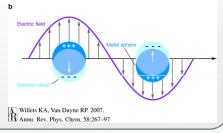
at 632.8nm, d~200 nm

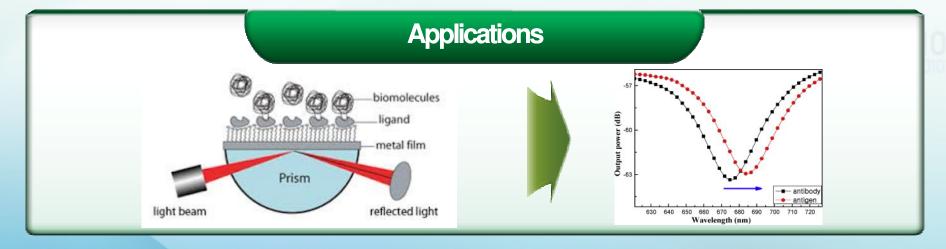
# Surface Plasmon Resonance (SPR) - Introduction3

#### Concept

- Collective oscillation of electrons at a metal-dielectric interface at a characteristic frequency
- Surface Plasmon Polariton (SPP) mode: longitudinal mode of EM field coupled with surface plasmon
- TM polarization can provide longitudinal EM field for SPP generation and forced oscillation of surface electrons
- Enhancement of wave-vector via higher refractive index light line
  - → Prism method, diffraction method or waveguide method
- Phase matching condition ightarrow  $k_{ex}^L = rac{\omega}{c} \sqrt{rac{\epsilon_m \epsilon_d}{\epsilon_m + \epsilon_d}}$
- SPR E-field distribution in the surface normal direction ightarrow  $E_d(r) = E_d(0)e^{-r\sqrt{k_{sp}^2-k_d^2}}$

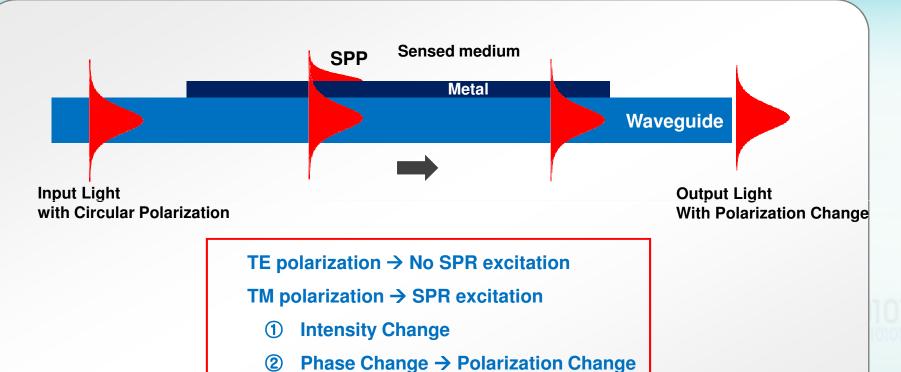






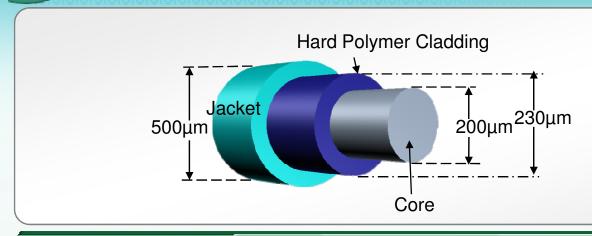
# Working Principle of the Sensing Device

#### **Simple Concept Diagram**



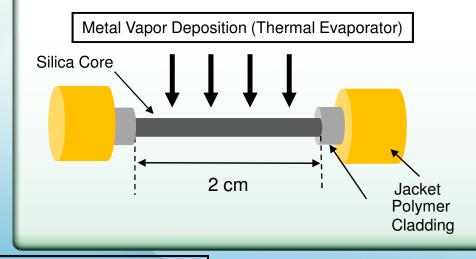
# Experimental Apparatus and Techniques (1)

Sensing Device Building Block: polymer-clad multimode fiber

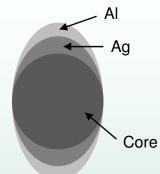


NA=0.37, JFTLH, Polymicro Technologies

#### **Bimetallic SPR Coating**



Expected Crosssection Profile



- Al coating for avoiding chemical instability of Ag
- · High enough sensitivity by SPR
- Avoid too much SPR attenuation
- · Enhanced birefringence
- Various penetration depth of evanescent field
  - → wide operating RI range
- Various SPR angle
  - → wide operating RI range

# Experimental Apparatus and Techniques (2)

#### Bimetalic coating of Ag and Al

- Non-golden coating to avoid too much attenuation of signal → operating RI range widened
- High enough sensitivity and signal-to-noise ratio
- The coated Ag-Al thickness: 7nm-30nm, 30nm-10nm, 20nm-5nm, 36nm-4nm

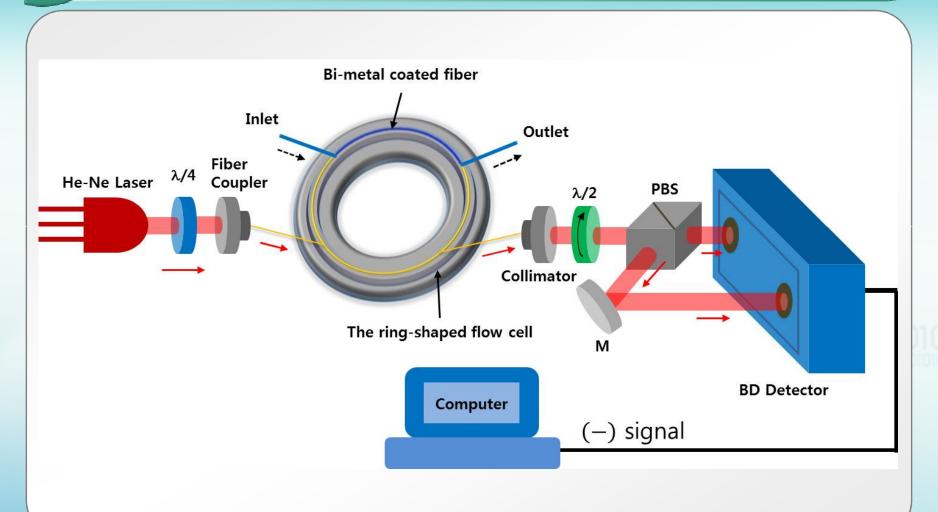
#### Fiber Device Installed at the Ring Shaped Flow Cell



- Polydimethylsiloxane (PDMS) used for the flow cell
- An inlet and an outlet ports extracted for the analyte solution input and output, respectively
- Ring shaped fiber ensuring many reflections
  - → enhanced sensitivity
- Wide distribution of incident angle to the multimode fiber
  - → wide operating RI range

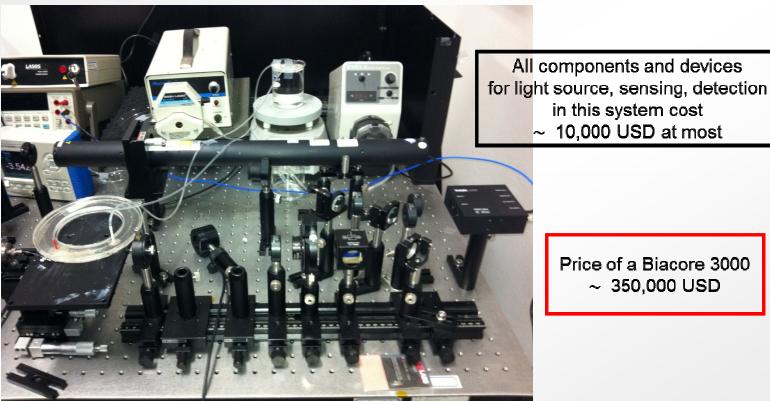
# Experimental Apparatus and Techniques (3)

#### **Schematic of Experimental Setup**



# Experimental Apparatus and Techniques (4)

#### **Experimental Setup (photo)**



in this system cost

Price of a Biacore 3000 ~ 350,000 USD

# Mathematical Description (1)

#### **Birefringence Detection Principle**

- Circular polarization

$$\begin{bmatrix} E_{out}^{H} \\ E_{out}^{V} \end{bmatrix} = \begin{pmatrix} R(-\xi) \begin{bmatrix} e^{-i\Gamma/2} & 0 \\ 0 & e^{i\Gamma/2} \end{bmatrix} R(\xi) \end{pmatrix} \begin{bmatrix} 1 \\ \pm i \end{bmatrix}$$

 $\Gamma \equiv \delta \phi_e - \delta \phi_o$  is the phase retardation of light through the SPR fiber device  $\xi$  the the angle between the *o*-axis of the SPR fiber device and a laboratory horizontal axis



$$\begin{bmatrix} E_{\lambda/2,out}^{H} \\ E_{\lambda/2,out}^{V} \end{bmatrix} = i \begin{bmatrix} -\cos 2\psi & \sin 2\psi \\ \sin 2\psi & \cos 2\psi \end{bmatrix} \begin{bmatrix} E_{out}^{H} \\ E_{out}^{V} \end{bmatrix}$$

 $\psi$  is the angle between the  $\lambda/2$  optic axis and a laboratory horizontal axis.

# Mathematical Description (2)

#### **Birefringence Detection Principle**

The two ports of the PBS output (s-port and p-port)

$$I_s = \frac{I_{out}}{2} [1 + \sin \Gamma \sin(2\xi - 4\psi)] \qquad I_p = \frac{I_{out}}{2} [1 - \sin \Gamma \sin(2\xi - 4\psi)]$$



#### The balanced detector output

$$I_{-} \equiv I_{s} - I_{p} = I_{out} \sin \Gamma \sin(2\xi - 4\psi)$$

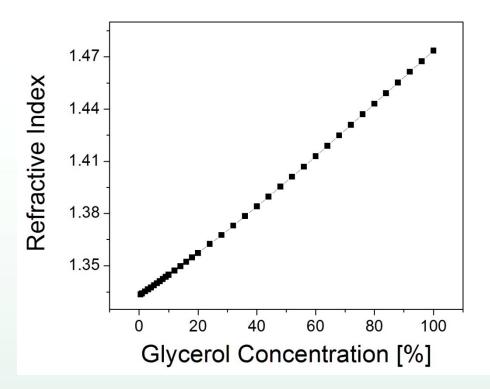


Rotatable  $\frac{\lambda}{2}$  enabling of max (-) and min(-) to be obtained

$$S \equiv \max(I_{-}) - \min(I_{-}) = 2I_{out} \sin \Gamma$$

# Results and Discussion (1)

#### **Glycerol Refractive Index**

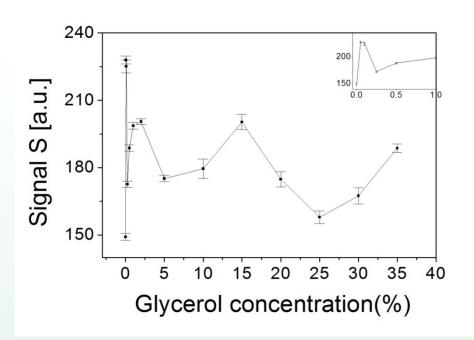


Glycerol Concentration based on Weight: C

Glycerol Index  $n \cong 0.0012 \times C[\%]$ 

# Results and Discussion (2)

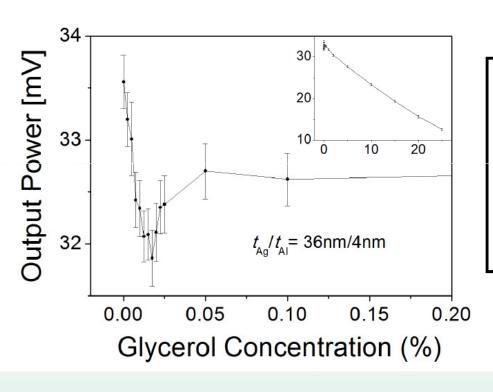
#### No metal coated fiber device



- No metal coated fiber device
- Highly nonlinear over the entire range of glycerol concentration used

# Results and Discussion (3)

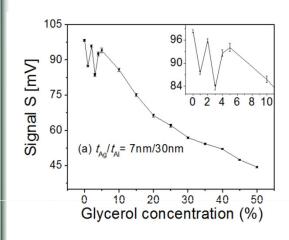
#### **Glycerol Measurement**

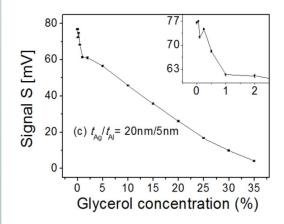


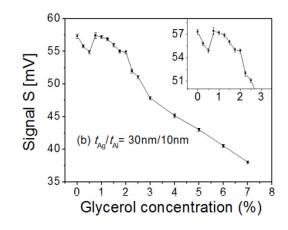
- Measurement of optical power only at the fiber output
- Highly nonlinear behavior at near zero
- Restricted operating range of concentration (RI)

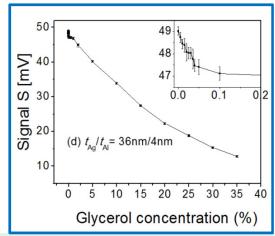
# Results and Discussion (4)

#### Fiber devices with SPR birefringence









- As Ag composition increases, i.e.,
   (a)→(d), less nonlinear behavior appears
- Two different sensitivity slopes appear at around 1% and 0.05% for (c) and (d)
- Sensitivity at concentration C near zero

$$\delta S/\delta C = 15.2 \text{mV/\%}$$
 (c)

$$\delta S/\delta C = 32.4 \text{mV/\%}$$
 (d)

> Minimum detectable C

$$5 \times 10^{-3}\% \ (9.3 \text{pM/L})$$

Minimum resolvable refractive index

$$5.8 \times 10^{-6} \text{RIU}$$

as experimentally achievable

Enlarged RI operating range: 0.05

# The Sensing System Characteristics (1)



## Good Sensitivity and Wide Operating Range

- ➤ Ring-shaped fiber device ensuring about 18 reflections → enhanced sensitivity
- Ag-Al (36nm-4nm) coating → high enough sensitivity, non-golden coating to avoid too much attenuation (wide RI operating range)
- ➤ Asymmetrical coating profile → various metal depth and various SPR angles
  - → Wide RI operating range
- $\triangleright$  Multimode fiber of 200  $\mu m$  core  $\rightarrow$  wide incident angle  $\rightarrow$  Wide RI operating range
- Newly developed Detection System for birefringence measurement
  - → Wide RI operating range

# The Sensing System Characteristics (2)



## Comparison with the other group results

Minimum Detectable RI (experimental)	Minimum Detectable RI (estimated)	Operaing range $(\times 10^{-3})$	Ref.	Remark
1.2×10 <sup>-4</sup>	5.5×10 <sup>-8</sup>	9.6	1	Mach-Zhender Type SPR Sensor (2004)
2×10 <sup>-5</sup>	Not mentioned	1.2	2	Single Mode Fiber SPR Sensor (1999)
<b>4×</b> 10 <sup>−6</sup>	Not mentioned	8.5	3	Single Mode Polarization Maintaining SPR Sensor (2003)
5×10 <sup>-5</sup>	Not mentioned	27	4	D-type Fiber Sensor (2007)
5×10 <sup>-4</sup>	Not mentioned	49	5	Single Mode SPR Sensor (1997)
1×10 <sup>-3</sup>	1.5×10 <sup>-6</sup>	4.2	6	SPR Heterodyne Interferometer Sensor (2011)
4×10 <sup>-5</sup>	Not mentioned	46	7	Miniaturized SPR fiber Sensor (1998)
5×10 <sup>-7</sup>	Not mentioned	2.6	8	SPR Phase detection Sensor (1996)
5.8×10 <sup>-6</sup>	To be estimated	50	Our Group	SPR birefringence Fiber Sensor (2013)

# The Sensing System Characteristics (3)



#### References used for comparison

#### References

- [1] S. Y. Wu, H. P. Ho, W. C. Law, C. L. Lin, S. K. Kong. Highly sensitive differential phase-sensitive surface plasmon resonance biosensor based on the Mach-Zehnder configuration. Optics Letters, 29, 2378-2380 (2004).
- [2] R. Slavík, J. Homola, J. Čtyroký. Single mode optical fiber surface plasmon resonance sensor. Sensors and Actuators B: Chemical, 54, 74-79 (1999).
- [3] M. Piliarik, J. Homola, Z. Manikova, J. Čtyroký. Surface plasmon resonance based on a single mode polarization maintaining optical fiber. Sensors and Actuators B: Chemical, 90, 236–242 (2003).
- [4] M. H. Chiu, C. H. Shih, M. H. Chi. Optimum sensitivity of single mode D-type optical fiber sensor in the intensity measurement. Sensors and Actuators B: Chemical, 123, 1120-1124 (2007).
- [5] A. J. C. Tubb, F. P. Payne, R. B. Millington, C. R. Lowe. Single-mode optical fibre surface plasmon wave chemical sensor. Sensors and Actuators B: Chemical, 41, 71-79 (1997).
- [6] J. Y. Lee, S. K. Tsai. Measurement of refractive index variation of liquids by surface plasmon resonance and wavelength-modulated heterodyne interferometry. Optics Communications, 284, 925–929 (2011).
- [7] R. Slavík, J. Homola, J. Čtyroký. Miniaturization of fiber optic surface plasmon resonance sensor. Sensors and Actuators B: Chemical, 51, 311-315 (1998).
- [8] S. G. Nelson, K. S. Johnston, S. S. Yee. High sensitivity surface plasmon resonance sensor based on phase detection. Sensors and Actuators B: Chemical, 35, 187–191 (1996).

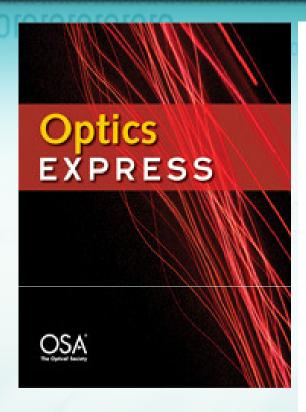
# The Sensing System Characteristics (4)



## The Benefits of our Sensing System

- Straightforward to Fabricate the Fiber Device (polymer-cladding)
- ✓ Ag-Al Combination for SPR Coating No Need to Use Expensive Gold
- ✓ Relatively Simple Detection System
- No Need of angular adjustment for SPR excitation
- ✓ No Need to Realize an Interferometer by Beam Recombination
  - → Easy Alignment (in-line polarization interferometer)
- ✓ Robustness to External Disturbance due to the Use of a Single Beam of Light compared to Dual Beam Interferometer scheme
- ✓ Relatively Compact Size compared to Prism based Optical Sensing System

## Relevant Publication



#### Bimetal coated optical fiber sensors based on surface plasmon resonance induced change in birefringence and intensity

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<sup>2</sup> Department of Nanophysics, Gachon University, South Korea
<sup>3</sup> Neuroscience Institute, Gil Hospital, Incheon, South Korea

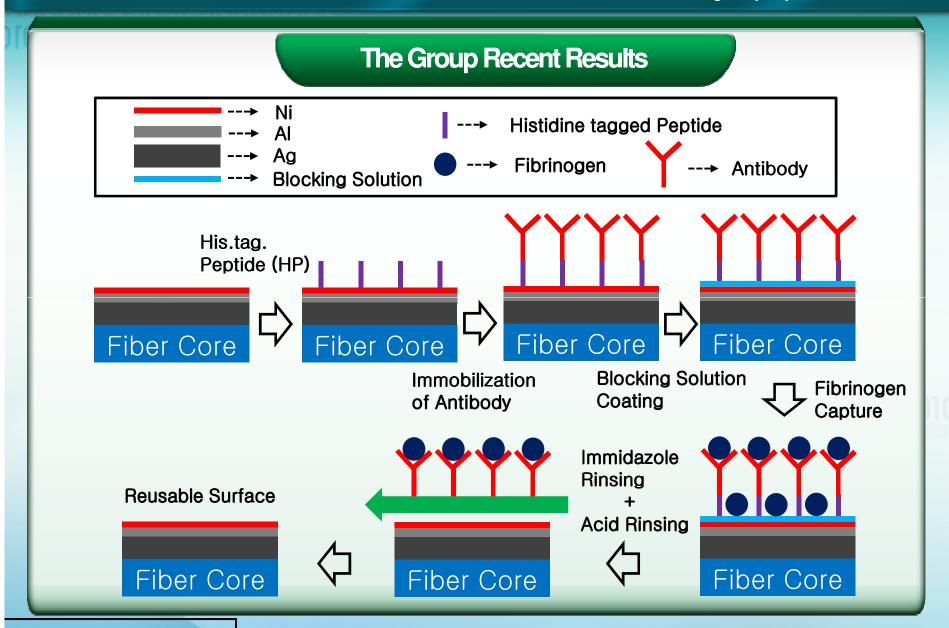
\*batu@gachon.ac.kr

Abstract: We present a surface plasmon resonance (SPR) based multimode fiber sensor with non-golden bimetallic coating. Our detection scheme used, which is capable of measuring the combined effects of SPR-induced birefringence and intensity changes, supported the minimum resolvable refractive index (RI) of  $5.8 \times 10^{-6}$ RIU with the operating RI range of 0.05 to be experimentally obtained at a single wavelength (632.8 nm) without non-spectroscopic techniques. The asymmetric profile of the thickness of the bimetal coating on the fiber core together with the inherent range of incidence angle for multimode propagation also contributed to the wide operating range. The SPR fiber device with the detection scheme demonstrated will be likely to be developed as a real-time label-free and highly sensitive diagnostic device of a wide operating range for biomedical and biochemical applications in a portable format.

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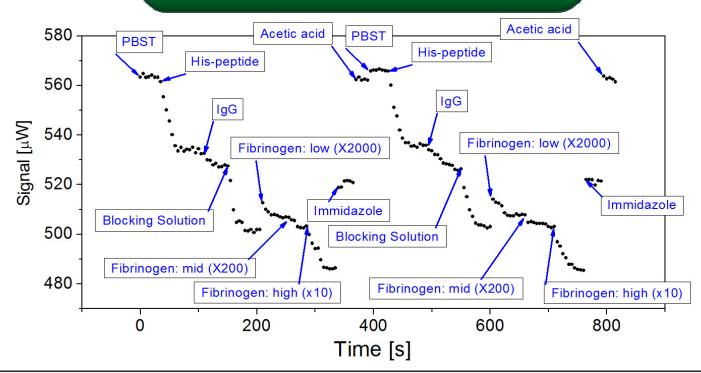
OCIS codes: (240.6680) Surface plasmons; (280.4788) Optical sensing and sensors; (060.2370) Fiber optics sensors.

## Additional Results Obtained Recently (1)



# Additional Results Obtained Recently (2)





PBST: Phosphate Buffered Saline with Tween 20, pH 7.4

His-peptide: Histidine-tagged Peptide (N-HHHHHHGGHWRGWVS-C  $1\mu g/ml$ 

Blocking Solution: Block ACE (AbD Serotec) 4g/L

IgG: Anti-fibrinogen IgG rabbit (324552 EMD millipore) 1.875 ng/ml

Acetic acid: 1M/L, pH 2.4, Immidazole: 20 mM/L

#### Fibrinogen from AD patient blood plasma

low (× 2000)  $\rightarrow$  dilution by 2000: 34.4  $\mu$ g/ml

mld (× 200)  $\rightarrow$  dilution by 200: 344  $\mu$ g/ml

high (× 10)  $\rightarrow$  dilution by 10: 6.9 mg/ml

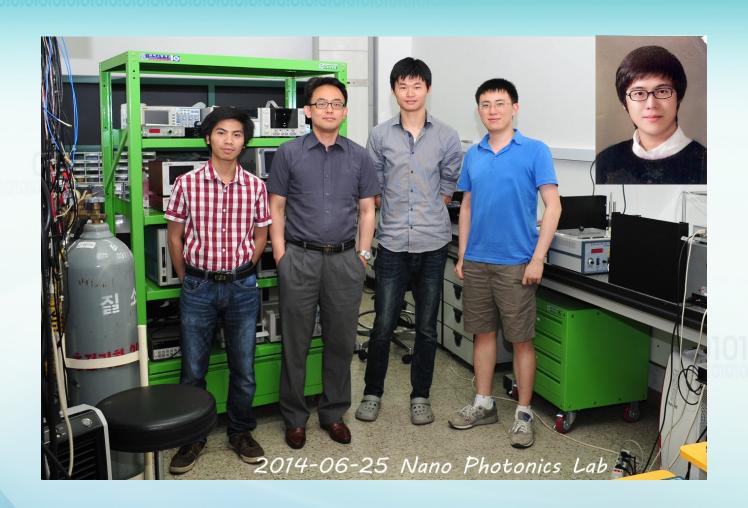
## Conclusion



## Summary

- SPR Birefringence assisted Optical Sensor Demonstration
- Ag-Al Bimetallic Coated Multimode Fiber for SPR Excitation
- Newly Developed Detection System for Birefringence
- Wide RI Operating Range of 0.05 demonstrated
- The Minimum Resolvable Index Resolution of  $5.8 \times 10^{-5}$  RIU
- The Minimum Detectable Concentration of Glycerol of 9.3 pico
   Mole/Liter
- Applicable for Chemical and Biological Sensing

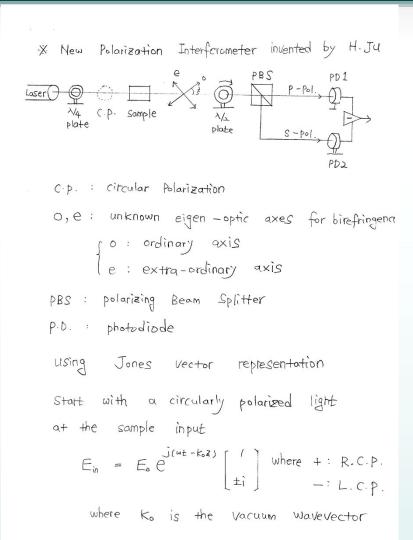
# Contributors



End

# Thanks for your attention Questions?

## Appendix - New Polarization Interferometer Detection (1)



· Sample rotation matrix 
$$R_s(\xi) = \begin{bmatrix} \cos \xi - \sin \xi \\ \sin \xi \cos \xi \end{bmatrix}$$

$$M = \begin{bmatrix} e^{-jk_0n_0l} & 0 \\ 0 & -jk_0n_0l \end{bmatrix}$$

$$= e^{-jk_0l(n_0+n_0)/2} \begin{bmatrix} e^{-jk_0l(n_0-n_0)/2} & 0 \\ 0 & e^{-jk_0l(n_0+n_0)/2} \end{bmatrix}$$

$$= e^{-jk_0l(n_0+n_0)/2} \begin{bmatrix} e^{-iT/2} & 0 \\ 0 & e^{iT/2} \end{bmatrix}$$

& Rotated Sample to be represented by

$$M_{+} = R_{s}(-\frac{1}{5}) M R_{s}(\frac{1}{5})$$

$$= \begin{bmatrix} \cos \beta & \sin \beta \\ -\sin \beta & \cos \beta \end{bmatrix} \begin{bmatrix} e^{-i7/2} & o \\ o & e^{i7/2} \end{bmatrix} \begin{bmatrix} \cos \beta & -\sin \beta \\ \sin \beta & \cos \beta \end{bmatrix}$$

(overall phase factor dismissed)

## Appendix - New Polarization Interferometer Detection (2)

$$M_{+} = \begin{bmatrix} \cos \beta & e^{-i7/4} & \sin \beta & e^{-i7/4} \\ -\sin \beta & e^{-i7/4} & \cos \beta & e^{-i7/4} \end{bmatrix} \begin{bmatrix} \cos \beta & -\sin \beta \\ \sin \beta & \cos \beta \end{bmatrix}$$

$$= \begin{bmatrix} \cos^{2}\beta & e^{-i7/4} & -\sin^{2}\beta & e^{-i7/4} \\ \sin \beta & \cos \beta & e^{-i7/4} & -\sin^{2}\beta & e^{-i7/4} \end{bmatrix}$$

$$= \begin{bmatrix} \cos^{2}\beta & e^{-i7/4} & -\sin^{2}\beta & e^{-i7/4} \\ \sin \beta & e^{-i7/4} & -\sin^{2}\beta & e^{-i7/4} \end{bmatrix}$$

$$= \begin{bmatrix} \cos^{2}\beta & e^{-i7/4} & -\sin^{2}\beta & e^{-i7/4} \\ -\sin^{2}\beta & -\sin^{2}\beta & e^{-i7/4} \end{bmatrix}$$

$$= \begin{bmatrix} \cos^{2}\beta & e^{-i7/4} & -\sin^{2}\beta & e^{-i7/4} \\ -\sin^{2}\beta & e^{-i7/4} & -\sin^{2}\beta & e^{-i7/4} \end{bmatrix}$$

$$= \begin{bmatrix} \cos^{2}\beta & e^{-i7/4} & -\sin^{2}\beta & e^{-i7/4} \\ -\sin^{2}\beta & e^{-i7/4} & -\sin^{2}\beta & e^{-i7/4} \end{bmatrix}$$

$$= \begin{bmatrix} \cos^{2}\beta & e^{-i7/4} & -\sin^{2}\beta & e^{-i7/4} \\ -\sin^{2}\beta & e^{-i7/4} & -\sin^{2}\beta & e^{-i7/4} \end{bmatrix}$$

$$= \begin{bmatrix} \cos^{2}\beta & e^{-i7/4} & -\sin^{2}\beta & e^{-i7/4} \\ -\sin^{2}\beta & e^{-i7/4} & -\sin^{2}\beta & e^{-i7/4} \end{bmatrix}$$

$$= \begin{bmatrix} \cos^{2}\beta & e^{-i7/4} & -\sin^{2}\beta & e^{-i7/4} \\ -\sin^{2}\beta & e^{-i7/4} & -\sin^{2}\beta & e^{-i7/4} \end{bmatrix}$$

$$= \begin{bmatrix} \cos^{2}\beta & e^{-i7/4} & -\sin^{2}\beta & e^{-i7/4} \\ -\sin^{2}\beta & e$$

$$E_{\text{out},p} = \frac{\cos T_{\lambda} + \sin T_{\lambda} \left( -i\cos^2 t + i\sin^2 t \mp \sin^2 t \right)}{\cos T_{\lambda} - i\sin T_{\lambda} \left( \cos^2 t \mp 2i\sin^2 t \cos t - \sin^2 t \right)}$$

$$= \frac{\cos T_{\lambda} - i\sin T_{\lambda} \left( \cos^2 t \mp 2i\sin^2 t \cos t \right)}{\cos T_{\lambda} - i\sin T_{\lambda} \left( \cos^2 t \mp i\sin^2 t \right)}$$

$$= \frac{\cos T_{\lambda} - i\sin T_{\lambda} \left( \cos^2 t \mp i\sin^2 t \right)}{\cos T_{\lambda} + i\sin T_{\lambda} \left( \cos^2 t - \sin^2 t \right)}$$

$$= \frac{1}{\cos T_{\lambda} + i\sin T_{\lambda} \left[ \cos^2 t - \sin^2 t \mp i\sin 2t \right]}$$

$$= \frac{1}{\cos T_{\lambda} + i\sin T_{\lambda} \left[ \cos^2 t - \sin^2 t \mp i\sin 2t \right]}$$

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$$= \frac{1}{\cos T_{\lambda} + i\sin T_{\lambda} \left[ \cos^2 t - \sin^2 t \mp i\sin 2t \right]}$$

$$= \frac{1}{\cos T_{\lambda} + i\sin T_{\lambda} \left[ \cos^2 t - \sin^2 t + i\sin 2t \right]}$$

$$= \frac{1}{\cos T_{\lambda} + i\sin T_{\lambda} \left[ \cos^2 t - \sin t \right]}$$

$$= \frac{1}{\sin t \cos t \left[ \cos t - \sin t \right]}$$

$$= \frac{1}{\sin t \cos t \left[ \cos t - \sin t \right]}$$

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$$= \frac{1}{\sin t \cos t \left[ \cos t - \sin t \right]}$$

## Appendix - New Polarization Interferometer Detection (3)

$$= i \left[ sin^{2} + -cos^{2} + , sin^{2} + cos^{2} + \right]$$

$$= i \left[ -cos^{2} + , sin^{2} + \right]$$

$$= i \left[ -cos^{2} + , sin^{2} + \right]$$

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$$\Rightarrow i \left[ -cos^{2} + , sin^{2} + \right]$$

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Therefore
$$E_{out} N_{\Delta} = A M_{\Psi,N_{\Delta}} E_{out}$$

$$= A i \left( -\cos 2\Psi, \sin 2\Psi \right) \left( \cos 7\Lambda - i\sin 7\Lambda e^{\mp 2i\beta} \right)$$

$$= A i \left( -\cos 2\Psi, \sin 2\Psi \right) \left( +i\cos 7\Lambda + i\sin 7\Lambda e^{\mp 2i\beta} \right)$$

$$= A i \left( -\cos 4\Psi (\cos 7\Lambda - i\sin 7\Lambda e^{\mp 2i\beta} \right)$$

$$\pm i\sin 2\Psi (\cos 7\Lambda + i\sin 7\Lambda e^{\mp 2i\beta} )$$

$$\pm i\cos 2\Psi (\cos 7\Lambda + i\sin 7\Lambda e^{\mp 2i\beta} )$$

$$\pm i\cos 2\Psi (\cos 7\Lambda + i\sin 7\Lambda e^{\mp 2i\beta} )$$

$$\pm i\cos 2\Psi (\cos 7\Lambda + i\sin 7\Lambda e^{\mp 2i\beta} )$$

$$+ i\sin 7\Lambda e^{\mp 2i\beta} (\cos 2\Psi + i\sin 2\Psi )$$

$$+ i\sin 7\Lambda e^{\mp 2i\beta} (\cos 2\Psi + i\sin 2\Psi )$$

$$= A \left[ E_{P,PD1} \right]$$

$$= A \left[ E_{P,PD1} \right]$$

$$= -i\cos 7\Lambda e^{\mp 2i\beta} (\cos 2\Psi + i\sin 2\Psi )$$

$$= E_{P,PD1} = -i\cos 7\Lambda e^{\mp 2i\beta} (\cos 2\Psi + i\sin 2\Psi )$$

$$= E_{P,PD1} = -i\cos 7\Lambda e^{\mp 2i\beta} (\cos 2\Psi + i\sin 2\Psi )$$

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## Appendix - New Polarization Interferometer Detection (4)

Ip = 
$$|E_0|^2 \left[ 1 \mp \sin \Gamma \sin (2\frac{1}{6} - 4\frac{1}{4}) \right]$$

Is =  $|E_0|^2 \left[ 1 \pm \sin \Gamma \sin (2\frac{1}{6} - 4\frac{1}{4}) \right]$ 

\* check energy conservation

Input intensity  $E_{in}^* E_{in} = A^*(1, \mp i) A \begin{pmatrix} 1 \\ \pm i \end{pmatrix}$ 

=  $2|A|^2 = 2|E_0|^2$ 

Output intensity  $I_p + I_g = 2|E_0|^2$ 

O Balanced Detector  $I_G$ 
 $I_G = I_p - I_s = \mp 2|E_0|^2 \sin \Gamma \sin (2\frac{1}{6} - 4\frac{1}{4})$ 

Max. of  $I_G = 2|E_0|^2 \sin \Gamma$ 

Max. of  $I_G = 2|E_0|^2 \sin \Gamma$ 

Min. of  $I_G = -2|E_0|^2 \sin \Gamma$ 

\* Consider  $\Gamma_0 = \frac{2\pi}{A}(n_e - n_o) l = \frac{2\pi}{A}l \Delta n = \alpha \Delta n$ 

( $\alpha = \frac{2\pi}{A}l$ ,  $\Delta n = n_e - n_o$ )

assuming  $\Delta n = b_G C$  ( $C: analyte concentration$ )

if  $C_0 \to C_0 + d_G$ , then  $\Delta n \to \Delta n + d(2n)$ 

then  $d(\Delta n) = b_G C_0$ 

Here  $d\Gamma_0 = \alpha d(\Delta n) = \alpha b_G C = \alpha const. dC_0$ 

## Appendix - New Polarization Interferometer Detection (5)

then 
$$Sin(\Gamma_0 + \delta\Gamma_0) \cong Sin\Gamma_0 + \delta\Gamma_0 \cos \Gamma_0$$
, for  $\delta\Gamma_0 \ll 1$   
 $using$   $f(x_0 + \delta x) \cong f(x_0) + \delta x f(x_0)$ , for  $\delta x \ll 1$   
 $\Rightarrow$   $Sin(\Gamma_0 + \delta\Gamma) / Sin\Gamma_0 = 1 + \delta\Gamma_0 \cot \Gamma_0$   
 $termind$  that  $\Gamma_0 = a\Delta n = abC_0 = \gamma C_0$   
 $\delta\Gamma_0 = ab\delta C_0 = \gamma \delta C_0$   
 $(\gamma = ab, constant)$ 

therefore there can be only one fitting parameter  $\eta$ 

renormalization w.r.t. the signal at the starting Co if 
$$Y = Y$$
. at  $C = C$ .

Subsequent  $Y$  can be normalized by  $Y$ .

then  $Y/Y$ . =  $1 + \gamma dc$ .  $cot(\gamma C_0)$ 

with fitting parameter  $\gamma$ 

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