Highly integrated biosensors based on fiber optics

Zhang, Mengying

2018

Zhang, M. (2018). Highly integrated biosensors based on fiber optics. Doctoral thesis,
Nanyang Technological University, Singapore.

<https://hdl.handle.net/10356/89954>

<https://doi.org/10.32657/10220/47180>

**NANYANG
TECHNOLOGICAL
UNIVERSITY**

SINGAPORE

**HIGHLY INTEGRATED BIOSENSORS
BASED ON FIBER OPTICS**

**ZHANG MENGYING
SCHOOL OF ELECTRICAL & ELECTRONIC
ENGINEERING**

2018

Highly Integrated Biosensors Based on Fiber Optics

Zhang Mengying

School of Electrical & Electronic Engineering

A thesis submitted to the Nanyang Technological University
in partial fulfillment of the requirement for the degree of
Doctor of Philosophy

2018

Acknowledgements

During my Ph.D. journey in the last four years, I received so much kind help and support from my professors, colleagues and beloved ones. I would like to express my sincere appreciations to them.

First and foremost, I would like to express my great gratitude towards my supervisors, Prof. Wei Lei and Prof. Shum Ping. Prof. Wei inspires me with innovative research ideas, equips me with experimental and analytical skills and guides me to overcome difficulties during my Ph.D. study. Under his patient guidance, I gradually get to know what research is. The professional attitude and learning skills he taught me will benefit my whole career. Prof. Shum has always been supportive throughout the years. He is always willing to share his valuable experience with me and introduce collaboration opportunities to me. I also received lots of encouragement from him, which gives me hope and courage to persist in research work.

I would like to extend my sincere thankfulness to Dr. Li Kaiwei, Dr. Wu Zhifang and Dr. Hu Juanjuan. They pass their precious research experience on to me unreservedly. Communicating with them has always helped me get a deeper understanding on my research topics. I also would like to thank my wonderful colleagues Dr. Huang Tianye, Dr. Xu Zhilin, Dr. Zhang Ting, Dr. Chen Ming, Dr. Chen Mengxiao, Dr. Jin Yunxia, Dr. Zhang Nan, Zhang Jing, Wu Tingting, Ma Shaoyang, Wang Zhe, Wang Zhixun, Yang Jiao and Qi Miao. They provide me with lots of kind help to my research work and enrich my campus life with much joy.

Last but not least, I express my love to my parents and grandparents. Their love gives me the greatest happiness and the courage to cope with any challenges.

Acknowledgements

Table of Contents

Acknowledgements	I
Abstract.....	V
List of Figures	VII
List of Abbreviations	XV
Chapter 1 Introduction.....	1
1.1 Background and Motivation.....	1
1.2 Objectives.....	5
1.3 Major Contributions.....	6
1.4 Organization	8
Chapter 2 Literature Review	10
2.1 Fiber-Optic Sensing Schemes.....	10
2.1.1 Long Period Fiber Grating.....	10
2.1.2 Side-Polished Optical Fiber.....	12
2.1.3 Microfiber	14
2.2 Fiber-Optic Magnetic Field Sensors.....	16
2.2.1 Magnetic Fluid	16
2.2.2 Magnetic Fluid and Optical Fiber Based Magnetic Sensors	19
2.3 Surface Plasmon Resonances	21
2.3.1 Drude Model.....	21
2.3.2 SPR Theory	22
2.3.3 LSPR Theory	25
2.3.4 Fiber-Optic SPR/LSPR Biosensors	28
2.4 Nanomaterials Based Plasmonic Biosensing	32
2.4.1 Graphene Enhanced Plasmonic Biosensing	34
2.4.2 TMO Based Plasmonic Biosensing	38
2.4.3 Macrocyclic Supramolecules Based Plasmonic Biosensing	42
Chapter 3 Magnetic Field Sensor Based on Magnetic Fluid Coated LPG	45
3.1 LPG Characterization.....	45
3.2 Detection of Magnetic Field.....	48
3.3 Summary.....	51
Chapter 4 Hybrid Graphene- on-Gold Plasmonic Fiber-Optic Biosensor.....	52
4.1 Design and Numerical Analysis	52
4.2 Fabrication and Characterization of Gold-Coated Side-polished Fiber	58
4.3 Graphene/Gold Hybrid Plasmonic Sensor.....	61

Table of Contents

4.3.1 Graphene Transfer.....	61
4.3.2 Characterization of Graphene/Gold Hybrid Plasmonic Sensor.....	64
4.4 ssDNA Detection	65
4.5 Summary.....	68
Chapter 5 Electron-Rich 2D MoO₃ for Highly Integrated Plasmonic Biosensing.....	69
5.1 Design and Construction of Biosensor.....	69
5.1.1 Biosensor Configuration	69
5.1.2 Synthesis and Characterization of MoO ₃ Nanoflakes	70
5.1.3 Integration of MoO ₃ Nanoflakes and Microfiber	74
5.2 BSA Detection.....	77
5.3 Numerical Analysis.....	79
5.4 Summary.....	82
Chapter 6 CD-Modified AuNPs Based Fiber-Optic LSPR Biosensor	83
6.1 Design and Configuration	84
6.2 Synthesis and Characterization of AuNPs	85
6.3 Selective Detection of Cholesterol.....	91
6.4 Summary.....	95
Chapter 7 Highly-Birefringent MOF Based SPR Sensor.....	97
7.1 Configuration and Principle.....	98
7.2 Phase Birefringence and Sensing Accuracy	101
7.3 Influencing Factors on SPR Behavior	104
7.4 Summary.....	107
Chapter 8 Summary and Future Work.....	108
8.1 Summary and Discussion	108
8.2 Future Work	110
Publications.....	112
References	115

Abstract

Benefited from the advantages of flexibility, miniaturization, immunity to electromagnetic interference and compatibility with today's well-developed optical fiber based telecommunication system, fiber-optic sensors show huge potentials with the increasing demand of comprehensive perception in every aspect of life. Especially in the practices of biosensing, optical fibers are prevailing platforms for highly-sensitive, real-time, label-free and in vivo detection due to their high degree of integration, dielectric nature, non-toxicity and chemical inertness. In this thesis, we investigate several approaches focusing on the proper design of optical fiber structure and the efficient integrations with functional materials to enhance the effectiveness of light-matter interaction and the reliability of biosensing output.

Firstly, we develop a highly sensitive magnetic field sensor based on magnetic-fluid-coated long period fiber grating (LPG). The emergence of optomagnetic biosensors in recent years brings the needs of all-optical, integrated and flexible magnetic field sensors. Benefited from the acute response of LPG to ambient medium and the remarkable magneto-optic properties of magnetic fluid, our proposed magnetic field sensor provides a superior sensitivity of 0.154 dB/Gauss. Secondly, we investigate the possibility of improving conventional fiber-optic plasmonic biosensors by employing a graphene/gold hybrid plasmonic structure. Introducing a graphene layer not only strengthens the surface plasmons but also acts as an excellent replacement of surface functionalization. We construct a biosensor that integrates such hybrid plasmonic architecture with a side-polished optical fiber and achieves a limit of detection (LOD) of ssDNA as low as 1 pM. Thirdly, we explore the potentials of adopting transition metal oxides as an alternative class of plasmonic 2D materials for biosensing in well-developed visible and near-infrared (NIR) optical windows, since plasmonics of common 2D materials locate intrinsically at mid-infrared range. Here we demonstrate the feasibility of integrating heavily-doped 2D MoO₃ with fiber-optic platform and achieving strong surface plasmons in NIR range, which facilitates low LOD of biomolecules. Fourthly, we realize one-step green synthesis of β -cyclodextrin (β -CD) capped gold nanoparticles. The macrocyclic supramolecular β -CD serves as

both reducing and stabilizing agent during synthesis and also biocompatible selective surface functionalization for target molecule recognition. Benefited from the highly efficient host-guest interaction between β -CDs and cholesterol molecules, we achieve an ultra-sensitive microfiber based cholesterol biosensor with good biocompatibility, specific selectivity and LOD as low as 5 aM. Lastly, we propose a highly-birefringent microstructured optical fiber (MOF) based plasmonic biosensor. Birefringence commonly exists in fiber-optic platforms and external perturbations would induce polarization crosstalk thereby destabilize the sensor output. We theoretically prove that the output instability due to polarization crosstalk can be effectively suppressed when the birefringence of MOF is larger than 2×10^{-4} . Here, we design a polarization maintaining MOF with birefringence as large as 4×10^{-4} , which can suppress the impact of polarization crosstalk to be negligible. Meanwhile, our proposed highly-birefringent MOF based plasmonic sensor also provides a high sensitivity of 3100 nm/RIU.

In the studies we conducted so far, it is shown that the vast possibilities of optical fiber design and the breakthroughs of functional nanomaterials facilitate promising potentials in achieving highly sensitive and highly integrated biosensors. Further improvements in the specificity, sensitivity, biocompatibility and integration of fiber-optic biosensors will be carried out in the near future.

List of Figures

Figure 1-1. Schematic illustration of conventional configuration of (a) SPR [5] and (b) LSPR [6].	1
Figure 1-2. Representative fiber-optic SPR/LSPR biosensing platforms based on (a) cascaded unclad optical fibers decorated with noble metal nanoparticles [11]; (b) unclad optical fiber coated with thin gold film [10]; (c) optical fiber endface integrated with metallic nanostructures [2].....	2
Figure 1-3. Magnetic nanoparticles assisted optical biosensor [54].	5
Figure 2-1. The schematic illustration of LPG and its mode couplings [60].	11
Figure 2-2. (a) The wavelength shift of LPG against surrounding refractive index [63]; (b) The wavelength shift of LPG resonant wavelength against a wide range of surrounding refractive index [64].	11
Figure 2-3. Schematic diagram of quartz block assisted side-polished fiber fabrication [82].	13
Figure 2-4. The propagation of the fundamental core mode through a tapered optical fiber [86].	14
Figure 2-5. The structural parameters of a taper transition [88].	15
Figure 2-6. The setup for fabricating an adiabatic tapered optical fiber [86].	16
Figure 2-7. Nanostructure of magnetic fluid particles [94].....	17
Figure 2-8. The magnetic nanoparticles gradually aggregate into (a) short needles, (b) columns mixed with short needles and (c) columnar glassy as the magnetic field strengthens; (d) The top view of hexagonally arranged columns [102].	18
Figure 2-9. (a) The side view and (b) the top view of the hexagonal columnar phase of magnetic fluid [101].	18
Figure 2-10. The schematic illustration of propagating SPR [124].	23
Figure 2-11. (a) The schematic illustration of Kretschmann configuration; (b) The plots of propagation constants of direct light in dielectric medium (k_s), the evanescent wave of total refractive incident beam at the prism-metal interface ($k_{ev} = k_p \sin \theta$), the evanescent wave of direct light in prism (k_p), the SPP propagating at the metal-dielectric interface ($k_{sp}(M/D)$) and the SPP propagating at the metal-prism interface ($k_{sp}(M/P)$) [123].	24
Figure 2-12. The schematic illustration of propagating SPR [129].	25
Figure 2-13. The formation of AuNPs using the Turkevich method [131].	27

Figure 2-14. The colors of aqueous solutions of gold nanospheres with increasing particle size. The particle sizes shown in (A-E) vary from 4 nm to 40 nm. All red bars represent 100 nm [133].	27
Figure 2-15. The redshift of LSPR peak as the AuNP size increases from 9 nm to 99 nm [142].	28
Figure 2-16. SPR/LSPR sensors based on (a) LPG [147]; (b) TFBG [175]; (c) tapered fiber with core diameter (ρ) of 50 μm and length of sensing region (L) of 2 mm [8]; (d) side-polished fiber [8]; (e) U-shaped fiber [146]; (f) patterned fiber end face [146].	29
Figure 2-17. Representative SPR/LSPR biosensors based on (a) PCF with hexagonal arranged air holes [12]; (b) PCF with liquid core [159]; (c) suspended-core MOF [163]; (d) semicircular channel MOF [166]; (e) semicircular channel MOF [165]; (f) exposed core MOF [168]; (g) exposed core grapefruit MOF [169]; (h) H-shaped MOF [170]. Λ : the pitch of photonic crystal air holes.	30
Figure 2-18 (a) A typical functionalization strategy of SPR immunosensor [40]. EDC/NHS: 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide/N-Hydroxysuccinimide. CNT: carbon nanotube. (b) AuNPs can form conjugation with numerous functional molecules mostly via gold-thiolate bonds [41].	32
Figure 2-19. (a) The hexagonal lattice of graphene. Each carbon atom is sp^2 hybridized [185]. (b) The band structures of graphene. VB and CB touch at the conical point [16].	34
Figure 2-20. Schematic illustration of the energy bands of graphene and metal (a) before and (b) after they are in contact. Φ_1 : the work function of metal. Φ_G : the work function of graphene [192].	36
Figure 2-21. Hybrid plasmonic architectures based on (a) monolayer graphene/gold [197]; (b) multilayer graphene/Py/gold [21]; (c) graphene oxide/gold [29]; (d) graphene-MoS ₂ /gold [31].	37
Figure 2-22. Free electrons are doped to TMOs via oxygen vacancies. (a) The pristine TMO lattice. (b) Two electrons are left in the lattice defect after the removal of an oxygen atom. Yellow spheres: metal cations. Red spheres: oxygen anions [203].	38
Figure 2-23. The polymorphs of (a) α -MoO ₃ (b) β -MoO ₃ (c) h-MoO ₃ [205].	38
Figure 2-24. A typical process of synthesizing α -MoO ₃ nanoflakes by liquid phase exfoliation [212].	40
Figure 2-25. (a) The SEM image of α -MoO ₃ nanoflakes [213]. (b) The TEM characterization of α -MoO ₃ nanoflakes [39]. The AFM characterization of (c) monolayer and bilayer α -MoO ₃ nanoflakes [212] and (d) multilayer α -MoO ₃ nanoflakes [201].	40
Figure 2-26. Molecular structures of some common macrocyclic supramolecules [282].	43

Figure 2-27. (a) Molecular structures and structural parameters of α -, β - and γ -CD [283]. (b) The side view and top view of the inclusion complexation formed by β -CD and cholesterol molecules [284].	43
Figure 2-28. Synthesis process of (a) carboxylatopillar[5]arene capped AuNPs [46]; (b) CD capped AuNPs [226]; (c) CD capped AgNPs, AuNPs and Agcore-Aushell/Au core-Agshell bimetallic nanoparticles [49].	44
Figure 3-1. The transmission spectrum of LPG.	46
Figure 3-2. Variation of the attenuation band of LPG as the surrounding refractive index increases.	47
Figure 3-3. Wavelength shift and transmission minimum of LPG against surrounding refractive index.	47
Figure 3-4. The experiment setup of magnetic field sensor.	48
Figure 3-5. Variation of LPG attenuation band along with increasing magnetic field strength.	49
Figure 3-6. Wavelength shift and transmission minimum of LPG against magnetic field	50
Figure 4-1. Configuration of proposed graphene-on-gold SPR biosensor. ssDNA molecules are adsorbed on single sheet of graphene through π -stacking interactions between the aromatics rings of nucleobases and honeycomb latticed carbon atoms.	53
Figure 4-2. The HE _{11y} mode patterns of side-polished optical fiber based SPR sensors (a) without and (b) with graphene enhancement. Red arrows: the electric field directions of HE _{11y} modes.	54
Figure 4-3. The gold film thickness is 50 nm. (a) Transmission spectra of conventional side-polished optical fiber based SPR sensor and graphene enhanced SPR sensor. (b) Comparison of sensitivities of conventional SPR and graphene enhanced SPR using wavelength interrogation (blue solid line and dashed line) and intensity interrogation (red solid line and dashed line).	54
Figure 4-4. The gold film thickness is 40 nm. (a) Transmission spectra of conventional side-polished optical fiber based SPR sensor and graphene enhanced SPR sensor. (b) Comparison of sensitivities of conventional SPR and graphene enhanced SPR using wavelength interrogation (blue solid line and dashed line) and intensity interrogation (red solid line and dashed line).	55
Figure 4-5. The gold film thickness is 30 nm. (a) Transmission spectra of conventional side-polished optical fiber based SPR sensor and graphene enhanced SPR sensor. (b) Comparison of sensitivities of conventional SPR and graphene enhanced SPR using wavelength interrogation (blue solid line and dashed line) and intensity interrogation (red solid line and dashed line).	55

Figure 4-6. Normalized electric field intensities of excited SPPs when no graphene layer, single layer graphene, 2-layer graphene and 3-layer graphene are deposited on the 30 nm gold film coated on the side-polished facet of fiber. (Inset) Distributions of normalized electric field intensity over the entire simulated geometry.....	57
Figure 4-7. Sensitivities corresponding to single, double and triple layers of graphene when using (a) wavelength interrogation and (b) intensity interrogation.	57
Figure 4-8. Schematic diagram of side-polished single-mode optical fiber.....	58
Figure 4-9. The SEM image of the cross section of the side-polished fiber.	59
Figure 4-10. Schematic diagram of side-polished single-mode optical fiber.....	59
Figure 4-11 (a) Transmission spectra of a side-polished fiber based SPR sensor with gold thickness of 30 nm. (b) Measured sensitivities that correspond to wavelength and intensity interrogations.....	60
Figure 4-12. (a) Microscopic view of the boundary of transferred single layer graphene (b) The boundary between the polished and the unpolished region of optical fiber which is fully covered with homogeneously deposited graphene.....	62
Figure 4-13. (a) Raman spectrum of monolayer CVD-grown graphene on copper foil. (b) Raman spectrum of transferred monolayer graphene on gold-coated fiber. (c) Raman spectra at 5 different positions along the longitude of optical fiber.	62
Figure 4-14. Comparison of transmission spectra of configurations with and without graphene.	63
Figure 4-15. The variations of transmission spectrum of (a) gold-coated side-polished fiber based plasmonic sensor and (b) graphene/gold hybrid plasmonic side-polished fiber based sensor.....	64
Figure 4-16. The comparison of the sensitivities before and after transferring graphene for (a) wavelength interrogation and (b) intensity interrogation.	64
Figure 4-17. (a) Change of transmission spectra of graphene enhanced SPR fiber sensor when detecting concentrations of ssDNA; (b) Variations of transmission minimum and resonant wavelength against ssDNA concentrations (log pM).....	66
Figure 4-18. (a) The variations of transmission spectrum as ssDNA concentration increases when there is no graphene on thin gold film. (b) The comparison of the sensitivities to ssDNA solutions with and without graphene transfer.....	67
Figure 5-1. Schematic diagram of fiber-optic biosensor integrated with heavily-doped MoO _{3-x} nanoflakes. Inset 1: Crystal structure of stable orthorhombic α -MoO ₃ . Inset 2: Molecular structure of BSA protein.	70
Figure 5-2. The XRD pattern of polycrystalline α -MoO ₃ powder	71

Figure 5-3. Color variations of MoO ₃ nanoflakes suspensions along with increasing doping extent.....	71
Figure 5-4. (a) Low-magnification TEM of the exfoliated MoO ₃ nanoflakes. (b) SAED pattern of MoO ₃ nanoflakes. (c) HRTEM of MoO ₃ nanoflakes. (d) AFM measurement of MoO ₃ nanoflakes. The average thickness of nanoflakes is ~2.8 nm and the lateral dimensions range from tens of nm to ~1 μm.	72
Figure 5-5. The evolvement of absorption spectrum from pristine MoO ₃ nanoflakes suspension (black curve) to increasing doping extent. 2 mL pristine MoO ₃ nanoflakes suspensions are added with 0, 50 μL, 60 μL, 70 μL and 80 μL 0.01 M NaBH ₄ respectively.	73
Figure 5-6. (a) XPS analysis of pristine MoO ₃ . (b) XPS analysis of highly doped MoO ₃ nanoflakes. Mo ⁶⁺ and Mo ⁵⁺ coexist after doping.	74
Figure 5-7. Real-time monitoring of the transmission intensity of microfiber within 745 nm – 755 nm as MoO _{3-x} nanoflakes are bonding to the microfiber surface.	75
Figure 5-8. (a) Morphology of MoO _{3-x} nanoflakes on the SiO ₂ (285 nm)/Si substrate. The nanoflakes are functionalized by the same method as microfiber functionalization. (b) AFM characterization of MoO _{3-x} nanoflakes dispersed on bare Si substrate without electrostatic attractions.	76
Figure 5-9. (a) Fluorescent microscopic images of MoO _{3-x} nanoflakes coated fibers that are functionalized with different concentrations of BSA molecules labelled with Cy3 dyes. (b) Absorption spectrum when MoO _{3-x} nanoflakes are mixed with different BSA concentrations. (c) Transmission spectra of the proposed biosensor when detecting incrementing BSA concentrations. (d) Linear response of transmission minimum as a function of BSA concentration in log-scale.	77
Figure 5-10. (a) Simulated plasmon resonance band with the deduced Drude model of MoO _{3-x} . Inset: HE ₁₁ mode profile of MoO _{3-x} nano-layer coated microfiber. (b) Simulated electric field distribution near the MoO _{3-x} nanolayer. Inset: Electric field distribution over the whole fiber diameter.	81
Figure 5-11. (a) Electric field distribution over the diameter of a bare microfiber. Inset: HE ₁₁ mode profile of the bare microfiber. (b) Electric field distribution over the diameter of a MoO _{3-x} coated microfiber. Inset: HE ₁₁ mode profile of the MoO _{3-x} coated microfiber.....	81
Figure 6-1. Schematic illustration of the proposed microfiber based biosensor. Inset 1: The molecular structure of β-CD. Inset 2: The molecular structure of cholesterol.....	84
Figure 6-2. The evolvement of AuNPs solution absorption during the synthesis process. Inset: The variation of solution color along with synthesis time.	85
Figure 6-3. The DLS measurements of AuNPs size distributions at different synthesis time.	86
Figure 6-4. The absorption of AuNPs solution after centrifugation and redispersion. Inset: the color of purified AuNPs solution.	87

Figure 6-5. SEM image of the as-prepared β -CD-capped AuNPs.	88
Figure 6-6. (a) Low-magnification TEM of β -CD-capped AuNPs. (b) HRTEM of a single β -CD-capped AuNP.....	88
Figure 6-7. (a) The AuNPs size distribution of 30 min synthesis time measured by DLS. (b) The comparison of AuNPs size distributions obtained from DLS measurement and TEM observation.	89
Figure 6-8. The ξ -potential value of the β -CD-capped AuNPs.	90
Figure 6-9. The ^1H NMR spectrum (300 MHz, D_2O) of the β -CD-capped AuNPs. Inset: Schematic β -CD structure associated with corresponding chemical shifts and interaction with AuNP surface.	90
Figure 6-10. The FTIR spectra of pristine β -CD and β -CD-capped AuNPs.	90
Figure 6-11. (a) C 1s XPS spectrum and (b) O 1s XPS spectrum of pristine β -CD; (c) C 1s XPS spectrum and (d) O 1s XPS spectrum of β -CD-capped AuNPs.	91
Figure 6-12. (a) The SEM image of the thinnest portion of microfiber. (b) The distribution of the immobilized β -CD-capped AuNPs on microfiber surface.	92
Figure 6-13. (a) The variation of transmission spectrum as the cholesterol concentration increases. (b) The response of transmission minimum against log-scale cholesterol concentration.	93
Figure 6-14. An interference study with the existence of common substances in human serum. The concentrations of interfering substances are added based on the realistic proportions in human serum.	95
Figure 7-1. Mesh sizes around the boundaries of gold layer in numerical model.....	98
Figure 7-2. (a) Schematic drawing of the proposed MOF structure; (b) x-polarized and (c) y-polarized core mode pattern calculated by FEM.....	99
Figure 7-3. Effective indices of core mode and surface plasmon mode with refractive index of analyte of 1.33 and gold layer thickness of 70 nm.	100
Figure 7-4. Changes of core mode transmission loss when refractive index of analyte increases from 1.33 to 1.34.	100
Figure 7-5. Mode patterns of (a) x- and (b) y-polarized core mode in conventional PCF with 50 nm gold layers and analyte refractive index of 1.38.	101
Figure 7-6. Loss spectra of MOF based SPR sensors when (a) $d_1/d_2=0.95$ (b) $d_1/d_2=0.4$ with analyte refractive index of 1.38.....	102
Figure 7-7. The relation between phase birefringence and the resonant wavelength offset..	103

List of Figures

Figure 7-8. (a) Loss spectra and (b) Sensitivity curves of proposed SPR sensor when gold thickness is 50, 60, 70 and 100 nm respectively. 105

Figure 7-9. Sensitivity curves when $d_1/d_2 = 1.0, 0.6, 0.5$ and 0.4 respectively. 106

List of Figures

List of Abbreviations

^1H NMR	Proton Nuclear Magnetic Resonance
2D	Two-Dimensional
AFM	Atomic Force Microscopy
AuNPs	Gold Nanoparticles
BSA	Bovine Serum Albumin
CB	Conduction Band
CD	Cyclodextrin
CVD	Chemical Vapor Deposition
Cy3	Cyanine 3
DI	Deionized
DLS	Dynamic Light Scattering
FEM	Finite Element Method
FTIR	Fourier-Transform Infrared Spectroscopy
HAuCl_4	Chloroauric Acid
HRTEM	High-Resolution Transmission Electron Microscopy
LOD	Limit of Detection
LPG	Long Period Fiber Grating
LSPR	Localized Surface Plasmon Resonance
MIR	Mid-Infrared
MOF	Microstructured Optical Fiber
MoO_3	Molybdenum Trioxide
MUA	11-Mercaptoundecanoic Acid

List of Abbreviations

MZI	Mach–Zehnder Interferometer
NIR	Near-Infrared
PAA	Poly(allylamine)
PBS	Phosphate Buffer Solution
PCF	Photonic Crystal Fiber
PCR	Polymerase Chain Reaction
PML	Perfectly Matched Layer
PSS	Poly(styrene sulfonate)
SAM	Self-Assembled Monolayer
SEM	Scanning Electron Microscope
SERS	Surface-Enhanced Raman Scattering
SMF	Single-Mode Fiber
SP	Surface Plasmon
SPP	Surface Plasmon Polariton
SPR	Surface Plasmon Resonance
TEM	Transmission Electron Microscopy
TFBG	Tilted Fiber Bragg Grating
TMO	Transition Metal Oxide
VB	Valence Band
WGM	Whispering Gallery Mode
WO ₃	Tungsten Oxide
XPS	X-ray Photoelectron Spectroscopy

Chapter 1 Introduction

1.1 Background and Motivation

Optical biosensors have been rapidly developed over the past decade thanks to their great potentials in highly sensitive, real-time, label-free and in vivo detection [1]. Widely applied optical biosensing techniques are surface plasmon resonance (SPR), localized surface plasmon resonance (LSPR), surface-enhanced Raman scattering (SERS), whispering gallery mode (WGM) resonators, etc. [2,3]. Under the trend of sensing system miniaturization, fiber-optic biosensors are favored by their compact size, flexibility, remote and in situ sensing capability. So far, various optical fiber based platforms have shown promising prospect in biosensing with high-degree of integration.

One crucial point of improving optical biosensing performance is to optimize the light-matter interaction. Among various forms of light-matter interaction, SPR and LSPR have captured intensive research interests due to their exceptional sensitivity. SPR/LSPR arises from the collective electron oscillations of noble metals or electron-rich semiconductors in resonance with incident light [4]. Conventionally SPR is implemented by coating a prism base with a thin noble metal film that excites resonant electron oscillations (Figure 1-1 (a) [5]), which are known as surface plasmon polariton (SPP). SPP can only be excited by TM-polarized light and it exponentially decays into the dielectric analyte thereby acutely responses to the variation of analyte refractive index. Generally, the shift of resonant angle or resonant wavelength at which light reflectance is minimum is used as the indication of biomolecules immobilization on the metal surface. If the thin metal film is replaced with metallic nanoparticles, resonant

Figure 1-1. Schematic illustration of conventional configuration of (a) SPR [5] and (b) LSPR [6].

electron oscillations can also be induced except that the surface plasmon is nonpropagating, which is the so-called LSPR. The excitation of LSPR is not restrained by the incident light polarization, thus it can be realized by both prism based reflection configuration and transmission configuration (Figure 1-1 (b) [6]).

However, the aforementioned SPR/LSPR configurations are limited by the bulky and non-flexible configuration especially under the increasing demand for portable, point-of-care or in vivo biosensing devices. Fortunately, such shortcoming can be addressed by optical fibers. Various optical fiber structures have been proven feasible and shown promising prospect for SPR/LSPR biosensing, such as fiber gratings, unclad fiber, side-polished fiber, microfiber, U-shaped fiber, etc. [2,7–11]. Figure 1-2 illustrates some typical configurations of fiber-optic SPR/LSPR biosensors.

Figure 1-2. Representative fiber-optic SPR/LSPR biosensing platforms based on (a) cascaded unclad optical fibers decorated with noble metal nanoparticles [11]; (b) unclad optical fiber coated with thin gold film [10]; (c) optical fiber endface integrated with metallic nanostructures [2].

In recent years, microstructured optical fiber (MOF) based SPR/LSPR sensors have drawn much research interest. MOFs possess fine arrangement of air holes that extend along the entire fiber. The fiber core dimension can be made very small to facilitate strong light-matter interaction while still maintaining flexibility and robustness thanks to the support of thin silica walls among air holes. The air holes surrounding the small fiber core can be infiltrated with gas or liquid analyte so that the strong evanescent field of guided light penetrates into the analyte. MOF based SPR/LSPR biosensor significantly improves the integration and also reduces the required sample volume. Several MOF structures have been proposed for SPR/LSPR

biosensor, for instances, selectively coated photonic crystal fiber (PCF) [12], semicircular channel MOF [13] and suspended-core MOF [14]. Since most MOF designs for SPR/LSPR biosensors are asymmetric in two orthogonal polarization directions, phase birefringence commonly exists. Hence, the resonant wavelengths corresponding to two polarizations are apart while their transmission dips partially overlap. As a consequence, external perturbations such as pressure, bending, twisting or inaccurate input polarization would result in the offset of resonant wavelength. Therefore, an MOF design that can suppress the measurement offset due to polarization crosstalk meanwhile providing highly sensitive biosensing performance would be promising.

Besides optimizing the configuration of fiber-optic platform, introducing functional nanomaterials is also a promising solution to enhance the plasmon-matter interaction [15]. The rapid development of two-dimensional (2D) materials in the past decade redefines the frontier of biosensing with high degree of integration and extremely low limit of detection (LOD). 2D materials show remarkable advantages in surface-to-volume ratio, near field confinement and in situ tunability of plasmonic properties [16,17]. Intrinsically the propagating SPR and LSPR can be supported by 2D materials and patterned 2D materials respectively in mid-infrared (MIR) or terahertz range [18,19]. Although 2D materials based plasmonic biosensing in MIR range has shown promising performance [20], it faces the challenges of achieving high degree of integration, compactness and cost effectiveness when it comes to practical applications. Hence the majority of researches focus on constructing hybrid plasmonic 2D materials/metal architectures, where the 2D materials deposited on conventional plasmonic thin metal film serve as a functional layer to promote the plasmon-matter interaction. Various hybrid plasmonic structures based on conventional prism configuration have been proposed, including graphene/gold [21–24], graphene oxide/gold [25–29], graphene-MoS₂/gold [30–32], etc., and they have proven the sensitivity enhancement benefited from the additional 2D materials functional layer. However, most of these studies are preliminary theoretical investigations and systematic exploration on such hybrid structures integrated with flexible waveguides (e.g. optical fibers) has yet to be conducted.

Since the intrinsic plasmonics of most common 2D materials locate within MIR and terahertz regions, employing heavily doped few-layer transition metal oxides (TMOs) as an alternative class of 2D plasmonic materials for frequently-used optical windows have attracted considerable attention recently. Benefited from their outer-d electrons, sufficient free carriers can be doped to TMOs via ionic intercalation to facilitate surface plasmons in visible and near-infrared (NIR) frequencies [33–35]. At the current stage, thin atomic layers of molybdenum trioxide (MoO_3) doped with abundant electrons are most widely studied due to the layered crystalized structure. Strong plasmonic peaks of 2D MoO_3 in visible or NIR range have been achieved through several approaches [34,36–39]. However, the biosensing capability of the highly integrated devices based on such plasmonic 2D MoO_3 or other TMOs remains unexplored.

Apart from the strong plasmon-matter interaction, surface functionalization that equips SPR/LSPR platforms with good biocompatibility, biomolecules immobilization and recognition is another key point to improve the biosensing performance. Conventional SPR/LSPR biosensors normally require tedious surface functionalization strategies to immobilize and recognize biomolecules [40,41]. Macrocyclic supramolecules are revealed to be an excellent molecular recognition element as they can form specific host-guest interaction with particular guest molecules. Also, they can reduce the cytotoxicity of noble metal nanoparticles [42]. Recently, one-step synthesis of macrocyclic supramolecules capped noble metal nanoparticles with good monodispersity have been demonstrated, indicating that the synthesis and the surface functionalization can be realized in one simple process [43–50]. However, the LSPR biosensing potential of macrocyclic supramolecules modified noble metal nanoparticles has not been comprehensively studied.

A new type of optomagnetic biosensor, in which magnetic nanoparticles are functionalized with molecular recognition element and mixed with sample fluid [51–53], emerges recently. Those magnetic nanoparticles are actuated by controllable magnetic field and rapidly accumulate at the detection area (Figure 1-3 [54]). The high refractive index of magnetic nanoparticles leads to substantial absorption and scattering of evanescent field so that effectively improves the sensitivity. Magnetic field

manipulated optical biosensor requires accurate measurement of applied field strength. Driven by the purpose of achieving compact and all-optical sensing system, optical fiber based magnetic field sensor attracts much attention. Due to its remarkable magneto-optic properties, magnetic fluid is considered as a promising material for magnetic field sensing. It is a colloidal suspension of surfactant-coated magnetic nanoparticles. Each nanoparticle can be viewed as a magnet that is driven to align with magnetic field direction. The change of optical properties of magnetic fluid during such phase transition can be detected by fiber-optic sensors. Various optical fiber based magnetic field sensors have been developed. Previous studies show the feasibility of using PCF [55], multimode interferometer [56], tilted fiber Bragg grating (TFBG) [57] and tapered fiber [58] for magnetic field sensing combined with magnetic fluid. A magnetic field sensor simply based on long period fiber grating (LPG), however, is rarely investigated.

Figure 1-3. Magnetic nanoparticles assisted optical biosensor [54].

1.2 Objectives

In this thesis, we aim to develop and validate well-designed fiber-optic platforms coupled with functional nanomaterials to achieve promising biosensing features, including high degree of integration, superior sensitivity, biocompatibility, molecular recognition, reliable output, flexibility, etc. The main objectives of our works are:

1) To develop a highly sensitive LPG and magnetic fluid based magnetic field sensor, aiming for accurate manipulation of magnetic nanoparticles when constructing all-fiber-based optomagnetic biosensors.

2) To systematically investigate the plasmonic properties of 2D materials/metal hybrid plasmonic structure when integrated with fiber-optic platforms. To be more specific, we theoretically and experimentally analyze the plasmon-matter interaction of graphene-on-gold hybrid structure deposited on a side-polished fiber. The constructed biosensor was adopted to detect ssDNA molecules as a demonstration of biosensing application.

3) To explore the biosensing potentials of recently emerged 2D TMOs as an alternative class of 2D plasmonic material in visible and NIR optical windows. Few-layer α -MoO₃ nanoflakes are synthesized and integrated with microfiber to realize highly sensitive detection of negatively charged protein molecules.

4) To investigate the LSPR behaviors of one-step synthesized gold nanoparticles (AuNPs) capped with a representative macrocyclic supramolecule, cyclodextrin (CD). Based on a microfiber platform, cholesterol molecules are adopted as target guest biomolecules to investigate the efficiency of host-guest interaction. Interference study is also conducted to verify the specific selectivity of the CD-capped AuNPs based fiber-optic biosensor.

5) To propose a highly-birefringent MOF that can effectively suppress the impact of undesired polarization on SPR biosensor output. Besides the output stability, the sensitivity of highly-birefringent MOF based SPR sensor is another important consideration.

1.3 Major Contributions

The novelty of the studies and my contributions to this thesis include:

1) *Develop a highly sensitive LPG based magnetic field sensor.* In this study, I fabricated a LPG and characterized its refractive index sensing capability. Then I designed the experimental setup and demonstrated the magnetic field sensing

capability of the LPG coated with magnetic fluid. The transmission spectrum of LPG varies in accord with the increase of magnetic fluid refractive index due to the phase transitions under the enhancing magnetic field strength. The acute response of LPG to the ambient environment variation results in the high sensitivity of magnetic field, which is superior to the state-of-the-art fiber-optic magnetic field sensors.

2) *Demonstrate a fiber-optic plasmonic biosensor based on graphene-on-gold hybrid plasmonic structure.* First, I carried out numerical analysis to verify that the addition of single graphene layer on thin gold film can enhance the SPP as well as the bulk refractive index sensing performance to the greatest extent compared with bilayer graphene/gold and multi-layer graphene/gold structures. Second, I fabricated a side-polished optical fiber and coated it with thin gold film and then characterized its SPR behavior. Then I deposited a single sheet of graphene on top of the thin gold film via wet-transfer method. Again, I characterized the SPR behavior of the graphene/gold hybrid structure and proved that additional graphene layer obviously enhances the SPR sensing performance. Lastly, I validated the proposed biosensing platform by ssDNA detection. A LOD as low as 1 pM is achieved, which is 3 orders of magnitude lower than the conventional SPR simply based on thin gold film.

3) *Realize a highly integrated biosensor based on 2D plasmonic MoO_{3-x} nanoflakes.* First, I synthesized and characterized 2D morphologies of MoO_3 nanoflakes. After doped with abundant electrons, the sub-stoichiometric MoO_{3-x} is formed and a strong plasmon resonance appears at NIR range. Then I integrated the MoO_{3-x} nanoflakes with microfiber via electrostatic interaction by facile layer-by-layer self-assembly of polyelectrolytes. The deposited MoO_{3-x} nanoflakes induce a strong plasmon resonance in the same NIR range on microfiber transmission spectrum and show good affinity to negatively charged biomolecules. To validate the proposed biosensor, I applied it in the detection of bovine serum albumin (BSA). A LOD as low as 1 pg/mL is achieved. I also carried out numerical calculation to deduce the Drude model parameters of electron-rich MoO_{3-x} based on the experimental results.

4) *Construct a biocompatible fiber-optic LSPR biosensor based on CD-modified AuNPs.* In this work, I synthesized β -CD-capped AuNPs in an eco-friendly and facile one-step process. The plasmonic property and the morphology of the β -CD-

capped AuNPs are then characterized. Then I integrated the synthesized AuNPs with a microfiber via electrostatic interaction and employed it in cholesterol detection. Benefited from the highly efficient host-guest interaction between β -CD and cholesterol molecules, the proposed fiber-optic biosensor achieves an ultralow LOD of cholesterol of 5 aM. I also conducted an interference study to verify the specific detection of the biosensor to cholesterol molecules. It shows that common interfering substances in human serum hardly affect the cholesterol detection.

5) *Design and analyze a highly-birefringent MOF based SPR sensor with high resistance to polarization crosstalk.* This study theoretically investigates the relation between phase birefringence and polarization crosstalk in MOF based SPR sensors. I carried out numerical analysis and found that commonly existed birefringence in MOF based SPR sensor designs induces considerable measurement offset when polarization crosstalk occurs unless the birefringence exceeds a threshold value, $\sim 2 \times 10^{-4}$. Therefore, I designed a MOF of which two central cladding air holes in the lateral direction are intentionally enlarged to introduce high phase birefringence to suppress the SPR sensing offset caused by polarization crosstalk. The proposed MOF structure provides a birefringence as high as $\sim 4.2 \times 10^{-4}$, which can suppress the offset to be negligible.

1.4 Organization

This thesis consists of 8 chapters:

Chapter 1 is an introduction. It introduces the background of optical fiber based biosensors and the recent development of functional nanomaterials, states the motivations and the objectives of our works and outlines the thesis organization.

Chapter 2 explains the concepts and the theories associated with fiber-optic sensing schemes, SPR/LSPR and relevant functional nanomaterials. It also reviews the state-of-the-art development of optical fiber based biosensors and functional nanomaterials in recent years.

Chapter 3 describes the experimental details and the results discussion of magnetic field sensor based on magnetic-fluid-coated LPG.

Chapter 4 numerically analyzes the design parameters of side-polished fiber based hybrid graphene-on-gold plasmonic biosensing platform, characterizes the plasmonic properties of the constructed hybrid structure and demonstrates its biosensing performance.

Chapter 5 demonstrates the synthesis and the characterization of heavily doped 2D MoO_{3-x} nanoflakes. It also describes how to construct and validate the highly integrated microfiber and nanoflakes based biosensing platform. The plasmonic behaviors of MoO_{3-x} nanoflakes are theoretically analyzed.

Chapter 6 constructs an LSPR fiber-optic biosensor based on β -CD-capped AuNPs. The eco-friendly synthesis and the characterization of the as-prepared AuNPs are presented in this chapter. An interference study is conducted to verify the specific molecular recognition of the proposed biosensor.

Chapter 7 shows the design of highly-birefringent MOF and numerically analyzes how it suppresses the output inaccuracy caused by polarization crosstalk.

Chapter 8 draws the conclusions and puts forward future research plans.

Chapter 2 Literature Review

This chapter reviews the background and the theories of state-of-the-art fiber-optic biosensors related to our research topics. First, we introduce some commonly employed optical fiber based sensing schemes in Section 2.1, including LPG, side-polished optical fiber and microfiber. Section 2.2 presents the magneto-optic properties of magnetic fluid and their potentials in magnetic field sensing. Previously reported magnetic fluid and optical fiber based magnetic field sensors are also summarized in this section. Section 2.3 explains the theories associated with SPR and LSPR. The state-of-the-art fiber-optic SPR/LSPR biosensors are also discussed in this section. Section 2.4 shows how some emerging nanomaterials, e.g. graphene, 2D TMOs and macrocyclic supramolecules, improve the performance of conventional plasmonic biosensing platforms and what potentials of these nanomaterials remained unexplored.

2.1 Fiber-Optic Sensing Schemes

2.1.1 Long Period Fiber Grating

LPG is a periodic perturbation of the refractive index of fiber core (Figure 2-1) [59]. It couples the forward-propagating fundamental core mode into several co-propagating cladding modes as long as the phase matching condition is satisfied. The high loss of the forward-propagating cladding modes leads to a series of attenuation bands at discrete wavelengths on the LPG transmission spectrum [60]. Each of the attenuation bands corresponds to a coupling from the fundamental core mode to a cladding mode. The phase matching condition is given by Equation (1) [61]:

$$\lambda_p = (n_{core}^{eff} - n_{p,clad}^{eff})\Lambda \quad (1)$$

where λ_p is the resonant wavelength of cladding mode of the p^{th} order. n_{core}^{eff} and $n_{p,clad}^{eff}$ are the effective refractive indices of the core mode and the p^{th} order cladding mode respectively. Λ is the period of grating, which is shown in Figure 2-1.

Figure 2-1. The schematic illustration of LPG and its mode couplings [60].

According to Equation (1) that the resonant wavelengths of LPG are dependent on the difference between the effective refractive indices of core mode and the corresponding cladding modes. The resonant wavelengths are therefore modulated by the surrounding refractive index of LPG as it influences the effective refractive indices of cladding modes. Equation (2) expresses the dependence of resonant wavelengths on surrounding refractive index [62]:

$$\frac{d\lambda_p}{dn_{sur}} = \frac{d\lambda_p}{dn_{p,clad}^{eff}} \frac{dn_{p,clad}^{eff}}{dn_{sur}} \quad (2)$$

where n_{sur} is the surrounding refractive index of LPG. The higher the order of cladding mode, the corresponding resonant wavelength is more sensitive to ambient refractive index [62,63]. The sensitivity also increases as the surrounding refractive index approaches to that of fiber cladding. The enhancement of sensitivity along with increasing ambient refractive index is shown by Figure 2-2 (a) [63]. When the

Figure 2-2. (a) The wavelength shift of LPG against surrounding refractive index [63]; (b) The wavelength shift of LPG resonant wavelength against a wide range of surrounding refractive index [64].

surrounding refractive index becomes closed to that of fiber cladding, the resonant dips on transmission spectrum are greatly weakened or even disappear. The resonant dips will reappear once the refractive index of ambient medium exceeds that of fiber cladding (Figure 2-2 (b)). The reappeared resonant wavelengths would no longer be varied by changing ambient refractive index [64].

The transmission minimum of the attenuation bands is a cosine-squared function of the coupling coefficient, κ , and the grating length, L [65,66]:

$$T = \cos^2(\kappa L) \quad (3)$$

The coupling coefficient κ reduces as the external perturbation enhances. The increase of ambient refractive index, bending or transverse load would decrease κ [65]. As the value of cosine-squared function fluctuates between 0 and 1, the variation trend of LPG transmission minimum is thereby dependent on its initial position. A resonant dip with its transmission minimum located at the valley (i.e. the lowest value) of the $\cos^2(\kappa L)$ curve is considered as “saturated”. Hence the transmission minimum of a saturated LPG increases with the ascending $\cos^2(\kappa L)$ curve when κ decreases. On the other hand, a transmission minimum located at point far from the valley of $\cos^2(\kappa L)$, which is corresponding to a “over-coupled” LPG, decreases along with reducing κ as the function curve is descending.

2.1.2 Side-Polished Optical Fiber

Side-polished optical fiber, which is also called D-shaped optical fiber, is a widely applied fiber configuration in fiber lasers [67–69], polarizers [70,71], numerous sensing applications [72–78], etc. Benefitted from the planar interface, side-polished fiber is a versatile platform for easy patterning of micro/nanostructures and easy deposition of functional layers or materials (e.g. gold thin film and 2D materials) [74–79]. The most frequently used fabrication method is to glue a stripped optical fiber in a V-groove of quartz block, and then polish the whole quartz block till strong enough evanescent field is exposed. Figure 2-3 illustrates the configuration and the cross-section of fixed side-polished fiber in V-groove [80]. To achieve acute response of

evanescent field to ambient environment, the distance between the polished facet and the fiber core should be kept comparable to the guided wavelength [81].

Figure 2-3. Schematic diagram of quartz block assisted side-polished fiber fabrication [82].

The attenuation coefficient α of the fundamental mode in side-polished fiber can be estimated by the following Vassalo's Formula [83]:

$$\alpha = \frac{4\sqrt{2\Delta}}{a(1+2b\Delta)} \frac{1-b}{K_1^2(V\sqrt{b})} \frac{\sqrt{b(V_{ex}^2 - bV^2)}}{V_{ex}^2} K_0\left(\frac{2\sqrt{b}Vd}{a}\right) \quad (4)$$

where a is the radius of fiber core, d is the distance from the polished facet to the center of fiber core. K_0 and K_1 are the modified Bessel function of the second kind of the zeroth and first order respectively. b is the normalized refractive index that is a function of effective refractive index N_{eff0}^2 :

$$b = \frac{N_{eff0}^2 - n_{clad}^2}{n_{core}^2 - n_{clad}^2} \quad (5)$$

Δ is relative refractive index difference:

$$\Delta = \frac{n_{core} - n_{clad}}{n_{core}} \quad (6)$$

V and V_{ex} are the normalized frequency parameters of the guide mode and external medium respectively:

$$V = \frac{2\pi a}{\lambda} \sqrt{n_{core}^2 - n_{clad}^2} \quad (7)$$

$$V_{ex} = \frac{2\pi a}{\lambda} \sqrt{n_{external}^2 - n_{clad}^2} \quad (8)$$

The exposed evanescent field at the polished interface penetrates into the external medium and decays exponentially in the perpendicular direction to the interface. The field intensity at the distance z from the interface is given by [84]:

$$I(z) = I_0 \exp\left(-\frac{z}{d_p}\right) \quad (9)$$

where I_0 is the initial intensity of incident light. θ is the angle of incidence to the normal of the interface. d_p is the penetration depth of the evanescent field where the electric field decays to e^{-1} of the initial intensity. It can be determined by:

$$d_p = \frac{\lambda}{2\pi \sqrt{n_{core}^2 \sin^2 \theta - n_{clad}^2}} \quad (10)$$

2.1.3 Microfiber

Optical microfibers or even nanofibers show great potentials in developing highly integrated devices with small footprints. They are also recognized by their strong evanescent field that facilitates highly efficient evanescent coupling in various optical components and devices including optical resonators, lasers and sensors [85]. Microfibers are mostly fabricated by tapering a standard single-mode optical fiber. As shown in Figure 2-4, a tapered optical fiber consists of a narrow waist with a constant thin diameter in the middle connected by two conical taper transitions. The first and the second transitions can be called “downtaper” and “uptaper” respectively [86]. The shape of downtaper and uptaper influences the mode propagation and coupling. For an adiabatically tapered optical fiber, of which the taper transitions are sufficiently gradual to minimize transmission loss, the guided core mode is gradually compressed due to the shrink of core diameter. After the core diameter is small enough, the core mode can no longer be confined within fiber core, but guided by the fiber cladding-air interface. Due to the high refractive index difference between fiber cladding and air, the

Figure 2-4. The propagation of the fundamental core mode through a tapered optical fiber [86].

propagating light is tightly confined in the microfiber waist (Figure 2-4). At the uptaper, the mode transformation process is reversed [87].

To realize adiabaticity, the structural parameters of taper transition should be properly designed. Figure 2-5 shows the structural parameters of taper transition. Let z represent the position along the longitude of tapered fiber, and $\rho(z)$ represent the fiber core radius at position z . Then the local taper angle $\Omega(z)$ is:

$$\Omega(z) = \tan^{-1} \left| \frac{d\rho}{dz} \right| \quad (11)$$

As $\Omega(z) \ll 1$ in practice, then the length of taper transition can be estimated as:

$$z_t \approx \frac{\rho}{\Omega} \quad (12)$$

The fundamental LP_{01} mode tends to couple to a higher order mode with the same azimuthal symmetry and the closest propagation constant β (i.e. LP_{02} mode). Let β_1 and β_2 be the propagation constants of LP_{01} and LP_{02} modes respectively. The coupling length, which is also called the beat length z_b , between the two modes is calculated as:

$$z_b = \frac{2\pi}{\beta_1 - \beta_2} \quad (13)$$

Figure 2-5. The structural parameters of a taper transition [88].

If the condition $z_t \gg z_b$ is satisfied everywhere along the microfiber, the mode coupling is negligible and the taper is considered as adiabatic [88]. Otherwise, the taper is nonadiabatic. In a nonadiabatic tapered fiber, the fundamental core mode LP_{01}^{core} couples to fundamental cladding mode LP_{01}^{clad} and higher order cladding modes

LP_{0m}^{clad} at the downtaper [89,90]. Those cladding modes propagate through the uniform central waist and couple back to the fiber core at uptaper, thus form a Mach–Zehnder interferometer (MZI). The phase difference $\Delta\Phi$ between two cladding modes can be found by $2\pi\Delta n_{eff}^m L/\lambda$, where Δn_{eff}^m effective refractive index difference, and L is the interference length. Such tapered fiber based MZI results in modal interference spectrum [90,91].

The microfibers are mostly fabricated by the heat-and-pull method. Figure 2-6 illustrates the fabrication setup. A standard optical fiber is stripped to expose the silica fiber cladding and fixed between two translation stages. A heat source with temperature at least 1700 °C (e.g. a small flame) is placed in the middle to soften the silica fiber so that the fiber can be stretched. To obtain a uniform central waist diameter, the heat source is scanned repeatedly over several centimeters at a constant speed which is the so-called flame brush technique [86,92].

Figure 2-6. The setup for fabricating an adiabatic tapered optical fiber [86].

2.2 Fiber-Optic Magnetic Field Sensors

2.2.1 Magnetic Fluid

Magnetic fluid is a synthesized liquids-like material that becomes strongly magnetized under magnetic field. It is a colloidal fluid consisting of nano-scaled magnetic particles such as magnetite (Fe_3O_4), nickel (Ni) and cobalt (Co) [93]. To prevent the magnetic nanoparticles from aggregation driven by van der Waals force, each particle is coated with 2-3 nm thick surfactant, which is generally fatty acid. Hence with no presence of

magnetic field, the surfactant-coated nanoparticles evenly suspend in the carrier liquid. The most common magnetic particle is Fe_3O_4 with a diameter of ~ 10 nm [94]. Figure 2-7 illustrates the nanostructure of magnetic fluid particles.

Figure 2-7. Nanostructure of magnetic fluid particles [94].

The remarkable magneto-optic effects such as birefringence, tunable refractive index and the Faraday Effect delivered by magnetic fluid have attracted much research attention especially in sensing applications. Although Fe_3O_4 is ferromagnetic in bulk volume, it becomes superparamagnetic when the size reduces to nano-scale and shows no hysteresis property unless it is applied with strong magnetic field beyond its threshold field [93,95–97]. When the superparamagnetic magnetic fluid is subjected to a magnetic field below the threshold, it undergoes phase transitions that lead to the variation of optical properties. The magnetic nanoparticles, which can be treated as permanent magnets, tend to align the magnetic moment with magnetic field direction and aggregate to chain-like clusters [98,99]. The phase transitions under gradually increased magnetic field strength have been deeply investigated by Islam *et al.* [100] and they are shown in Figure 2-8. As the applied magnetic field strength gradually increases, the magnetic nanoparticles gradually cluster due to the dipole-dipole interaction to form short needles in alignment with the field direction (Figure 2-8 (a)). As the field strength further increases, more magnetic nanoparticles are magnetized to aggregate and some short needles elongate into columns (Figure 2-8 (b)). Finally, all the clusters of nanoparticles evolve into long columns along the magnetic field direction, which is a phase called “columnar glassy” (Figure 2-8 (c)). Figure 2-8 (d)

shows the top view of the columnar phase of magnetic fluid. When the magnetic field reaches certain strength, the repulsive forces among the columnar clusters lead to a hexagonal arrangement of those columns which is relatively stable. The hexagonal structure of columnar clusters induced by relatively high magnetic field strength has also been reported by Yang *et al.* [101]. As shown in Figure 2-9 (a), the side view of columnar phase is a one-dimensional periodic distribution of parallel columns. The top view, which is shown in Figure 2-9 (b), shows a hexagonal pattern similar to that of Figure 2-8 (d).

Figure 2-8. The magnetic nanoparticles gradually aggregate into (a) short needles, (b) columns mixed with short needles and (c) columnar glassy as the magnetic field strengthens; (d) The top view of hexagonally arranged columns [102].

Figure 2-9. (a) The side view and (b) the top view of the hexagonal columnar phase of magnetic fluid [101].

The agglomeration of magnetic nanoparticles driven by applied magnetic field increases the refractive index of magnetic fluid. Chen *et al.* studied the relation between the refractive index of magnetic fluid, n_{MF} , and magnetic field intensity, and they found that the $n_{MF} - H$ curve fits well with the Langevin function [103]. As long as the Langevin function applies, the refractive index of magnetic fluid increases with enhancing magnetic field. Similar trends are also observed in other studies [104–106].

2.2.2 Magnetic Fluid and Optical Fiber Based Magnetic Sensors

The variation of the refractive index during phase transitions makes magnetic fluid a promising material for optical based magnetic field sensors. In recent years, fiber-optic magnetic field sensors have been intensively investigated owing to their compactness, flexibility and remote sensing capability. Numerous structures of optical fiber have been proposed for magnetic field sensing. Due to the differences in employed fiber structures and the types of magnetic fluid, the sensitivities and measuring thresholds vary from one to another. The sensitivities of optical fiber based magnetic field sensors can be categorized in terms of sensing parameters, such as wavelength shift, transmission intensity and output power. Wang *et al.* proposed a single-mode-multimode-single-mode fiber based magnetic field sensor by monitoring the wavelength shift. They achieved a sensitivity of -16.86 pm/Oe [107]. Gao *et al.* monitored the variation of output power of PCF under magnetic field and obtained a sensitivity of 0.011 $\mu\text{W/Oe}$ [55]. Zheng *et al.* used a TFBG to detect the phase transitions of magnetic fluid and achieved a sensitivity of 147 nW/Oe [57]. Various researches deliver sensitivities in terms of transmission intensity (e.g. dB/mT). For instances, Lin *et al.* proposed to adopt multimode interferometer to sense magnetic field and their sensitivity was -0.1939 dB/mT [56]. Tapered fiber based magnetic field sensor has been demonstrated by Miao *et al.*, they achieved a sensitivity of 0.13056 dB/Oe [58]. Chen *et al.* reported a sensitivity of 0.748 dB/mT achieved by employing the single-mode-multimode-single-mode fiber structure [108].

Table 1 compares the magnetic fluid and optical fiber based magnetic field sensors with the common non-fiber based magnetic field sensors [109–113]. Different types of magnetic field sensors have their own measurement ranges and resolutions thereby can be suitable for different applications. For instance, search coil is favored by the simple configuration and the broadest measurement range. However, it cannot detect static magnetic fields since its working principle is based on the Faraday's law of induction [109,110]. The most sensitive low-field sensor is superconducting quantum interference device (SQUID) which is mainly used in astronomy, geological and medical applications. However, SQUID is also the most expensive magnetic field sensor as it has to be operated at very low temperature even near absolute zero [109,110,112]. Hall effect sensors are the most widely applied magnetic field sensors due to their broad measurement range, cost effectiveness and high accuracy especially for high field strength of > 1 T. The measurement ranges of the aforementioned fiber-optic magnetic field sensors fall within 0.1-60 mT, which overlap with the lower range of Hall effect sensors (Table 1). Besides achieving high degree of integration with the magnetic nanoparticles assisted optomagnetic biosensors, it would be more advantageous if the fiber-optic magnetic field sensors can provide comparable resolutions to the commonly used Hall effect sensors. However, the resolutions of the great majority of previously studied fiber-optic magnetic field sensors are still uncompetitive. As discussed in Section 2.1.1, LPG provides merits of high sensitivity to ambient refractive index, simple configuration and multi-parameter measurement [62,114,115], which has not been proposed for magnetic field sensing and we believe it would bring better sensing performance.

Table 1. Comparison of common magnetic field sensing mechanisms.

Mechanism	Range (mT)	Resolution (nT)	Pros	Cons
Search coil	10^{-10} - 10^6	Variable	Broadest measurement range	Unable to detect static fields
SQUID	10^{-9} -0.1	10^{-4}	Highest sensitivity	Operating below the superconducting transition temperature; Most expensive
Fluxgate	10^{-4} -0.5	0.1	Versatile; Low power consumption	Expensive
Magneto-resistance	10^{-3} -5	10	Low cost; Good temperature stability	Demagnetization/destroyed by large magnetic fields

Hall effect	$0.1-3 \times 10^4$	100	High yield; Reliable for large field measurement (> 1 T)	Nonlinearity
Optical fibers	0.1-60	Variable	Remote sensing; Flexibility; Miniaturization	Temperature sensitive

2.3 Surface Plasmon Resonances

SPR is the collective oscillations of free electrons at the interface between a metal and a dielectric medium [116]. There are two distinct forms of SPR: propagating SPR which is the term “SPR” normally refers to and localized SPR (LSPR) [15,117]. The theories behind these two prominent biosensing techniques and the state-of-the-art SPR and LSPR biosensors as well as their prospects will be discussed in this section.

2.3.1 Drude Model

To understand the interaction between light and metals or heavily doped semiconductors that are abundant with free conduction electrons, it is fundamental to understand the Drude model, which is a classical conductivity model widely adopted and proven to be accurate for the optical properties of electron-rich materials. Based on the assumption that the free electrons in conduction band are independent and do not interact with each other, the complex dielectric function is given by [118]:

$$\varepsilon(\omega) = \varepsilon' + i\varepsilon'' = 1 - \frac{\omega_p^2}{\omega(\omega + i/\tau)} \quad (14)$$

where τ is the relaxation time which is inversely proportional to the electron density, N [119]. The inverse of τ , $1/\tau$, is defined as the collision frequency γ . γ characterizes the damping of electron oscillations in response to electromagnetic field and numerically equals to the linewidth of the plasmon resonance band [120]. ω_p is the bulk plasma frequency which is the characteristic frequency of conduction electrons and it is defined as:

$$\omega_p = \sqrt{\frac{Ne^2}{\varepsilon_0 m^*}} \quad (15)$$

where ε_0 is the free space permittivity, and m^* is the effective mass of free electrons. Expanded from Equation (14), the real part and the imaginary part of $\varepsilon(\omega)$ can be respectively expressed as:

$$\varepsilon' = 1 - \frac{\omega_p^2}{(\omega^2 + \gamma^2)} \quad (16)$$

$$\varepsilon'' = \frac{\omega_p^2 \gamma}{(\omega^2 + \gamma^2)\omega} \quad (17)$$

Since the Drude model only takes the conduction electrons into consideration, offset often occurs between the theoretical model and experimental observation. An effective revision is to introduce the contribution from the positive ion core by adding a constant to the real part of dielectric function, ε' [121]. Then the overall expression becomes:

$$\varepsilon(\omega) = \varepsilon_b - \frac{\omega_p^2}{(\omega^2 + \gamma^2)} + i \frac{\omega_p^2 \gamma}{(\omega^2 + \gamma^2)\omega} \quad (18)$$

where ε_b denotes the background permittivity which is the response from core polarization [34,122]. The plasmon resonance frequency is determined by:

$$\omega_{sp} = \sqrt{\frac{\omega_p^2}{1 + 2\varepsilon_{dielectric}} - \gamma^2} \quad (19)$$

where $\varepsilon_{dielectric}$ represents the dielectric constant of ambient dielectric medium.

2.3.2 SPR Theory

SPR is the coupling between the evanescent electromagnetic wave and the propagating surface plasmon wave, which is also called SPP [123]. SPP is a TM-polarized electromagnetic wave that propagates parallel to the interface between the metal film and dielectric medium. Figure 2-10 illustrates the transverse electromagnetic field of SPP. SPP is strongest at the thin metal surface and exponentially decays into the dielectric medium.

Figure 2-10. The schematic illustration of propagating SPR [124].

Figure 2-11 (a) illustrates the conventional SPR configuration, a Kretschmann-Raether silica prism coated with a thin noble metal film beyond which is a semi-infinite dielectric medium. SPR occurs when the phase matching condition is satisfied [123,125,126]. By solving the Maxwell equations for the interface of a semi-infinite metal layer and a dielectric medium, the propagation constant of SPP is given by [126]:

$$K_{sp} = \frac{\omega}{c} \sqrt{\frac{\epsilon_{metal}\epsilon_{dielectric}}{\epsilon_{metal} + \epsilon_{dielectric}}} \quad (20)$$

where ω is the frequency of the TM-polarized incident light, and c is the light velocity. ϵ_{metal} and $\epsilon_{dielectric}$ are the dielectric constants of the metal layer and the dielectric medium respectively. The function curve of K_{sp} is plotted in Figure 2-11 (b). The propagation constant of light that transmits in dielectric medium can be expressed as [126]:

$$k_s = \frac{\omega}{c} \sqrt{\epsilon_{dielectric}} \quad (21)$$

It can be seen from Figure 2-11 (b) that K_{sp} will always be larger than k_s regardless of light frequency. Therefore, there could never be phase matching between SPP and direct light in dielectric medium. The propagation constant of the evanescent wave of the total reflected incident light at the interface between the prism and dielectric medium (air in this case) is:

$$K_{ev} = \frac{\omega}{c} \sqrt{\epsilon_{prism}} \sin\theta \quad (22)$$

where ϵ_{prism} is the dielectric constant of silica. θ is the angle of light incidence. The function curves in Figure 2-11 (b) indicate that K_{ev} intercepts with $K_{sp} (M/D)$, which is the propagation constant of SPP at the interface between metal layer and dielectric medium, at a certain frequency of light. On the other hand, the propagation constant of SPP at the interface between prism and metal layer, $K_{sp} (M/P)$, will never cross the function curve of K_{ev} . This implies that SPR could only be excited on the metal-dielectric interface. Therefore, it can be concluded that the phase matching condition of SPR is the equating of propagation constants of the evanescent wave of total reflected incident light at the prism-metal interface and the SPP at the metal-dielectric interface:

$$\frac{\omega}{c} \sqrt{\epsilon_{prism}} \sin(\theta_{res}) = \frac{\omega}{c} \sqrt{\frac{\epsilon_{metal} \epsilon_{dielectric}}{\epsilon_{metal} + \epsilon_{dielectric}}} \quad (23)$$

where θ_{res} the resonant incident angle at which the phase matching condition is satisfied.

Figure 2-11. (a) The schematic illustration of Kretschmann configuration; (b) The plots of propagation constants of direct light in dielectric medium (k_s), the evanescent wave of total refractive incident beam at the prism-metal interface ($K_{ev} = k_p \sin \theta$), the evanescent wave of direct light in prism (k_p), the SPP propagating at the metal-dielectric interface ($K_{sp}(M/D)$) and the SPP propagating at the metal-prism interface ($K_{sp}(M/P)$) [123].

Since the right expression of Equation (23) is obtained by solving the Maxwell equations at the interface of an assumptive semi-infinite metal layer and a semi-infinite dielectric medium. Considering the real situation where the metal layer thickness is

finite and the high refractive index the silica prism affects K_{sp} (M/D), the phase matching condition can be more precisely expressed as [127]:

$$\frac{\omega}{c} \sqrt{\epsilon_{prism}} \sin(\theta_{res}) = \frac{\omega}{c} \sqrt{\frac{\epsilon_{metal} \epsilon_{dielectric}}{\epsilon_{metal} + \epsilon_{dielectric}}} + \Delta\beta \quad (24)$$

The second term, $\Delta\beta$, of the right expression of Equation (24) denotes the effects of finite metal layer thickness and high refractive index of prism. $\Delta\beta$ decreases as the metal layer thickness increases.

In most fiber-optic SPR, the wavelength interrogation method is employed. The sensitivity of wavelength interrogation, S_λ (nm/RIU), is the shift of resonant wavelength divided by the change of analyte refractive index [127]:

$$S_\lambda = \frac{\delta\lambda}{\delta n_a} = \frac{n_p \epsilon'_{metal}}{\frac{n_p}{\lambda} n_a^3 \left(\frac{1}{\epsilon'_{metal}} - 1 \right) + \frac{dn_p}{d\lambda} n_a (n_a^2 + \epsilon'_{metal})} \quad (25)$$

Therefore, the sensitivity of wavelength interrogation is determined by n_a , the refractive index of analyte, and n_p , the refractive index of prism, and also ϵ'_{metal} , the real part of the dielectric constant of metal layer.

2.3.3 LSPR Theory

When light interacts with a noble metal nanoparticle that is smaller than the wavelength, the excited surface plasmon is nonpropagating due to the restriction of particle size, thereby it is called localized SPR. LSPR can be treated as the oscillation of the electron

Figure 2-12. The schematic illustration of propagating SPR [129].

cloud with respect to the positive ionic core induced by the incident electric field (Figure 2-12) [128,129]. The electron oscillation is strongest when the oscillation frequency resonances with the incident light frequency. To understand the LSPR behaviors in depth, Mie theory describing the scattering and absorption of light by a nanoparticle with diameter much smaller than wavelength ($d \ll \lambda$) is a proper model.

Based on the Mie theory, the extinction cross-section of a homogeneous conducting spherical nanoparticle can be deduced as:

$$\sigma_{ext} = 9 \left(\frac{\omega}{c} \right) (\varepsilon_{dielectric})^{\frac{3}{2}} V \frac{\varepsilon_{metal}''}{(\varepsilon_{metal}' + 2\varepsilon_{dielectric})^2 + (\varepsilon_{metal}'')^2} \quad (26)$$

where V is the volume of spherical nanoparticle. It can be seen from Equation (26) that the extinction cross-section reaches maximum when the condition $\varepsilon_{metal}' = -2\varepsilon_{dielectric}$ is met. At visible or NIR frequencies, $\gamma \ll \omega_p$. Then according to Equation (16), we can simplify the real part of dielectric function of noble metal to:

$$\varepsilon_{metal}' = 1 - \frac{\omega_p^2}{\omega^2} \quad (27)$$

At the oscillations resonance where $\varepsilon_{metal}' = -2\varepsilon_{dielectric}$, we can obtain the expression of LSPR resonant frequency:

$$\omega_{LSPR} = \frac{\omega_p}{\sqrt{2\varepsilon_{dielectric} + 1}} \quad (28)$$

Taking $\varepsilon_{dielectric} = n_{dielectric}^2$ for dielectric medium, the LSPR resonant wavelength is impacted by the ambient refractive index as follows:

$$\lambda_{LSPR} = \lambda_p \sqrt{2n_{dielectric}^2 + 1} \quad (29)$$

Based on the aforementioned theories, LSPR can be supported by any metal, alloy or semiconductor with proper complex dielectric constant. Although copper, aluminum and zinc oxide nanostructures have been investigated for LSPR sensing, gold and silver plasmonic nanosensors are overwhelmingly studied and employed. This is due to the poor resistance of non-noble metals to corrosion and oxidation that depresses the plasmonic sensitivity. Hence benefited from their chemical stability, AuNPs are most widely applied in complex biological sensing [130].

The most popular conventional synthesis method of AuNPs was proposed by Turkevich in 1951 [131]. In this method, chloroauric acid (HAuCl_4) solution is heated to boiling point and added with sodium citrate under good mechanical stirring. The citrate functions as both stabilizing and reducing agent [132]. Figure 2-13 shows reaction process of reducing gold ions to gold atoms capped with citrate in Turkevich

Figure 2-13. The formation of AuNPs using the Turkevich method [131].

Figure 2-14. The colors of aqueous solutions of gold nanospheres with increasing particle size. The particle sizes shown in (A-E) vary from 4 nm to 40 nm. All red bars represent 100 nm [133].

method. The synthesized aqueous AuNPs solutions possess peak extinctions at visible frequencies. The size of AuNPs impacts the LSPR behaviors. As shown in Figure 2-14, the variation of particle size leads to the change of solution colors, indicating the shift of resonant frequencies [133]. All the red bars in Figure 2-14 represent 100 nm. It has been reported that very small AuNPs with diameter less 5 nm show no LSPR absorption. For AuNPs of 5-50 nm, their sharp LSPR resonance peaks range from 520 nm to 530 nm. As the particle size grows larger, the absorption band undergoes redshift meanwhile broadens [129]. Figure 2-15 shows the variation of LSPR absorption band along with the increasing of AuNPs size. Unlike SPP, the inducement of LSPR is not limited to total reflected TM-polarized light. It can be induced directly by the incident electromagnetic field [117]. Therefore, the configurations of LSPR sensors include not only prism, but also direct extinction measurements [134,135], lab-on-a-chip platforms [136–138], and certainly optical fibers [2,139–141].

Figure 2-15. The redshift of LSPR peak as the AuNP size increases from 9 nm to 99 nm [142].

2.3.4 Fiber-Optic SPR/LSPR Biosensors

Compared with the Kretschmann-Raether prism, solution-based extinction measurement and lab-on-a-chip platform, optical fiber based SPR/LSPR is favored by its miniaturization, flexibility, remote and in situ sensing capability and low

consumption of clinic samples. The phase matching condition also applies to fiber-optic SPR, except that the incident angle varies from the critical angle to 90° in optical fibers [123]. At the phase matching point, the effective refractive index of core mode equals to that of surface plasmon mode [143]. The attenuation of the fiber core mode L_c (dB m^{-1}) is given by [144,145]:

$$\frac{40\pi}{\ln(10)\lambda} \text{Im}(n_{eff}) = 8.686 \times k_0 \text{Im}(n_{eff}) \quad (30)$$

where k_0 is the wave vector in free space, and $\text{Im}(n_{eff})$ is the imaginary part of the core mode effective refractive index. The resonant dip on fiber-optic SPR transmission spectrum corresponds to the largest transmission loss of the core mode.

Since SPR is generated by the coupling between the evanescent field of the total reflected light in silica prism and SPP at the metal-dielectric interface and LSPR is the collective oscillations of electron clouds in resonance with the incident light, the exposure of relatively strong evanescent field is crucial in the design of fiber-optic SPR/LSPR sensor. So far, many optical fiber structures have been proven to be feasible for SPR/LSPR sensing. They can mainly be classified into 3 categories: grating-

Figure 2-16. SPR/LSPR sensors based on (a) LPG [147]; (b) TFBG [175]; (c) tapered fiber with core diameter (ρ) of $50 \mu\text{m}$ and length of sensing region (L) of 2 mm [8]; (d) side-polished fiber [8]; (e) U-shaped fiber [146]; (f) patterned fiber end face [146].

assisted fibers, geometry-modified fibers and microstructured fibers [146]. Grating-assisted fibers are basically LPG and TFBG [147–149], since they couple the core mode into cladding modes of which the mode effective indices are modulated by surrounding refractive index. Common geometry-modified fibers are unclad fiber of which the fiber cladding is etched [150–152], side-polished fiber [153–155], tapered fiber [156,157], U-shaped fiber [9,158], etc. Figure 2-16 illustrates some representative configurations of SPR/LSPR biosensors based on grating-assisted and geometry-modified optical fibers.

MOFs significantly improve the integration of SPR/LSPR sensor as the cladding air holes could be used as microfluidic channels infiltrated with gas or liquid analyte [144]. The dimension of the fiber core of MOF can be made very small without

Figure 2-17. Representative SPR/LSPR biosensors based on (a) PCF with hexagonal arranged air holes [12]; (b) PCF with liquid core [159]; (c) suspended-core MOF [163]; (d) semicircular channel MOF [166]; (e) semicircular channel MOF [165]; (f) exposed core MOF [168]; (g) exposed core grapefruit MOF [169]; (h) H-shaped MOF [170]. A : the pitch of photonic crystal air holes.

compromising the flexibility and the robustness. The strong evanescent field owing to the small core dimension effectively interacts with the infiltrated analyte in cladding air holes, thereby strong plasmon-matter interaction with a long interaction distance could be achieved. Numerous MOF structures have been proposed for SPR/LSPR biosensors. For instances, PCFs with hexagonal arranged air holes are the most common MOF structures. The evanescent field of guided core mode interacts with the thin gold film selectively coated on the inner wall of peripheral holes and excites SPP that is sensitive to the RI of infiltrated analyte (Figure 2-17 (a)). The hollow core of PCF can also be coated with thin gold film and serves as a microfluidic channel as shown in Figure 2-17 (b) [159]. Since SPP can only be excited on the small portion of cylindrical thin gold film that perpendicular to the core mode polarization direction, the hexagonal MOFs can hardly achieve a sensitivity higher than 2000 nm/RIU due to limited light-matter interaction [159–162]. Therefore, enhancing the interaction between core mode and thin gold film is the prime purpose in many MOF structural designs. One solution is to decrease the fiber core dimension. For instance, suspended-core fiber as shown in Figure 2-17 (c) is favored due to its small solid core dimension and large cladding air holes. Thereby the strong evanescent field of guided light effectively excites surface plasmons of AuNPs or thin gold films decorated in the vicinity of fiber core [163]. MOF with semicircular channels is another popular solution for enhancing light-matter interaction [159,164–167]. As illustrated in Figure 2-17 (d) and (e), the semicircular channels enlarge the interaction area between guided core mode and thin gold layer. Meanwhile, the large semicircular channels facilitate easy liquid infiltration. Such approaches can effectively improve the sensitivity to 3000 nm/RIU and above. For easy deposition of thin metal film or nanoparticles, exposed core MOFs which are the modified structures of commercially available suspended-core MOFs and grapefruit MOFs are promising solutions (Figure 2-17 (f) and (g)) [168,169]. Another open-structured MOF, H-shaped fiber, is proposed for high sensitivity, easy access to thin fiber core and free flow of analyte (Figure 2-17 (h)) [170]. It can be seen from Figure 2-17 that most MOF designs are asymmetric in two orthogonal polarization directions (x- and y-polarization) when achieving higher sensitivity or easy deposition of plasmonic materials, phase birefringence commonly exists in MOF based SPR/LSPR sensors. Due to the cylindrical geometry of MOF air

holes, both two orthogonal core mode polarizations can excite SPP. The phase birefringence induces the offset between the resonant wavelengths of two orthogonal polarizations based on Equation (24). The polarization that is perpendicular to the larger portion of inner wall thin metal film is normally monitored for plasmonic sensing. However, external perturbations such as pressure, bending or twisting and inaccurate input polarization would lead to the existence of undesired polarization thereby a shifted resonant wavelength. To address this issue, a polarization-maintaining MOF would be a promising solution to suppress the effects of polarization crosstalk.

2.4 Nanomaterials Based Plasmonic Biosensing

Optical fiber based SPR/LSPR has been employed in various practical biosensing applications such as the detections of bacteria [171], food poisoning [172,173] and proteins [174–177]. Surface functionalization of thin gold films and AuNPs is often required for targeting a specific biomolecule. In addition, despite the inert nature of gold, surface functionalization of AuNPs to diminish cytotoxicity should also be taken into consideration [178,179]. Self-assembled monolayer (SAM) is an extensively applied surface functionalization strategy [180]. Since gold possesses high reactivity with thiols (-SH), molecules with thiol groups can form highly ordered SAM via strong gold-thiolate bonds (Au-S) (Figure 2-18) [41,180]. Figure 2-18 (a) shows a typical surface functionalization strategy of thin gold film for SPR immunosensor [40]. A

Figure 2-18 (a) A typical functionalization strategy of SPR immunosensor [40]. EDC/NHS: 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide/N-Hydroxysuccinimide. CNT: carbon nanotube. (b) AuNPs can form conjugation with numerous functional molecules mostly via gold-thiolate bonds [41].

SAM of 11-Mercaptoundecanoic acid (MUA) is formed on gold film via Au-S bonds. The MUA monolayer adsorbs specific antigens which immobilize the corresponding antibodies in the analyte. The formation of the antigen-antibody complexes at the metal film surface varies the local refractive index which modulates the propagation constant of SPP, thereby changes the phase matching condition. For AuNPs, surface functionalization strategies like ligand substitution, polymer deposition, biomolecule coating, etc. have been proven effective to meet goals of both biocompatibility and specific molecular recognition (Figure 2-18 (b)) [178–181].

Besides the specific biomolecule recognition, another consideration is the influence of surface functionalization on plasmonic sensitivity. As the strength of surface plasmons exponentially decays from the interfaces of thin gold film and AuNPs, the closer the captured biomolecules to the interface, the higher the plasmonic sensitivity would be [117,128,182]. A study proves that the target biomolecules binding activity is observable only if the SAM layer is kept within 20 nm [128]. Another study compares the sensitivities corresponding to two functionalization strategies with different recognition layer thickness [182]. One strategy is to modify AuNPs surface with a layer of 4.24 nm antibody. The other is to functionalize a layer of peptide as thin as 0.96 nm. It shows that keeping the surface functionalization within 1 nm significantly improves the sensitivity and the LOD of the LSPR biosensor. Based on the distance-dependent plasmonic sensitivity and the requirement of biomolecule recognition, the recent emergence of 2D materials and supramolecular chemistry has attracted great attention. In our works, 2D materials such as graphene and few-layer MoO_3 are employed as both the booster of plasmon-matter interaction and the biointerface in highly integrated fiber-optic plasmonic biosensors. Also, CD, a representative supramolecule is adopted as both reducing and capping agent in one-step synthesis of biocompatible AuNPs and also the biointerface for molecular recognition.

2.4.1 Graphene Enhanced Plasmonic Biosensing

Ever since its discovery in 2004, graphene has always been a hot research spot owing to its remarkable structural, chemical, electrical, mechanical and optical properties. For instances, it possesses large specific surface area of $2630 \text{ m}^2\text{g}^{-1}$, high transparency of 97.3%, high carrier mobility of $2 \times 10^5 \text{ cm}^2\text{V}^{-1}\text{s}^{-1}$, exceptionally large thermal conductivity of $5000 \text{ Wm}^{-1}\text{K}^{-1}$ [183]. Therefore, graphene plays a key role in improving performance of electrochemical, nanoelectronic and optical sensors in biochemical applications [184].

Graphene is a free-standing 2D carbon crystal arranged in honeycomb lattice. Carbon atoms in graphene are connected with each other via sp^2 -hybridized bonding (Figure 2-19 (a)) [185]. The $2p_z$ orbitals of two adjacent carbon atoms evolve into delocalized π (bonding) band which forms the valence band (VB), and π^* (anti-bonding) band which forms the conduction band (CB) [186]. Each carbon atom provides one π electron to the lower VB and the upper CB is kept empty [16]. The VB and CB are degenerate at the Dirac point at each corner of the Brillouin zone (Figure 2-19 (b)). Therefore, pristine graphene can be treated as a semiconductor or semimetal with zero bandgap.

Figure 2-19. (a) The hexagonal lattice of graphene. Each carbon atom is sp^2 hybridized [185]. (b) The band structures of graphene. VB and CB touch at the conical point [16].

Since monolayer of graphene is only one-atom thick ($\sim 0.34 \text{ nm}$), its white light adsorption is only 2.3% and its reflectivity is negligible. The light absorption proportionally increases with the number of graphene layers [187]. The complex refractive index of graphene within the visible range is given by [188]:

$$n_{\text{graphene}} = 3.0 + i \frac{C}{3} \lambda \quad (31)$$

where $C = 5.446 \mu\text{m}^{-1}$ and λ is the vacuum wavelength. The high optical transparency, the broadband plasmonic properties and the extremely high surface-to-volume ratio allow graphene to be well integrated into optical sensors as a sensitive film [189]. When modeling the electromagnetic properties of graphene, the one-atom thick layer can be equivalent to a conductivity surface [190,191]. Assuming that the single graphene layer is laterally infinite and no external magnetic field is applied, the surface conductivity of graphene arises from intraband contribution $\sigma_{\text{intra}}(\omega, \mu_c, \Gamma, T)$ and interband contribution $\sigma_{\text{inter}}(\omega, \mu_c, \Gamma, T)$:

$$\begin{aligned} \sigma(\omega, \mu_c, \Gamma, T) &= \sigma_{\text{intra}}(\omega, \mu_c, \Gamma, T) + \sigma_{\text{inter}}(\omega, \mu_c, \Gamma, T) = \\ &= \frac{je^2(\omega - j2\Gamma)}{\pi\hbar^2} \left[\frac{1}{(\omega - j2\Gamma)^2} \int_0^\infty \varepsilon \left(\frac{\partial f_d(\varepsilon)}{\partial \varepsilon} - \frac{\partial f_d(-\varepsilon)}{\partial \varepsilon} \right) d\varepsilon - \int_0^\infty \frac{f_d(-\varepsilon) - f_d(\varepsilon)}{(\omega - j2\Gamma)^2 - 4(\varepsilon/\hbar)^2} d\varepsilon \right] \end{aligned} \quad (32)$$

where μ_c is chemical potential, Γ is electron scattering rate, $\hbar$ is the reduced Planck's constant that equals to $h/2\pi$, ε denotes energy and $f_d(\varepsilon)$ is Fermi-Dirac Distribution Function which is given by:

$$f_d(\varepsilon) = \left(e^{\frac{\varepsilon - \mu_c}{k_B T}} + 1 \right)^{-1} \quad (33)$$

where k_B is Boltzmann's constant. The first integral in Equation (32) associates with the intraband contribution and the second integral corresponds to the interband contribution.

Propagating and localized SPR can be sustained by graphene and patterned graphene structures respectively in MIR and terahertz frequencies [16,18–20]. One huge advantage of graphene is the tunability of SPR by adjusting the carrier density by doping and electrical gating [16]. Coupled with the unprecedented field confinement and good biocompatibility, graphene brings exciting prospects for highly integrated biosensing in MIR range [20]. However, graphene plasmons in MIR range are hardly compatible with today's well developed optical communication system in visible and NIR frequencies. Intensive research efforts have been focused on constructing graphene/metal hybrid plasmonic structure to employ graphene as an enhancement to conventional SPR as well as a functional layer. When graphene is in contact with a

Figure 2-20. Schematic illustration of the energy bands of graphene and metal (a) before and (b) after they are in contact. Φ_1 : the work function of metal. Φ_G : the work function of graphene [192].

metal, the difference between the work functions of graphene and metal leads to the transfer of charges thereby the doping of graphene [183]. Figure 2-20 illustrates the electrons flow when graphene seamlessly contacts with a metal with a higher work function [192]. Graphene has a work function of 4.5 eV. When it contacts with a metal of which the work function is higher than 5.4 eV (e.g. the work function of gold is 5.54 eV), electrons transfer from graphene to the surface of metal to equilibrate the Fermi levels [193,194]. Hence the graphene becomes p-type doped. The charge transfer increases the electron density at metal surface, thereby enhances the strength of SPP [195].

In recent years, numerous studies have proven the great potentials of applying 2D material/metal hybrid film-like architectures to the conventional Kretschmann configuration based SPR sensor for sensitivity enhancement. Hybrid plasmonic sensing platforms such as monolayer graphene/gold [196,197], multilayer graphene/gold [21–24], graphene oxide/gold [25–29], reduced graphene oxide/gold [198], graphene-MoS₂/gold [30–32], etc. have been proposed and investigated. Figure 2-21 shows some representative configurations of 2D material/metal hybrid plasmonic biosensing platforms. One significant motivation is that graphene strengthens the intensity of SPP on the metal surface. This is due to the transport of electrons from graphene to gold when the two materials are in contact as explained above. Besides the SPP

Figure 2-21. Hybrid plasmonic architectures based on (a) monolayer graphene/gold [197]; (b) multilayer graphene/Py/gold [21]; (c) graphene oxide/gold [29]; (d) graphene-MoS₂/gold [31].

enhancement, graphene provides another attractive advantage to biosensing. Profited from its honeycomb lattice arrangement of carbon atoms, graphene forms π -stacking interaction with aromatic rings which commonly exist in biomolecules [199]. Hence the biomolecules could be stably immobilized on graphene surface and vary the local refractive index that intimates to the SPP propagation surface. Moreover, as aforementioned, owing the evanescent nature of SPP at the perpendicular direction to the metal-dielectric interface, the sensitivity of SPR decreases with the increasing thickness of surface functionalization [200]. The one-atom thickness of graphene offers huge superiority over conventional surface functionalization strategies.

Although the mechanism of how graphene enhances the Kretschmann prism based SPR biosensing has been widely investigated, most of these researches are preliminary theoretical analysis. In addition, a systematic study of integrating such 2D material/metal hybrid structure with miniaturized and flexible optical fibers to achieve highly integrated and highly sensitive biosensing remains blank.

2.4.2 TMO Based Plasmonic Biosensing

The in situ plasmonic tunability and the exceptional field confinement bring 2D materials extensive research attention. Also, 2D materials possess remarkable surface-to-volume ratio that facilitates highly efficient target biomolecules immobilization resulting in enhanced plasmon-matter interaction. Considering the surface plasmons of common 2D materials like graphene and MX_2 intrinsically locate within MIR or terahertz regions which are not accessible to the frequently used optical window, in recent years heavily doped ultrathin TMOs have been studied as an alternative class of plasmonic 2D materials aiming for the visible and NIR frequencies [34,35,201,202]. Profited from their unique character of outer-d valence electrons, TMOs are able to achieve sufficient free carrier concentrations for surface plasmons via ionic intercalation. Tailoring the ionic intercalation process can introduce aliovalent

Figure 2-22. Free electrons are doped to TMOs via oxygen vacancies. (a) The pristine TMO lattice. (b) Two electrons are left in the lattice defect after the removal of an oxygen atom. Yellow spheres: metal cations. Red spheres: oxygen anions [203].

Figure 2-23. The polymorphs of (a) α -MoO₃ (b) β -MoO₃ (c) h-MoO₃ [205].

heteroatoms or lattice vacancies to tune the carrier concentrations of TMOs [203]. Taking the most commonly investigated TMOs, tungsten oxide (WO_3) and MoO_3 , as examples, a large amount of free electrons can be doped by inducing oxygen vacancy defects. An oxygen atom is a dianion. The removal of an oxygen atom from TMO lattice leaves a doubly ionized point defect in the vacancy (Figure 2-22), meaning that two free electrons are introduced to the conduction band [33,203]. Such oxygen vacancies induced doping can facilitate enough electron concentration to support LSPR in the visible or NIR regions [33–35]. Recently, the tunable LSPR of 2D MoO_3 has been most widely studied [34,35,38].

There are three polymorphs of MoO_3 , the stable orthorhombic α - MoO_3 (Figure 2-23 (a)), the metastable monoclinic β - MoO_3 (Figure 2-23 (b)) and the hexagonal h-MoO_3 (Figure 2-23 (c)) [204,205]. It can be seen from Figure 2-23, among the three polymorphs, 2D morphology of α - MoO_3 can be easily acquired due to the layered crystalized structure. Each two adjacent atomically thin planar units of α - MoO_3 form a double-layer with thickness of 1.4 nm. Distorted MoO_6 octahedra are joined by sharing zigzag edges. The adjacent double-layer units are held together by the weak van der Waals force [206].

2D few-layer α - MoO_3 nanoflakes or nanosheets can be obtained via various methods including top-down exfoliation and bottom-up synthesis. Originated from the discovery of graphene, mechanical exfoliation is a low-cost and straightforward method to get high quality crystalline 2D α - MoO_3 nanosheets [207]. However, it suffers from low yield [208]. Oxidizing few-layer MoS_2 nanoflakes can be a high yield synthesis method to acquire 2D MoO_3 nanoflakes. Nevertheless, the quality of MoO_3 nanoflakes is compromised by impurities and hydration during the oxidation process [38,209]. Another high yield method is liquid phase exfoliation which is also the most widely applied method [36,37,201,210–213]. Liquid phase exfoliation is a facile three-step process as shown in Figure 2-24. α - MoO_3 powder is ground and undergone sonication in solvent (e.g. water/ethanol). The exfoliated few-layer α - MoO_3 nanoflakes can be retrieved from the supernatant after centrifugation [212]. Figure 2-25 shows the representative morphologies of α - MoO_3 nanoflakes characterized by scanning electron microscope (SEM), transmission electron microscopy (TEM) and

Figure 2-24. A typical process of synthesizing α - MoO_3 nanoflakes by liquid phase exfoliation [212].

Figure 2-25. (a) The SEM image of α - MoO_3 nanoflakes [213]. (b) The TEM characterization of α - MoO_3 nanoflakes [39]. The AFM characterization of (c) monolayer and bilayer α - MoO_3 nanoflakes [212] and (d) multilayer α - MoO_3 nanoflakes [201].

atomic force microscopy (AFM). From the thickness of nanoflakes measured by AFM, the number of double-layer planar units can be deduced as the thickness of a double-layer unit is fixed at 1.4 nm. As shown in Figure 2-25 (c) and (d), the α - MoO_3

nanoflakes obtained by liquid phase exfoliation can be the mixture of monolayer, bilayer and multilayer. As an n-type semiconductor with a bandgap of 3.2 eV, pristine α -MoO₃ only induces absorption in UV frequencies [39]. After ionic intercalation, the oxygen vacancies in resultant sub-stoichiometric MoO_{3-x} behave as shallow donors and support LSPR in visible and NIR ranges [214]. A few methods have been proposed to introduce oxygen vacancies in α -MoO₃ nanoflakes, such as hydrogen spill-over [34,36], NaBH₄ reduction [39] and light stimulation [37,38]. The essence of these methods is to generate and intercalate H⁺ ions to MoO₃ lattice. The intercalated H⁺ ions mainly interact with the corner-sharing oxygen atoms in the lattice, leading to the formation of -OH₂ groups and hydrogen molybdenum bronze (H_xMoO₃, 0 < x ≤ 2) [36,215,216]. Eventually, water molecules are formed and released from the lattice, inducing oxygen vacancies and the formation of MoO_{3-x}. The reaction can be represented by the following expressions [36]:

Although the mechanism of inducing LSPR in heavily doped MoO₃ nanoflakes has been thoroughly investigated, the potential of implementing such 2D plasmonic material in biosensing is seldom explored. Previous researchers studied the mixture of different concentrations of bovine serum albumin (BSA) solution and α -MoO₃ nanoflakes solution [37,38,201]. They showed that negatively charged protein molecules have high affinity to α -MoO₃ nanoflakes due to van der Waals forces and electrostatic interaction as α -MoO₃ nanoflakes are positively charged. Moreover, owing to the repellent between the negatively charged BSA molecules and electrons at the surface of nanoflakes, the increase of BSA concentration reduces the free electron density at nanoflakes surface leading to the decrease of plasmon resonance peak. This unique biosensing mechanism where α -MoO₃ nanoflakes act as both the plasmonic material and the surface functionalization has yet to be applied in highly integrated optical platforms.

2.4.3 Macrocyclic Supramolecules Based Plasmonic Biosensing

Besides 2D materials, macrocyclic supramolecules can also be excellent surface functionalization for plasmonic biosensing. Macrocyclic supramolecules, such as CDs, pillararenes, calixarenes and cucurbiturils (Figure 2-26), are recognized by their macrocyclic cavities and favored by their selective molecular recognition capability via host-guest interaction, where macrocyclic supramolecules function as host molecules to form inclusion complexations with certain guest molecules. The driving force of forming host-guest interaction is noncovalent interaction such as hydrophobic association, electrostatic attraction, van der Waals force, π -stacking interaction, etc. [217]. Encouragingly, such host-guest interaction provides even higher efficiency in recognizing and capturing target molecules than the conventional biomolecule-ligand binding [218].

In conjunction with noble metal nanoparticles, macrocyclic supramolecules not only serve as biorecognition elements but also improve the biocompatibility of nanoparticles as well as the stabilizing performance [42,218,219]. Moreover, macrocyclic supramolecules have another huge advantage of being the surface functionalization layer, i.e. their cavity heights are generally less than 1 nm [220–222], which is comparable to 2D materials. Among the various macrocyclic supramolecules, CD has attracted most attention in biological applications due to their good water solubility, nontoxicity and biocompatibility [42]. A CD molecule is a macrocyclic linkage of several D-glucose units via α -1,4-glucose bonds. α -, β - and γ -CD are three common formations of CD that consist of six, seven and eight glucose units respectively (Figure 2-27 (a)). Figure 2-27 (a) compares the structural parameters of α -, β - and γ -CD. CD is a torus-shaped cavity with the hydroxyl groups oriented towards outside and the methinic protons reside inside. Hence CD cavity has hydrophilic external surface and hydrophobic inner surface [42]. Therefore, the formation of inclusion complexations is mainly driven by the hydrophobic association between the hydrophobic groups in guest molecule and the interior of CD cavity [171]. Common guest molecules of CD are adamantane, lithocholic acid, ferrocene, cholesterol, etc. [220]. The stability of the host-guest interaction is largely dependent on the cavity

size. For instance, the cavity of β -CD most tightly fits with the sterol group (Figure 2-27 (b)), making β -CD a highly efficient cholesterol receptor in many biomedical applications [224,225].

Compared with functionalizing the macrocyclic supramolecules to noble metal nanoparticles surface via post-processing surface modification, capping the nanoparticles with supramolecules during the synthesis would be much more efficient. Several studies have been carried out to realize macrocyclic supramolecules modified noble metal nanoparticles in one-step synthesis [43–50]. These synthesis methods are similar to the Turkevich method as explained in Section 2.3.3, except that supramolecules are added instead of sodium citrate as the capping agent. However, the majority of these attempts either introduce harsh reducing reagents (e.g. NaBH_4 , NaOH , thiols) or rely on high PH condition, which would be detrimental in biological applications [46,49,226]. Figure 2-28 demonstrates some typical one-step synthesis

Figure 2-26. Molecular structures of some common macrocyclic supramolecules [282].

Figure 2-27. (a) Molecular structures and structural parameters of α -, β - and γ -CD [283]. (b) The side view and top view of the inclusion complexation formed by β -CD and cholesterol molecules [284].

process of macrocyclic supramolecules modified metal nanoparticles. Carboxylatopillar[5]arene (Figure 2-28 (a)) and CD (Figure 2-28 (b)) have been employed as the capping agents with the existence of strong reducing reagents NaBH_4 . Core-shell bimetallic nanoparticles can also be synthesized under alkaline condition (PH 10-12) (Figure 2-28 (c)) [45,49]. The completely eco-friendly synthesis of supramolecules capped metal nanoparticles has only recently been demonstrated by Zhao *et al.* [227]. In their approaches, AuNPs are synthesized in mild conditions (PH 7.0-7.4) and CDs are served as both reducing and stabilizing agent. Although macrocyclic supramolecule modified nanoparticles have been proposed and synthesized, they are mainly utilized in constructing self-assemblies [46,47,227]. Currently, their LSPR biosensing potential has not been comprehensively explored.

Figure 2-28. Synthesis process of (a) carboxylatopillar[5]arene capped AuNPs [46]; (b) CD capped AuNPs [226]; (c) CD capped AgNPs, AuNPs and Agcore-Aushell/Au core-Agshell bimetallic nanoparticles [49].

Chapter 3 Magnetic Field Sensor Based on Magnetic Fluid Coated LPG

Optomagnetic biosensors, in which magnetic nanoparticles bonded with target biomolecules are manipulated via controllable magnetic field, effectively improve the efficiency of biomolecule detection. The manipulation of magnetic nanoparticles requires accurate measurement of applied field strength. Driven by the purpose of achieving highly integrated all-optical biosensing systems, fiber-optic magnetic field sensor attracts much attention. In parallel, magnetic fluid shows remarkable magneto-optic properties and becomes promising material for magnetic field sensing. Although various specific optical fiber structures coupled with magnetic fluid have been proposed to measure the field strength, a fiber-optic magnetic field sensor with improved sensitivity and simplified configuration still needs to be explored. LPG is favored due to the outstanding sensitivity to ambient environment and the simplicity of configuration for multi-parameter measurement. In this work, we propose a magnetic sensor based on LPG coated with the magnetic fluid, providing with high sensitivity and reduced cost.

In this chapter, Section 3.1 presents the characterization of LPG we fabricated for magnetic field sensing. Section 3.2 introduces the setup for magnetic field measurement and analyzes the sensing performance of magnetic fluid coated LPG.

3.1 LPG Characterization

We write the LPG on a standard single-mode fiber (SMF) using the ultraviolet irradiation method [66]. The grating period of LPG is $450\text{ }\mu\text{m}$ and the grating length is 30 mm. Figure 3-1 plots the transmission spectrum of LPG, of which the resonant wavelength corresponding to the highest order cladding mode (LP_{06}) [228] is at 1590.8

Figure 3-1. The transmission spectrum of LPG.

nm. We characterize the sensitivity of LPG to the ambient refractive index by immersing it into refractive index matching liquids. The refractive indices of matching liquids, which are made by mixing glycerol and water with different volume concentrations, range from 1.3323 to 1.4472. The variation of the attenuation band of the highest order cladding mode along with increasing surrounding refractive index is shown in Figure 3-2. As expected from Equation (1) and (2), the resonant wavelength undergoes a blue shift as the ambient refractive index increases.

Figure 3-3 plots the shift of resonant wavelength and also the change of transmission minimum of LPG against increasing surrounding refractive index. The shift of resonant wavelength is in agreement with that of Figure 2-2 (a), and it fits well with a cubic function. The transmission minimum of the attenuation band of LPG experiences a fall and a rise. This can be explained by Equation (3) that the transmission minimum is a function of $\cos^2(\kappa L)$. The initial coupling of LPG locates at the descending slope of cosine square function as the coupling coefficient decreases till the “valley” of cosine square curve is reached. As the coupling coefficient further decreases with the increasing refractive index, the transmission minimum increases along with the ascending $\cos^2(\kappa L)$ curve.

Figure 3-2. Variation of the attenuation band of LPG as the surrounding refractive index increases.

Figure 3-3. Wavelength shift and transmission minimum of LPG against surrounding refractive index.

3.2 Detection of Magnetic Field

After the characterization, we seal the LPG in a capillary tube with an inner diameter of 450 μm . The capillary is infiltrated with magnetic fluid EMG605, which is a water-based suspension of Fe_3O_4 particles. The volume concentration of Fe_3O_4 particles is 3.9% and the nominal diameter is 10 nm. We stabilize the magnetic fluid coated LPG in the middle of a pair of electromagnets (EM4-HVA LakeShore). Meanwhile, the magnetic field strength is measured by a gaussmeter (Model 425, Lake Shore). The experiment setup is illustrated in Figure 3-4. Before the experiment, the temperature between the two electromagnets is monitored for 40 minutes under a field strength of ~ 700 Gauss (G). The temperature varies from 23.9°C to 24.4°C . According to the thermal sensitivities reported by Hu *et al.* ($47.4 \text{ pm}/^\circ\text{C}$) [229] and Chaubey *et al.* ($0.06 \text{ nm}/^\circ\text{C}$) [230] and the thermo-optic coefficient of magnetic fluid reported by Chen *et al.* ($-10^{-4}/^\circ\text{C}$) [103], we consider the thermal effects during the magnetic field detection can be neglected. After the monitoring of temperature, we adjust the field strength back to 0 and subject the LPG to be perpendicular to the direction of magnetic field. Then we gradually increase the magnetic field strength from 0 to ~ 110 G.

Figure 3-4. The experiment setup of magnetic field sensor.

Figure 3-5 shows the change of LPG attenuation band as the magnetic field strength increases. The red dashed line is the attenuation band of the bare LPG exposed in air. It can be seen that the resonant dip significantly deepens by 12.5 dB when the LPG immerge into magnetic fluid (blue solid line). Also, there is a blue shift of resonant wavelength from 1590.8 nm to 1582.9 nm. According to the fitting curve in Figure 3-6, we estimate the refractive index of magnetic fluid to be ~ 1.39 , which agrees

reasonably well with that in [57]. Then the attenuation band further shifts to shorter wavelengths in the meanwhile becomes shallower and broader as the applied field strength increments from 0 to ~110 G. We estimate that the magnetic fluid refractive index increases from ~1.39 to ~1.41, as the resonant wavelength shifts from ~1583 nm to ~1580 nm. The increase of magnetic fluid refractive index is in agreement with previous studies [104–106], as explained in Section 2.2.1. The magnetic particles gradually aggregate into columns along the magnetic field direction, which leads to the increase of refractive index. The significant reduction of attenuation band depth of ~19 dB is caused by the increasing magnetic fluid refractive index as well as the enhancing absorption and scattering effects during the phase transitions [108,231], which have been demonstrated in Section 2.2.1. According to Figure 3-3, our LPG is “over-coupled”. The transmission minimum decreases with increasing external perturbation till the “valley” is reached. Hence we observe an enhancement of attenuation band when the surrounding material of LPG changes from air to magnetic fluid. As the magnetic field strength increases from 0 to ~110 G, the increase of transmission

Figure 3-5. Variation of LPG attenuation band along with increasing magnetic field strength.

minimum means that the LPG is at the “saturated” or slightly “under-coupled” position when field strength is 0. Thereby, the resonant dip moves up along with the ascending $\cos^2(\kappa L)$ curve. The slightly different positions of the “valley” in Figure 3-3 and Figure 3-5 is due to the different impacts of different surrounding materials on the LPG coupling coefficient. In Figure 3-3, the coupling coefficient is merely reduces by increasing ambient refractive index. In Figure 3-5, however, the external perturbation not only consists of refractive index but also the absorption and scattering induced by magnetic particles. Therefore, the “saturated” coupling of LPG occurs at a slightly smaller refractive index.

Figure 3-6 plots the resonant wavelength shift and the transmission minimum against the enhancing magnetic field strength. The wavelength shift linearly decreases till the field strength approaches ~110 G. The cease of wavelength shift indicates the saturated phase transition of magnetic fluid. As explained in Section 2.2.1, the hexagonal arrangement of columnar clusters of magnetic particles is relatively stable. The transmission minimum linearly and steeply increases along with the incrementing field strength. Based on the fitting function in Figure 3-6, our proposed magnetic field

Figure 3-6. Wavelength shift and transmission minimum of LPG against magnetic field

sensor provides a sensitivity of ~ 0.154 dB/G, which is higher than those of [56,58,108]. Moreover, as the transmission intensity resolution of optical spectrum analyzer can reach 0.001 dB, theoretically the resolution of our proposed sensor can be estimated to be 650 nT, which is superior than all the previously reported fiber-optic magnetic field sensors [55–58,107,108] and comparable to that of the Hall effect sensors (Table 1). The measurement range of a magnetic field sensor is limited by the threshold field strength at which the sensor starts to response. Profited from the excellent sensitivity of LPG and the acute phase transitions of the employed magnetic fluid, the measurement threshold of our proposed sensor is as low as ~ 7.4 G. Therefore, the magnetic fluid coated LPG is promising in relatively low magnetic field detection compared with previously reported fiber-optic magnetic field sensors that most measurement thresholds start from 20 G or even higher [55,56,58,107,108]. The reliability of the magnetic field sensor can be further improved by introducing temperature compensation to eliminate the temperature crosstalk [232,233]. For example, a fiber Bragg grating (FBG) can be cascaded to the LPG based magnetic field sensor to calibrate the temperature perturbation without responding to the ambient refractive index change [232].

3.3 Summary

We demonstrate a magnetic field sensor based on LPG coated with magnetic fluid. Benefited from the acute response of LPG to ambient environment and the tunable optical properties of magnetic fluid under applied field, our proposed sensor provides a superior sensitivity of ~ 0.154 dB/G as well as a high resolution of 650 nT. This work takes a step further in the optical fiber based magnetic field sensors and shows prospect of implementing all-fiber-based optomagnetic biosensors.

Chapter 4 Hybrid Graphene-on-Gold Plasmonic Fiber-Optic Biosensor

Integrating 2D materials into conventional plasmonic sensors delivers unprecedented enhancement on sensing performance. Although various hybrid 2D material/metal plasmonic sensing platforms have been proposed, most of these studies are preliminary theoretical investigations. In this work, we systematically investigate the influence of 2D material on hybrid plasmonic photonic structure on the SPP excitation as well as the sensing performance. To be more specific, we numerically analyze and experimentally demonstrate an optical fiber based plasmonic biosensor seamlessly integrated with the graphene-on-gold hybrid structure.

In this chapter, Section 4.1 introduces the design and configuration of our proposed hybrid plasmonic biosensor. It also presents the eigenmode analysis to optimize the structural parameters. Section 4.2 presents the fabrication and characterization of a conventional SPR sensor based on a side-polished optical fiber coated with thin gold film. Section 4.3 shows the construction of graphene-on-gold hybrid architecture and how the additional graphene layer improves the sensing capability. Section 4.4 presents the ssDNA detection using our proposed graphene-on-gold fiber-optic biosensor. It also proves that the hybrid structure provides superior biosensing performance than the conventional thin gold film.

4.1 Design and Numerical Analysis

We propose an optical fiber based SPR biosensor seamlessly integrated with the graphene-on-gold hybrid structure. Figure 4-1 illustrates the configuration of our proposed biosensor. Considering the cylindrical geometry of optical fiber is not suitable for the transfer of large-area single-layer graphene, we decide to use side-polished fiber

of which the flat polished facet can better preserve the integrity as well as prevent the wrinkles of graphene sheet. To do so, a standard SMF is side-polished to expose the evanescent field of core mode and a thin gold film is coated on the side-polished facet. Single sheet of graphene is then deposited on top of the gold film to enhance the excited SPP as well as to bond with biomolecules. A polychromatic light source couples into the fiber core. The peak transmission loss of the output spectrum occurs at the resonance at which the phase matching condition is satisfied. We use both wavelength and intensity interrogations to characterize the SPR behaviors. The nucleobases of analyte ssDNA are enriched with carbon rings so that ssDNA molecules can be stably bonded to graphene sheet through π -stacking interaction.

Figure 4-1. Configuration of proposed graphene-on-gold SPR biosensor. ssDNA molecules are adsorbed on single sheet of graphene through π -stacking interactions between the aromatics rings of nucleobases and honeycomb latticed carbon atoms.

We carry out numerical analysis using the mode analysis in FDTD Solutions of Lumerical to verify that the graphene enhanced SPR provides better performance even for bulk refractive index sensing. In the simulation, the fiber core diameter is 8 μm and the polished fiber cladding facet just coincides with the perimeter of fiber core. The refractive indices of fiber core and cladding are set based on the Sellmeier equations of fused silica and GeO_2 -doped silica respectively [234]. Firstly, we investigate how the gold film thickness impacts the SPR behaviors of our proposed biosensor. As discussed in Section 2.3.2, SPP is TM-polarized electromagnetic wave. Hence only guided core modes with polarization perpendicular to the thin gold film (i.e. y-polarized modes) can excite SPP. Although the standard SMF becomes multimode at visible

wavelengths, the incident light power is predominantly coupled into the fundamental core mode at normal incidence [235,236]. Hence we focus on analyzing the SPR behaviors of y-polarized fundamental core mode (i.e. HE_{11}^y) in the simulation. Figure 4-2 shows the HE_{11}^y mode patterns without and with the deposition of single graphene sheet. The addition of graphene layer strengthens the excited SPP, which enhances the attenuation of HE_{11}^y mode.

Figure 4-2. The HE_{11}^y mode patterns of side-polished optical fiber based SPR sensors (a) without and (b) with graphene enhancement. Red arrows: the electric field directions of HE_{11}^y modes.

Generally the thickness of thin gold film of optical fiber based SPR sensor ranges from 30 nm to 50 nm [237–239]. We set the gold film thickness as 50 nm, 40 nm and 30 nm respectively and compare their SPR sensing performances. Figure 4-3, 4-4 and 4-5 show the transmission spectra, sensitivities of wavelength interrogation

Figure 4-3. The gold film thickness is 50 nm. (a) Transmission spectra of conventional side-polished optical fiber based SPR sensor and graphene enhanced SPR sensor. (b) Comparison of sensitivities of conventional SPR and graphene enhanced SPR using wavelength interrogation (blue solid line and dashed line) and intensity interrogation (red solid line and dashed line).

Figure 4-4. The gold film thickness is 40 nm. (a) Transmission spectra of conventional side-polished optical fiber based SPR sensor and graphene enhanced SPR sensor. (b) Comparison of sensitivities of conventional SPR and graphene enhanced SPR using wavelength interrogation (blue solid line and dashed line) and intensity interrogation (red solid line and dashed line).

Figure 4-5. The gold film thickness is 30 nm. (a) Transmission spectra of conventional side-polished optical fiber based SPR sensor and graphene enhanced SPR sensor. (b) Comparison of sensitivities of conventional SPR and graphene enhanced SPR using wavelength interrogation (blue solid line and dashed line) and intensity interrogation (red solid line and dashed line).

and intensity interrogation corresponding to 50 nm, 40 nm and 30 nm gold film thickness respectively.

It can be seen from the above figures, with a graphene layer added, the peak transmission loss enhances meanwhile shifts to a longer wavelength. The peak loss enhancement is due to the enhanced SPP excitation caused by graphene as explained in Section 2.4.1. The redshift of resonant wavelength is owing to the high refractive index of graphene, as explained by Equation (31). As the refractive index of analyte

increases, the graphene enhanced sensor undergoes a larger wavelength redshift as well as a larger peak loss enhancement, leading to the improved sensitivities in both wavelength and intensity interrogations. As the gold thickness decreases, the resonant peak shifts to shorter wavelengths and the peak transmission loss enhances. This can be explained by Equation (24) that the propagation constant increases along with decreasing gold thickness, thus the phase matching condition is satisfied at a larger effective refractive index which corresponds to a shorter wavelength. Moreover, a thinner gold film makes it easier for the electric field of SPP to penetrate through, hence the intensity of SPP strengthens. The addition of a single sheet of graphene improves SPR sensitivities of both wavelength and intensity interrogations for all gold film thickness. Graphene on 50 nm gold film shows advantage in wavelength interrogation. It provides sensitivity as large as 1264 nm/RIU. However, the intensity interrogation sensitivity of 50 nm is much smaller compares with that of 40 nm and 30 nm. Graphene on 30 nm gold film possesses tremendous advantage in the intensity interrogation sensitivity. It provides a sensitivity - 897%/RIU, which is several times larger than that of 50 nm. Considering the resonant wavelength shift of SPR is driven by the variation of local refractive index, and the peak transmission loss enhancement is caused by both refractive index change and molecular scattering, we decide to use intensity interrogation as it is more affected by the adsorption of biomolecules to the SPP propagation surface. Therefore, we choose the gold film thickness as 30 nm.

Then we investigate the relation between number of graphene layers and SPP excitation. In the first scenario, a 30 nm gold film, beyond which is dielectric liquid medium, is coated on top of the side-polished facet. The blue curve in Figure 4-6 shows the normalized electric field distribution of SPP excited by thin gold film. The zero position is the boundary between gold film and side-polished facet. The inset of Figure 4-6 plots the electric field distributions over the entire simulated configuration, which includes the dielectric medium, thin gold film, fiber core and fiber cladding. In agreement with theory, the electric field of guided core mode is Gaussian distributed and that of SPP is the strongest at the thin film surface and exponentially decays into the dielectric medium. We add single layer of graphene on top of the gold film in the following scenario. As shown by the black curve in Figure 4-6, the intensity of SPP considerably enhances by ~30.2% with the addition of single graphene sheet. We also

Figure 4-6. Normalized electric field intensities of excited SPPs when no graphene layer, single layer graphene, 2-layer graphene and 3-layer graphene are deposited on the 30 nm gold film coated on the side-polished facet of fiber. (Inset) Distributions of normalized electric field intensity over the entire simulated geometry.

Figure 4-7. Sensitivities corresponding to single, double and triple layers of graphene when using (a) wavelength interrogation and (b) intensity interrogation.

investigate the impact of multiple graphene layers on the SPR behaviors. Two or more graphene layers would depress the SPP intensity instead of further boosting it. The increase of graphene layers leads to the gradual decrease of SPP due to the energy loss of electrons induced by additional graphene layer [195]. Therefore, single sheet of graphene maximizes the SPP intensity.

Figure 4-7 compares the sensitivities of single, double and triple graphene layers. For wavelength interrogation, the sensitivities corresponding to single, double and triple graphene layers are 1039.18, 1037.55 and 1036.73 nm/RIU respectively. And the sensitivities of intensity interrogation are -897.15, -871.61 and -847.36%/RIU respectively. Hence multiple layers of graphene compromise the SPR sensing performance compared with single layer, since the SPP intensity weakens as the number of graphene layer increases. Therefore, our proposed biosensor is composed of single graphene sheet deposited on 30 nm gold film with high sensitivity and easy accomplishment.

4.2 Fabrication and Characterization of Gold-Coated Side-polished Fiber

We use the commonly adopted method as shown in Section 2.1.2 to fabricate the side-polished optical fiber. An SMF is firstly fixed in a groove of a silica block using epoxy, and then polished the entire silica block till the fiber core is exposed. The side view of the fabricated side-polished fiber is shown in Figure 4-8. Figure 4-9 illustrates the cross-section of the deepest polishing depth. It matches well with the structure we constructed for simulation that the polished facet just coincides with the perimeter of fiber core. To examine the surface quality, we have measured the surface roughness of the side-polished fiber sample using AFM. Figure 4-10 shows that the surface height deviation of the side-polished fiber is 6.24 nm. The polished facet is further coated with a 30 nm gold film by electron beam evaporation. We characterize the SPR behaviors

Figure 4-8. Schematic diagram of side-polished single-mode optical fiber.

Figure 4-9. The SEM image of the cross section of the side-polished fiber.

Figure 4-10. Schematic diagram of side-polished single-mode optical fiber.

of the resulting gold-coated side-polished fiber. A polychromatic light source with the wavelength range from 400 nm to 700 nm transmits through a linear polarizer and couples into the SMF. The output light is received by a spectrometer with spectral resolution of 0.38 nm. We adjust the angle of linear polarizer meanwhile monitoring the transmission spectrum of side-polished fiber. When the peak transmission loss on spectrum reaches the lowest point, we fix the angle of polarizer as it corresponds to the HE_{11}^y mode. The gold-coated side-polished facet sequentially immerses in refractive index matching liquids, which are NaCl solutions with different concentrations with the refractive indices ranging from 1.3326 to 1.3497. Figure 4-11 (a) shows the

characterization results. The resonant wavelength shifts to longer wavelengths and the peak loss enhances along with increasing analyte refractive index. As plotted in Figure 4-11 (b), both resonant wavelength shift and transmission minimum show linear relation against analyte refractive index. This phenomenon matches with the abovementioned simulation results. The corresponding sensitivities of wavelength and intensity interrogations are ~ 414 nm /RIU and $\sim 391\%$ /RIU, respectively. The experimental sensitivities are less than those of simulation due to uneven polishing depth and process-induced surface roughness. As discussed in Section 2.1.2, the deeper

Figure 4-11 (a) Transmission spectra of a side-polished fiber based SPR sensor with gold thickness of 30 nm. (b) Measured sensitivities that correspond to wavelength and intensity interrogations.

the polishing depth is, the higher the sensitivity is [240]. Based on the side view of side-polished fiber shown in Figure 4-8, the deepest polishing depth is at the central region of the side-polished facet and gradually shallows away from the center of side-polished fiber. Hence the sensing performance of our fabricated side-polished fiber is a compositive result of the high sensitivity of deep-polished region and the relatively lower sensitivity of shallow-polished region. Also, surface roughness has considerable impact on the performance of plasmonic sensors, and cannot be achieved to be perfectly smooth in the fabricated side-polished fiber. Surface polariton would be attenuated by radiating or scattering into other surface-polariton states if roughness exists [241]. A study has found that, if the surface height deviation is larger than 5 nm, the excited surface plasmon will be considerably scattered leading to destructive coupling and degradation of sensing performance [242]. Since our surface height deviation is 6.24 nm, which is slightly higher than 5 nm, surface roughness is a considerable factor to lower the sensing performance in our experimental study. Besides the fine polishing we adopted in the experiment, surface roughness could be further improved by chemical etching of the polished facet, for example, using HF solution.

4.3 Graphene/Gold Hybrid Plasmonic Sensor

4.3.1 Graphene Transfer

Following the characterization, we transfer single sheet of graphene on top of the thin gold film by the wet-transfer approach [243]. We use a commercial 1 cm × 1 cm single-layer graphene grown on copper foil via chemical vapor deposition (CVD). Firstly, a few hundred nanometers of PMMA thin film is spin-coated on the top surface of graphene sheet. After the PMMA film is solidified, we float the whole copper foil on 8.33% ammonium persulfate $(\text{NH}_4)_2\text{S}_2\text{O}_8$ solution to etch the copper foil beneath graphene. Then the remaining PMMA coated graphene sheet is transferred to float on deionized (DI) water for several times to remove the residual ions. We locate the floating graphene sheet on top of gold coated side-polished facet of the fiber, and gradually lift it out of water with the graphene sheet attached on the side-polished facet.

After drying the graphene-coated fiber in a 37°C oven for 12 hours, the PMMA thin film is removed by acetone.

Figure 4-12 (a) shows the boundary of transferred single-layer graphene. The sensing area of side-polished fiber has an effective length of ~1 mm. The strip in the middle is the groove of silica block in which the SMF is fixed with epoxy. Hence the effective sensing area of the side-polished fiber is much smaller than the size of graphene sheet. During the process of graphene transfer, we locate the sensing area of the side-polished fiber to be at the center of the square graphene. Therefore, the

Figure 4-12. (a) Microscopic view of the boundary of transferred single layer graphene (b) The boundary between the polished and the unpolished region of optical fiber which is fully covered with homogeneously deposited graphene.

Figure 4-13. (a) Raman spectrum of monolayer CVD-grown graphene on copper foil. (b) Raman spectrum of transferred monolayer graphene on gold-coated fiber. (c) Raman spectra at 5 different positions along the longitude of optical fiber.

boundary of transferred graphene is at least 3 to 4 mm away from the sensing area. Even though the boundary of graphene is a bit torn, the effective sensing area of side-polished fiber is fully covered with well-preserved single-layer graphene sheet. Figure 4-12 (b) shows the boundary between the polished and the unpolished region of optical fiber which right under the center of transferred graphene sheet. It can be seen that the whole area is covered with homogeneously deposited graphene.

Figure 4-13 (a) and (b) show the Raman spectra of the monolayer CVD-grown graphene on copper foil and the monolayer graphene transferred onto the gold-coated side-polished optical fiber, respectively. The peak locations of G and 2D bands are at $1589\text{ cm}^{-1} \pm 2\text{ cm}^{-1}$ and $2678\text{ cm}^{-1} \pm 2\text{ cm}^{-1}$ respectively. The intensity ratios of 2D to G peaks in Figure 4-13 (a) and (b) are 2.70 and 2.26 respectively, which indicate the monolayer of graphene [244]. To verify the consistency of the monolayer graphene after wet transfer, we collect Raman spectra at 5 different locations along the fiber longitude. Figure 4-13 (c) plots the peak locations of G and 2D bands of positions that are 0, 0.2 cm, 0.4 cm, 0.6 cm and 0.8 cm from the edge of graphene. Both the two bands vary within $\pm 2\text{ cm}^{-1}$ as the data-collecting position changes.

Figure 4-14 compares the transmission spectra of plain gold film and graphene coated gold film on side-polished fiber when immersing in DI water. In agreement with simulation, the SPR resonant wavelength undergoes a redshift from 577.2 nm to 579.3

Figure 4-14. Comparison of transmission spectra of configurations with and without graphene.

nm with the addition of a graphene layer. Meanwhile, the graphene sheet obviously decreases the transmission minimum from 52.97% to 48.27%.

4.3.2 Characterization of Graphene/Gold Hybrid Plasmonic Sensor

We carry out experiments to verify that the graphene enhanced plasmonic sensor provides better performance even for bulk refractive index sensing. First, we fabricate and characterize another side-polished optical fiber coated with 30 nm gold film. The gold-coated side-polished facet sequentially immerses in the same refractive index matching liquids. Figure 4-15 (a) shows the variation of the transmission spectrum as the analyte refractive index increases. As expected, the resonant wavelength shifts to

Figure 4-15. The variations of transmission spectrum of (a) gold-coated side-polished fiber based plasmonic sensor and (b) graphene/gold hybrid plasmonic side-polished fiber based sensor.

Figure 4-16. The comparison of the sensitivities before and after transferring graphene for (a) wavelength interrogation and (b) intensity interrogation.

longer wavelengths and the peak loss enhances along with increasing refractive index. Following the characterization of gold-coated side-polished fiber, we transfer a single-layer graphene on top of the gold film using the same wet transfer method. Then we characterize such graphene/gold hybrid plasmonic sensor using the same method. Figure 4-15 (b) shows the characterization results. When immersing in DI water, the resonant wavelength undergoes a redshift from 579.9 nm to 582.3 nm with the addition of a graphene layer. Meanwhile, the additional graphene sheet decreases the transmission minimum from 52.55% to 49.89%. These spectrum variations induced by graphene transfer is very similar to that shown in Figure 4-14. As the refractive index gradually increases, it is obvious that the wavelength shift and the peak transmission loss enhancement are larger than those of Figure 4-15 (a).

Figure 4-16 compares the sensitivities of wavelength and intensity interrogations before and after transferring single-layer graphene. As shown in Figure 4-15 (a), the sensitivity of wavelength interrogation increases from 352.29 nm/RIU to 417.73 nm/RIU after the graphene transfer. Also, the sensitivity of intensity interrogation increases from -427.76%/RIU to -462.01%/RIU (Figure 4-16 (b)). Therefore, in agreement with the simulation, the graphene/gold hybrid structure could effectively improve the plasmonic sensing performance.

4.4 ssDNA Detection

Lastly, we validate the biosensing capability of our proposed sensor by detecting ssDNA, as ssDNA quantitation is a critical process in many biomedical techniques such as DNA sequencing, cloning, gene expression and polymerase chain reaction (PCR) [245]. We use 7.3 kDa 24-mer (5'-CTT CTG TCT TGA TGT TTG TCA AAC-3') ssDNA (Integrated DNA Technologies) with concentrations ranging from 1 pM to 10 μ M. 24-mer is a commonly used oligonucleotide probe length in the detections of human diseases-causing peptides and bacteria such as amyloid- β peptide [246], *Streptococcus pyogenes* [247], *Enterobacteriaceae* [248] and *Arcobacter butzleri* [249]. Using the same setup with aforementioned characterization, we flow various concentrations of ssDNA to the sensing area of the graphene enhanced SPR

sensor, and wait for 8 minutes to ensure that ssDNA molecules fully interact with gold film or graphene. Then we inject DI water to flush away the unbonded or weakly adsorbed ssDNA molecules and then record the stabilized transmission spectrum. Figure 4-17 (a) plots the magnified transmission spectra with various ssDNA concentrations. Same with the trend when sensing bulk refractive index, the resonant dip deepens and also shifts to longer wavelengths as the concentration increments. This phenomenon is caused by the adsorption of ssDNA molecules on graphene sheet. The bonding of ssDNA varies the local refractive index as well as scatters evanescent field

Figure 4-17. (a) Change of transmission spectra of graphene enhanced SPR fiber sensor when detecting concentrations of ssDNA; (b) Variations of transmission minimum and resonant wavelength against ssDNA concentrations (log pM).

that intimates to the SPP propagation surface, thereby causes higher transmission loss. Also, the propagation constant of SPP is modified so that the phase matching condition of SPR is satisfied at a longer wavelength. We also observe a distinguishable enhancement of peak transmission loss when ssDNA concentration is as small as 1 pM. Figure 4-17 (b) plots the linearly decreasing transmission minimum and the gradually saturated increasing resonant wavelength against log pM concentration. Therefore, using transmission minimum as the measuring parameter, our proposed biosensor

Figure 4-18. (a) The variations of transmission spectrum as ssDNA concentration increases when there is no graphene on thin gold film. (b) The comparison of the sensitivities to ssDNA solutions with and without graphene transfer.

provides a linear response over a wide detection range of log scale ssDNA concentration from 1 pM to 10 μ M.

Furthermore, we experimentally compare the biosensing performance of the cases with and without a single-layer graphene deposited on the gold film. We use a gold-coated side-polished fiber to detect the ssDNA solutions with concentrations ranging from 1 pM to 10 μ M. Figure 4-18 (a) shows the variation of transmission spectrum as the ssDNA concentration increases. It can be seen that when the ssDNA concentrations are as low as 1 pM and 10 pM, the variation of spectrum is hardly distinguishable. When the ssDNA concentration increases to 1 nM, we can observe a distinguishable enhancement of peak transmission loss of 0.1%. Therefore the hybrid graphene/gold plasmonic structure improves the LOD from 1 nM to 1 pM. The improvement of LOD is benefited from the improved adsorption of ssDNA molecules to graphene due to the π - π interactions. In Figure 4-18 (b), we compare the sensitivities to ssDNA solutions in two cases with and without graphene transfer. It is obvious that the graphene/gold hybrid structure not only improves the LOD but also provides a two times higher sensitivity.

4.5 Summary

We demonstrate a fiber-optic biosensor based on graphene-on-gold hybrid architecture. We prove by both numerical analysis and experimental demonstration that the deposition of graphene on the thin gold film effectively enhances the excited SPP, thus promotes the SPR sensitivities in both wavelength and intensity interrogations. Coupled with biomolecules adsorption capability, graphene enhanced SPR fiber sensor delivers distinctive sensing performance, leading to the realization of the prospect of highly sensitive, highly integrated, flexible and miniaturized in situ biosensors.

Chapter 5 Electron-Rich 2D MoO₃ for Highly Integrated Plasmonic Biosensing

2D plasmonic materials facilitate exceptional light-matter interaction and enable in situ plasmon resonance tunability. However, surface plasmons of 2D materials intrinsically locate at MIR range that are hardly accessible for practical applications. To address this fundamental challenge, heavily-doped MoO₃ nanoflakes have captured considerable research efforts to achieve tunable plasmonic properties in visible and NIR region. However, the feasibility of integrating plasmonic MoO₃ nanoflakes in a sensing carrier, as well as its potential for biological detection, still remain unexplored. In this work, we synthesize few-layer α -MoO₃ nanoflakes that are heavily doped with free electrons via H⁺ intercalation. The resultant sub-stoichiometric MoO_{3-x} nanoflakes provide strong plasmon resonance located at ~735 nm. Integrated with microfiber, the MoO_{3-x} nanoflakes show good affinity to negatively charged biomolecules and provide a detection limit of BSA as low as 1 pg/mL.

In this chapter, Section 6.1 introduces the design of MoO_{3-x} based fiber-optic biosensing platform. It also describes in details how to synthesize and characterize MoO_{3-x} nanoflakes and how to integrate the nanoflakes with microfiber. Section 6.2 presents the biosensing performance of our proposed MoO_{3-x} based plasmonic sensor. Section 6.3 numerically analyzes the plasmonic behaviors of MoO_{3-x} coated microfiber.

5.1 Design and Construction of Biosensor

5.1.1 Biosensor Configuration

Figure 5-1 schematically illustrates our proposed biosensing platform that the surface of microfiber is covered with a thin layer of heavily-doped α -MoO₃. The strong evanescent field of microfiber effectively excites the surface plasmons of MoO₃ nano-

Figure 5-1. Schematic diagram of fiber-optic biosensor integrated with heavily-doped MoO_{3-x} nanoflakes. Inset 1: Crystal structure of stable orthorhombic α -MoO₃. Inset 2: Molecular structure of BSA protein.

layer. BSA molecules are then immobilized onto the surface of MoO₃ nanoflakes and interact with surface plasmons leading to the change of transmission spectrum. 2D morphology of α -MoO₃ nanoflakes can be easily synthesized by liquid phase exfoliation due to the layered crystalized structure as demonstrated in Section 2.4.2.

5.1.2 Synthesis and Characterization of MoO₃ Nanoflakes

0.4 g α -MoO₃ (Alfa Aesar) powder is ground for 1 hour and then dissolved in 50 mL solution of ethanol/DI water (1:1, v/v). As shown by the X-ray crystallography pattern in Figure 5-2, the α -MoO₃ powder we used is polycrystalline. After 2 hours of sonication, the α -MoO₃ solution undergoes 20 min centrifugation with 10000 rpm. 15 mL of lucid supernatant with MoO₃ nanoflakes evenly dispersed is then collected. After adding with 600 μ L 0.01 M NaBH₄ (Alfa Aesar), the color of supernatant turns into dark blue. The doping of free carriers is realized by the H⁺ intercalation process, which induces oxygen vacancies in MoO₃ nanoflakes. As we gradually add NaBH₄ to the suspension of pristine MoO₃ nanoflakes, sub-stoichiometric MoO_{3-x} [201,250] forms and the color of supernatant evolves from colorless to dark blue (Figure 5-3).

Figure 5-2. The XRD pattern of polycrystalline α -MoO₃ powder

Figure 5-3. Color variations of MoO₃ nanoflakes suspensions along with increasing doping extent.

The morphology of the exfoliated MoO₃ nanoflakes is characterized by TEM and high-resolution TEM (HRTEM). The low-magnification TEM clearly indicates that as-prepared α -MoO₃ samples are flake-like in shape (Figure 5-4 (a)). The square array of diffraction dots in the corresponding selected area electron diffraction (SAED) pattern (Figure 5-4 (b)) reveals the single crystal nature of each orthorhombic α -MoO₃ nanoflake. The lattice fringes of α -MoO₃ nanoflakes can be clearly observed under HRTEM, and the interval between two adjacent fringes is ~ 2.3 Å, corresponding to the d-spacing of the (2 0 0) plane [251] (Figure 5-4 (c)). The thicknesses and the lateral dimensions of the MoO₃ nanoflakes are assessed by AFM. It shows that the average nanoflake thickness is ~ 2.8 nm (Figure 5-4 (d)), exactly the thickness of two double-layer planar units.

Figure 5-4. (a) Low-magnification TEM of the exfoliated MoO_3 nanoflakes. (b) SAED pattern of MoO_3 nanoflakes. (c) HRTEM of MoO_3 nanoflakes. (d) AFM measurement of MoO_3 nanoflakes. The average thickness of nanoflakes is ~ 2.8 nm and the lateral dimensions range from tens of nm to ~ 1 μm .

We also investigate the variation of the absorption of MoO_3 nanoflakes under different free electrons doping concentrations. Before doping, pristine MoO_3 nanoflakes only absorb ultraviolet wavelengths while barely induce loss to visible and NIR bands (the black curve in Figure 5-5), which can be explained by the bandgap of MoO_3 (~ 3.2 eV) [35]. The absorption spectra start to show an increment beyond 700 nm which gradually evolves into a distinct absorption peak associated with plasmon resonance (Figure 5-5). Along with the increasing doping extent, the absorption

increases steadily and meanwhile, the resonant wavelength undergoes a blue-shift from 767 nm to 738 nm. The blueshift of wavelength along with the enhancing doping concentration is predictable since the plasma frequency is directly related to the electron density ($\omega_p \propto n^{1/2}$) described by the Drude model [252], meaning that the increase of free electron density in sub-stoichiometric MoO_{3-x} leads to the increase of surface plasmon frequency that corresponds to a shorter resonant wavelength.

Figure 5-5. The evolvement of absorption spectrum from pristine MoO₃ nanoflakes suspension (black curve) to increasing doping extent. 2 mL pristine MoO₃ nanoflakes suspensions are added with 0, 50 μ L, 60 μ L, 70 μ L and 80 μ L 0.01 M NaBH₄ respectively.

The formation of sub-stoichiometric MoO_{3-x} is further verified by X-ray photoelectron spectroscopy (XPS) measurements shown in Figure 5-6 (a) and (b). Before the H⁺ intercalation, only two binding energy peaks locate at 233.1 eV and 236.2 eV correlated with Mo⁶⁺ 3d_{5/2} and Mo⁶⁺ 3d_{3/2}, respectively (Figure 5-6 (a)). After the doping of free carriers, the lower oxidation state Mo⁵⁺ with binding energy peaks at 231.9 eV and 235.1 eV, coexists with Mo⁶⁺ in MoO_{3-x} samples [253]. Evaluated from the peak areas corresponding to the two oxidation states, Mo⁶⁺ and Mo⁵⁺ ions account for 71.7% and 28.3%, respectively (Figure 5-6 (b)). The increased free electron density of sub-stoichiometric MoO_{3-x} originates from the two leftover electrons per oxygen vacancy once an oxygen atom is removed from the oxide as explained in Section 2.4.2.

These leftover electrons facilitate the collective oscillations at the surface of MoO_{3-x} nanoflakes at the resonant frequency.

Figure 5-6. (a) XPS analysis of pristine MoO₃. (b) XPS analysis of highly doped MoO₃ nanoflakes. Mo⁶⁺ and Mo⁵⁺ coexist after doping.

5.1.3 Integration of MoO₃ Nanoflakes and Microfiber

The microfiber is fabricated using the heat-and-pull method as explained in Section 2.1.3. It is tapered from a standard SMF. The whole length of the tapered fiber consisting of two identical taper transitions and the central uniform waist is 30 mm. The waist diameter is 2 μ m and the waist length is $\sim$ 10 mm. Based on Equation (11), the taper angle $\Omega(z) \ll 1$. Hence the tapered fiber is adiabatic. To stably immobilize the MoO_{3-x} nanoflakes, we adopt polyelectrolytes to functionalize the fiber surface. Since MoO_{3-x} is positively charged [254], it undergoes strong electrostatic attraction to polyanions. Therefore, we functionalize the microfiber with self-assembled poly(allylamine) (PAA)/poly(styrene sulfonate) (PSS) bilayer to introduce evenly distributed negative charges on the outer surface. We immobilize the microfiber in a flow chamber and fill up the chamber with DI water. Then we flow 100 μ L 1.0 M NaOH (Alfa Aesar) solution into the chamber and monitor the real-time transmission intensity of the microfiber. The transmission intensity stabilizes in about 10 min. Then the microfiber as well as the chamber are rinsed with DI water for 5 times. 100 μ L 0.05 wt% positively charged PAA (Sigma-Aldrich) is then flowed into the chamber and stagnated for 20 min, meanwhile the real-time transmission of microfiber tends to

steady intensity. After 5 times rinsing with DI water, 100 μL 0.05 wt% PSS (Sigma-Aldrich) carried with negative charges is flowed into the chamber and stagnated for 20 min. Again, the microfiber is rinsed with DI water for 5 times to wash away redundant PSS. Now the microfiber is functionalized with evenly distributed negative charges. Then the functionalized microfiber is immersed in 50 μL MoO_{3-x} solution. We monitor the real-time transmission intensity of microfiber within 745 nm – 755 nm. As shown in Figure 5-7, the transmission intensity keeps steady before adding the MoO_{3-x} nanoflakes. After adding the MoO_{3-x} nanoflakes, the transmission intensity suddenly declines and then gradually tends to a steady level meaning the deposition of nanoflakes on microfiber surface tends to saturation. This phenomenon is a typical self-assembly process of plasmonic nanomaterials to optical fibers.

Figure 5-7. Real-time monitoring of the transmission intensity of microfiber within 745 nm – 755 nm as MoO_{3-x} nanoflakes are bonding to the microfiber surface.

We characterize the morphology of the immobilized MoO_{3-x} nanoflakes using SEM. Low accelerating voltages (≤ 5 kV) are suitable for observing the surface morphology. Since microfiber is made of insulating SiO₂ that the electrons strike on it accumulate at the surface as there is no conducting path to the ground [255]. Observing microfiber surface morphology suffers from the charging effect that the MoO_{3-x} nanoflakes cannot be clearly seen. To address the charging issue, we functionalize a

Figure 5-8. (a) Morphology of MoO_{3-x} nanoflakes on the SiO₂ (285 nm)/Si substrate. The nanoflakes are functionalized by the same method as microfiber functionalization. (b) AFM characterization of MoO_{3-x} nanoflakes dispersed on bare Si substrate without electrostatic attractions.

SiO₂ (285 nm)/Si substrate with MoO_{3-x} nanoflakes using exactly the same method as microfiber functionalization. The top thin SiO₂ film is the same material as microfiber, thus we can achieve the same functionalization effectiveness on the thin SiO₂ film surface. Also, the interaction volume of electron beam at low accelerating voltage is less than 1 μm [256]. Hence the insulating SiO₂ layer is thin enough that considerable interaction volume lies in the conductive Si substrate beneath so that the amount of electrons accumulated on specimen surface is significantly reduced. Figure 5-8 (a) shows the SEM image of the morphology of MoO_{3-x} nanoflakes on the SiO₂ (285 nm)/Si substrate. The large bright color areas are the connected MoO_{3-x} nanoflakes. It can be seen the negatively charged PAA/PSS bilayer effectively adsorbs the positively charged MoO_{3-x} nanoflakes that the nanoflakes spread over the great majority of the area. Some individual MoO_{3-x} nanoflakes intersperse among the large-area connected nanoflakes (red circled areas in Figure 5-8 (a)). The sizes of scattered individual nanoflakes are comparable to those in AFM characterization (red circled areas in Figure 5-8 (b)), where the MoO_{3-x} nanoflakes disperse on bare Si substrate without electrostatic attractions. Therefore, the electrostatic interaction significantly promotes the MoO_{3-x} deposition on microfiber surface that the nanoflakes expand to micro-size in the lateral dimension.

5.2 BSA Detection

To validate the proposed plasmonic fiber-optic sensor, we apply it to the detection of BSA. BSA is a well-known negatively charged protein so that it can be efficiently adsorbed to MoO_{3-x} nanoflakes surfaces via electrostatic interactions as well as collective van der Waals forces [254]. To verify the affinity between the negatively charged BSA molecules and the positively charged MoO_{3-x} nanoflakes, we functionalize the MoO_{3-x} coated fibers with different concentrations of cyanine 3 (Cy3) dye labeled BSA molecules and observe them under a fluorescence microscope. Four microfibers with diameters of ~10 μm are prepared and immobilized with a nano-layer of MoO_{3-x} using the abovementioned functionalization process. Then the four

Figure 5-9. (a) Fluorescent microscopic images of MoO_{3-x} nanoflakes coated fibers that are functionalized with different concentrations of BSA molecules labelled with Cy3 dyes. (b) Absorption spectrum when MoO_{3-x} nanoflakes are mixed with different BSA concentrations. (c) Transmission spectra of the proposed biosensor when detecting incrementing BSA concentrations. (d) Linear response of transmission minimum as a function of BSA concentration in log-scale.

microfibers are respectively immersed in 100 μL Cy3-BSA (Nanocs Inc.) solutions with concentrations of 0, 10 $\mu\text{g/mL}$, 20 $\mu\text{g/mL}$, and 40 $\mu\text{g/mL}$ for 20 min. The four microfibers are then rinsed with DI water to wash away non-adsorbed Cy3-BSA molecules. Figure 5-9 (a) presents the fluorescent microscopic images of four microfibers functionalized with 0, 10 $\mu\text{g/mL}$, 20 $\mu\text{g/mL}$, and 40 $\mu\text{g/mL}$ Cy3-BSA, respectively. The even brightness along the fiber at each concentration indicates the even distribution of the stably adsorbed Cy3-BSA molecules, which also implies the uniformity of the immobilized MoO_{3-x} nano-layer. As expected, the brightness enhances as the Cy3-BSA concentration increases, indicating the incrementing quantity of adsorbed Cy3-BSA molecules.

To investigate the impact of the bonded BSA molecules on the plasmonic behaviors of heavily-doped MoO_{3-x}, we measure the absorption spectra of MoO_{3-x} suspensions mixed with different concentrations of BSA. 1 mL of MoO_{3-x} suspensions is blended with 2 mL of BSA solutions with concentrations of 100 ng/mL, 1 $\mu\text{g/mL}$, and 10 $\mu\text{g/mL}$, respectively. As shown in Figure 5-9 (b), the peak absorption of MoO_{3-x} slightly reduces when adding with relatively small BSA concentration of 100 ng/mL. The plasmonic peak intensity further attenuates as the BSA concentration increases. This is owing to the repulsion between the negatively charged BSA molecules and the free electrons at MoO_{3-x} nanoflakes surface, which reduces the free electron density participated in the plasmonic resonance [201,202].

As MoO_{3-x} nanoflakes are bonded to the microfiber surface, a plasmon resonance centered at 735 nm forms on the transmission spectrum (the black curve in Figure 5-9 (c)). 100 μL of BSA analyte with concentrations range from 1 pg/mL to 100 ng/mL are sequentially tested using the MoO_{3-x} coated microfiber. The resonance on the transmission spectrum gradually attenuates as the BSA concentration increases. The shallowing of plasmon resonance can be explained by the reduction of free carrier density. An obvious weakening of the plasmon resonance appears when the BSA concentration is as low as 1 pg/mL. Compared with the detection limit of 100 ng/mL obtained from the absorption measurement shown in Figure 5-9 (b), such a low detection limit of the proposed fiber-optic biosensor is benefited from the full utilization of the high aspect ratio of 2D MoO_{3-x} nanoflakes. As the MoO_{3-x} is

immobilized by electrostatic attraction, only a nano-scaled layer of nanoflakes can stably attach to the microfiber, and additional layers of MoO_{3-x} with positive charges repel each other which will be washed away. This leads to the fact that the surface of immobilized MoO_{3-x} nanoflakes fully interacts with the BSA molecules and 100 μ L of analyte is a considerably large amount compared with the nano-scale MoO_{3-x}. Therefore, this fiber-based biosensing platform effectively reduces the required amounts of 2D plasmonic material and biological analyte. Furthermore, the transmission minimum corresponding to the peak plasmon resonance increases linearly with the log-scale increment of BSA concentration (Figure 5-9 (d)).

The reproducibility of the MoO_{3-x} based fiber-optic plasmonic biosensing device we designed is mainly determined by the reproducibility of microfiber fabrication and MoO_{3-x} immobilization procedure. As the microfiber is fabricated via the heat-and-pull method as introduced in Section 2.1.3, the structural parameters of microfiber (i.e. waist diameter, waist length and taper transition length) can be very well controlled during fabrication if the flame size, the scanning speed and the scanning length of flame, and the pulling speed and the pulling length of translation stages are fixed. Hence we can repeatedly fabricate microfibers with same structural parameters and same sensing behaviors. The immobilization of MoO_{3-x} nanoflakes on microfiber is also highly reproducible. The surface functionalization of PAA/PSS bilayer has even thickness and very good surface smoothness, thus it hardly induces perturbations on the output spectrum. And based on Figure 5-8 (a) and Figure 5-9 (a), the immobilized MoO_{3-x} nanoflakes as well as the BSA molecules can evenly distribute on microfiber surface. As long as the concentrations and volumes of MoO_{3-x} nanoflakes solution used for surface functionalization is fixed, the sensing performance of the fiber-optic plasmonic device can be highly reproducible.

5.3 Numerical Analysis

As the heavily doped MoO_{3-x} nanoflakes show quasi-metallic plasmonic properties, the complex dielectric constant of MoO_{3-x} can be described by the Drude Model as explained in Section 2.3.1. Based on the plasmon resonance band shown in Figure 5-9

(c) (the black curve in Figure 5-9 (c)), the resonance locates at 735 nm corresponding to the resonant frequency ω_{sp} of 1.687 eV. Also, the linewidth of resonance band is 180.7 nm, thus γ can be calculated to be 0.416 eV. As the transmission spectrum is obtained when the biosensor is surrounded by DI water, $\epsilon_{dielectric}$ is substituted with 1.333. Hence, the plasma frequency ω_p can be deduced as 3.327 eV. We carry out eigenmode analysis where the fiber diameter is constructed to be 2 μm which exactly equals to that of the microfiber in our experiment. The thickness of MoO_{3-x} nano-layer surrounding the microfiber is set to be 5.6 nm, which is the thickness of two stacked layers of MoO_{3-x} nanoflakes. During the calculation, we keep adjusting the value of ϵ_b to match the theoretical and experimental results. ϵ_b is found to be 3.52 by fitting the simulated resonant wavelength to 735 nm. The deduced parameters are summarized in Table 2. The parameters in Table 2 are their average values since there is size distribution of MoO_{3-x} nanoflakes.

Table 2. Drude Model Parameters of MoO_{3-x}

ω_{sp} (eV)	γ (eV)	ϵ_m	ω_p (eV)	ϵ_b
1.687	0.416	1.333	3.327	3.520

Based on the Drude model parameters in Table 2, we carry out eigenmode analysis to simulate the electromagnetic field distribution of MoO_{3-x} nanoflakes coated microfiber. As discussed in Section 2.1.3, the fiber core at microfiber waist is too small to confine a guided core mode at the core-cladding interface. In this case, the fundamental HE₁₁ mode is guided by the cladding-air interface [257,258]. We calculate the plasmon resonance band as plotted in Figure 5-10 (a) and it matches well with the experimental spectrum. The inset of Figure 5-10 (a) presents the HE₁₁ mode profile of the MoO_{3-x} coated microfiber. The evanescent field distributed in the vicinity of MoO_{3-x} nano-layer surface can be clearly observed. The electric field distribution of the entire HE₁₁ mode profile is shown in the inset of Figure 5-10 (b), while Figure 5-10 (b) plots the magnified electric field distribution in the vicinity of MoO_{3-x} nano-layer. MoO_{3-x} nano-layer strongly absorbs and confines the electric field of the guided mode in fiber, which gives rise to the attenuation band in transmission spectrum.

Figure 5-10. (a) Simulated plasmon resonance band with the deduced Drude model of MoO_{3-x}. Inset: HE₁₁ mode profile of MoO_{3-x} nano-layer coated microfiber. (b) Simulated electric field distribution near the MoO_{3-x} nanolayer. Inset: Electric field distribution over the whole fiber diameter.

Figure 5-11 compares the electric field distributions over the entire microfiber diameter without and with the nano-layer of MoO_{3-x}. For a bare microfiber, the electric field distribution matches well with the Gaussian distribution (Figure 5-11 (a)). The HE₁₁ mode profile of bare microfiber is shown in the inset of Figure 5-11 (a). When the microfiber is coated with a nano-layer of MoO_{3-x}, the electric field remains the Gaussian distribution except that the additional MoO_{3-x} layer strongly absorbs and confines a portion of the guided mode (Figure 5-11 (b)). The evanescent field in the vicinity of fiber surface becomes stronger in the HE₁₁ mode profile (The inset of Figure 5-11 (b)), leading to a better biosensing performance.

Figure 5-11. (a) Electric field distribution over the diameter of a bare microfiber. Inset: HE₁₁ mode profile of the bare microfiber. (b) Electric field distribution over the diameter of a MoO_{3-x} coated microfiber. Inset: HE₁₁ mode profile of the MoO_{3-x} coated microfiber.

5.4 Summary

For the first time, we integrate 2D plasmonic MoO_{3-x} nanoflakes with optical biosensing platform and demonstrate that when integrated with microfiber, a small amount of MoO_{3-x} nanoflakes would induce strong plasmon resonance in NIR and provide a promising detection of protein molecules. We also deduce the Drude model parameters of quasi-metallic MoO_{3-x} via eigenmode analysis. This work proves the unprecedented potentials of employing TMOs as an alternative class of 2D plasmonic materials in highly integrated plasmonic devices compliant with frequently used and cost-effective optical system.

Chapter 6 CD-Modified AuNPs Based Fiber-Optic LSPR Biosensor

LSPR of AuNPs has become a prominent biosensing technique as it facilitates highly sensitive and label-free detection of biomolecular quantification, binding and dissociation. Especially when integrated with fiber-optic probes, it brings the feasibility of miniaturized, remote and even in vivo biosensing. Biocompatibility is of crucial importance for in vivo biosensing. Despite the inert nature of gold, further surface functionalization of AuNPs to diminish cytotoxicity is often required. Meanwhile, surface functionalization should also serve as selective biointerface without compromising the sensitivity. Macrocyclic supramolecule-modified AuNPs is revealed to simultaneously satisfy biocompatibility, selective molecular recognition as well as high sensitivity. Although several attempts have been carried out to save post-processing surface modification by capping AuNPs with macrocyclic supramolecules during the synthesis, the majorities introduce harsh reducing reagents (e.g. NaBH_4 , NaOH , thiols, etc.) which would be detrimental in biomedical practices. Also, the LSPR biosensing potential of the macrocyclic supramolecule-modified AuNPs has not been comprehensively explored. Therefore, in this work, we realize completely “green” synthesis of biocompatible, high-quality and monodisperse β -CD-capped AuNPs. We decorate the biocompatible AuNPs on the surface of a microfiber to realize a highly sensitive and highly integrated biosensing device with good molecular selectivity.

In this chapter, Section 6.1 introduces the architecture of our proposed biosensing platform. Section 6.2 describes the synthesis procedures of β -CD-capped AuNPs and the characterization of the as-prepared AuNPs. Section 6.3 presents the detection of cholesterol molecules using the β -CD-capped AuNPs coated fiber-optic biosensor. It also proves the exclusive selectivity of β -CD-capped AuNPs to cholesterol molecules via interference study.

6.1 Design and Configuration

Figure 6-1 schematically illustrates our β -CD-capped AuNPs based fiber-optic biosensor. Each AuNP is equipped with many β -CD molecules through the conjunction of the carboxyl groups of the oxidized β -CDs and the gold surface [227]. The β -CD-capped AuNPs are immobilized onto the surface of a microfiber via electrostatic force. A considerable portion of the evanescent field leaks out due to the thin diameter of microfiber and excites strong LSPR of the AuNPs. The cholesterol molecules are attracted to the macrocyclic cavities of β -CDs via host-guest interaction and perturb the surface plasmons resulting in the variation of the transmission spectrum. As discussed in Section 2.4.3, the host-guest interactions between CDs and guest molecules are mainly driven by the hydrophobic associations. The cavity size of β -CD most tightly fits with the sterol group of cholesterol molecule (Figure 2-27 (b)), resulting in highly efficient adsorption of target cholesterol molecules.

Figure 6-1. Schematic illustration of the proposed microfiber based biosensor. Inset 1: The molecular structure of β -CD. Inset 2: The molecular structure of cholesterol.

6.2 Synthesis and Characterization of AuNPs

The β -CD-capped AuNPs are synthesized in an eco-friendly way, where β -CD functions as both reducing and stabilizing agent. 35 mL of DI water, 5 mL of phosphate buffer solution (PBS, 0.1 M, pH 7.0), 10 mL of 0.01 M β -CD aqueous solution and 1 mL of 0.01 M HAuCl_4 are added to a round bottom flask. Then the mixed solution is heated to 100 °C for 60 min with vigorous stir. During the heating process, the solution color gradually evolves from nearly colorless to light purple and then stabilizes at light red (see the color evolution in the Inset of Figure 6-2). We measure the absorption of the β -CD-capped AuNPs solution at different reaction time. As shown in Figure 6-2, when the reaction time is 20 min, at which the solution color is light purple, a weak and broad absorption peak appears at 535 nm. The weak peak is due to the low concentration of synthesized AuNPs in the solution. After 30 min of reaction time, since when the solution color remains at light red, sharp absorption peaks with resonant wavelength at 521 nm are observed. According to Figure 2-15 in Section 2.3.3, we can

Figure 6-2. The evolvement of AuNPs solution absorption during the synthesis process. Inset: The variation of solution color along with synthesis time.

roughly estimate the nanoparticle sizes are stabilized at ~20 nm. To obtain a clear picture of the AuNPs size distribution, we characterize the β -CD-capped AuNPs solutions by dynamic light scattering (DLS). As shown in Figure 6-3, at 20 min, the AuNPs sizes have a broad distribution around 83 nm. This is in accordance with the absorption curve in Figure 6-2 that the larger particle sizes lead to a longer LSPR wavelength. The broad particle size distribution also explains the corresponding broad absorption spectrum in Figure 6-2 (the black curve). Similar with the solution color and the absorption spectra, the DLS result also stabilizes after reaction time of 30 min. It can be seen from Figure 6-3 that the AuNPs sizes stabilize around ~18 nm during 30 min to 60 min with a much narrower size distribution. It can be concluded from Figure 6-2 and Figure 6-3 that 30 min of synthesis time can deliver β -CD-capped AuNPs with good enough plasmonic resonance and monodispersity. Therefore, we finalize our synthesis time at 30 min.

Figure 6-3. The DLS measurements of AuNPs size distributions at different synthesis time.

To purify the AuNPs, the cooled solution undergoes centrifugation with 8000 rpm for 8 min. The precipitates are collected and redispersed in 5 mL DI water for next-step characterizations and optical biosensing. After the purification, we get a more

condensed AuNPs solution with ruby-red color (Inset of Figure 6-4). The peak absorption remains at 521 nm but with a much sharper plasmonic resonance. The linewidth of resonance band is as narrow as 47 nm, which is competitive with conventionally synthesized AuNPs.

Figure 6-4. The absorption of AuNPs solution after centrifugation and redispersion. Inset: the color of purified AuNPs solution.

Figure 6-5 shows the SEM observation of the as-prepared β -CD-capped AuNPs with synthesis time of 30 min. We can see the homogeneous particle size distribution in SEM and the AuNPs tend to contiguously attach to each other after the solvent fully evaporates. From the SEM image, we can estimate the average diameter of β -CD-capped AuNPs is ~ 19 - 20 nm, which matches well the DLS measurement in Figure 6-3. A clear picture of AuNPs morphology can be provided by TEM and HRTEM. The TEM image shown in Figure 6-6 (a) indicates that the AuNPs have almost uniform spherical structures, and the particle diameters mostly range from ~ 18 nm to ~ 21 nm, which is also in accordance with DLS results. The comparison between the particle size distributions obtained from DLS and TEM is shown in Figure 6-7. Due to the limited nanoparticle samples in TEM characterization, the TEM based size distribution is narrower. We can conclude the good crystallinity of the β -CD-capped AuNPs from the distinct lattice fringes under HRTEM (Figure 6-6 (b)). The (1 1 1) plane can be clearly observed. The ξ -potential value of the β -CD-capped AuNPs is -33 mV (Figure 6-8),

meaning that our as-prepared AuNPs are negatively charged at surface. The AuNPs in solution are kept from aggregation by the electrostatic repulsion. The proton nuclear magnetic resonance (^1H NMR) spectrum of the β -CD-capped AuNPs in D_2O shown in Figure 6-9 indicates that the macrocyclic structure of β -CD is well preserved on AuNPs surface after the synthesis process [259]. The well-maintained macrocyclic structure can be further verified by the Fourier-transform infrared spectroscopy (FTIR) (Figure 6-10). The FTIR spectra of β -CD and β -CD-capped AuNPs have very similar profiles except that the band corresponding to hydroxyl group becomes much narrower after

Figure 6-5. SEM image of the as-prepared β -CD-capped AuNPs.

Figure 6-6. (a) Low-magnification TEM of β -CD-capped AuNPs. (b) HRTEM of a single β -CD-capped AuNP.

the formation of AuNPs, which indicates that the hydroxyl groups of β -CD molecules mainly participate in reducing Au^{3+} ions to metallic Au^0 . To obtain a precise characterization of the transformation of β -CD featured groups during AuNPs synthesis, we carry out XPS measurements for pristine β -CD and as-synthesized β -CD-capped AuNPs (Figure 6-11). As shown in Figure 6-11 (a), The C 1s XPS spectrum of pristine β -CD consists of three peaks located at 284.7 eV, 286.4 eV and 287.6 eV, corresponding to C–C, C–OH and O–C–O bonds respectively. There is only one peak at 532.8 eV in O 1s spectrum, which is contributed by C–OH or C–O–C bonds in β -CD (Figure 6-11 (b)) [227]. After the formation of β -CD-capped AuNPs, we can observe an obvious shrink of C–OH peak in the C 1s XPS spectrum (Figure 6-11 (c)). The peak area of C–OH decreases from 65.9% in Figure 6-11 (a) to 60.7% in Figure 6-11 (c), indicating the reduction of hydroxyl groups that is in accordance with the FTIR observation. Meanwhile, a new peak appears at 289.1 eV, which is correlated with the O–C=O bond [260]. Hence as expected, a new peak appears at 531.0 eV in the O 1s spectrum (Figure 6-11 (d)), corresponding to the C=O bond [261]. Therefore, we can conclude from XPS results that after reducing Au^{3+} to Au^0 , the reacted hydroxyl groups of β -CD molecules are oxidized to carboxyl groups. The newly formed carboxyl groups strongly interact with the AuNPs surface via O–Au bond (Inset of Figure 6-9) and effectively stabilizes the AuNPs [227,261].

Figure 6-7. (a) The AuNPs size distribution of 30 min synthesis time measured by DLS. (b) The comparison of AuNPs size distributions obtained from DLS measurement and TEM observation.

Figure 6-8. The ξ -potential value of the β -CD-capped AuNPs.

Figure 6-9. The ^1H NMR spectrum (300 MHz, D_2O) of the β -CD-capped AuNPs. Inset: Schematic β -CD structure associated with corresponding chemical shifts and interaction with AuNP surface.

Figure 6-10. The FTIR spectra of pristine β -CD and β -CD-capped AuNPs.

Figure 6-11. (a) C 1s XPS spectrum and (b) O 1s XPS spectrum of pristine β -CD; (c) C 1s XPS spectrum and (d) O 1s XPS spectrum of β -CD-capped AuNPs.

6.3 Selective Detection of Cholesterol

The microfiber is fabricated by tapering a standard SMF using the heat-and-pull method described in Section 2.1.3. The thinnest portion of microfiber has a diameter of 4 μm (Figure 6-12 (a)) and a length of ~ 8 mm. Electrostatic deposition of polyelectrolyte is a facile yet efficient surface functionalization technique [262]. Since the β -CD-capped AuNPs have been proven to be negatively charged, we functionalize the microfiber surface with a layer of positively charged PAA to adsorb AuNPs via electrostatic interaction. A homogeneous layer of PAA is deposited on microfiber surface using the same method as described in Section 5.1.3. The purified AuNPs solution is diluted by 3 times for the decoration of microfiber surface. 50 μL of the diluted AuNPs solution is flowed into the chamber and stagnated for 10 min. Then we

rinse the chamber with DI water for 5 times to flush away the redundant and weakly adsorbed AuNPs. Figure 6-12 (b) shows the surface morphology of microfiber immobilized with β -CD-capped AuNPs.

Figure 6-12. (a) The SEM image of the thinnest portion of microfiber. (b) The distribution of the immobilized β -CD-capped AuNPs on microfiber surface.

It can be seen that the AuNPs evenly spread on fiber surface other than packing together as shown in Figure 6-5, indicating the homogeneous distribution of the positively charged PAA and the stable immobilization of AuNPs. As the AuNPs are gradually attached on microfiber surface, an attenuation band centered at 530.7 nm appears on the transmission spectrum and gradually deepens. The black curve in Figure 6-13 (a) is the stabilized transmission spectrum after the redundant AuNPs are removed by rinsing. The reason for the redshift of resonance peak from 521.5 nm as shown in Figure 6-4 to 530.7 nm in Figure 6-13 (a) is due to the high refractive index of silica microfiber, since the LSPR resonant wavelength is proportional to $\sqrt{2n_{dielectric}^2 + 1}$ at optical frequencies, where $n_{dielectric}$ is the refractive index of ambient dielectric material as explained in Equation (29) [263]. The β -CD-capped AuNPs decorated microfiber is sequentially immersed in 200 μ L aqueous cholesterol solutions with concentrations range from 5 aM to 0.5 μ M. We can observe a distinguishable deepening of the attenuation band when the cholesterol concentration is as low as 5 aM (the red curve in Figure 6-13 (a)). Such low limit of detection is benefited from the highly efficient interaction between β -CD and cholesterol molecules. The formation of host-guest inclusion complexations at AuNPs surface increases the local refractive index as well as the scattering of evanescent field, leading to a higher transmission loss.

As the cholesterol concentration increments, the resonance peak keeps descending and then tends to ease when the concentration is higher than 5 nM (Figure 6-13 (a)). Meanwhile, the resonant wavelength undergoes a redshift from 530.7 nm to 531.4 nm, verifying the increase of surrounding refractive index. As the adsorbed cholesterol molecules only perturb the evanescent field within 1-2 nm distance from AuNPs surface as discussed in Section 2.4.3, the overall effective refractive index of the whole

Figure 6-13. (a) The variation of transmission spectrum as the cholesterol concentration increases. (b) The response of transmission minimum against log-scale cholesterol concentration.

penetration depth of surface plasmon is not largely increased. Hence the resonant wavelength shift is not obvious. Taking the transmission minimum as the sensing parameter, our proposed biosensor provides a linear response within a wide range of log-scale cholesterol concentration from 5 aM to 5 nM (Figure 6-13 (b)). It can be seen from Figure 6-13 (b) the response tends to saturate when cholesterol concentration is larger than 5 nM. Limited by the poor water solubility of cholesterol molecules [264], only concentrations no more than 0.5 μ M are prepared and tested.

To verify the reliability of our proposed biosensor in practical applications, we carry out an interference study for the commonly present compounds in human serum, including glutamic acid, cysteine, ascorbic acid and dopamine [227,265,266]. For each tested cholesterol concentration, the interfering substances are diluted to their corresponding concentrations based on the realistic proportions in human serum [227]. For example, when 5 fM cholesterol is tested, glutamic acid, cysteine, ascorbic acid and dopamine solutions with concentrations of 0.15 fM, 0.31 fM, 0.13 fM and 3.75×10^{-21} M respectively are sequentially introduced. Figure 6-14 presents the real-time monitoring of the average transmission intensity within 530-535 nm when we detect 50 aM – 5 fM cholesterol while introducing the interfering substances. It shows that each time when the cholesterol is added, the average transmission intensity quickly descends by ~1%, which matches with the descending trend of transmission minimum shown in Figure 6-13 (b). Introducing the interfering substances induces slight but tolerable fluctuations on transmission intensity. Each addition of interfering substance leads to slow and very small-scale decrease of transmission intensity. After the intensity is stabilized, the redundant substances are flushed away by rinsing with DI water (the blue arrows in Figure 6-14). We can see that the rinse almost brings the intensity back to the level before the interfering substances are added. The negligible impact of interfering substances on the biosensing performance is due to the much weaker host-guest interaction between the interfering compounds and β -CDs compared with the cholesterol- β -CD inclusion complexation and also the relatively low concentrations of interfering substances in human serum. As the interaction between β -CDs and guest molecules is mainly driven by hydrophobic attraction, the hydrophobic groups in guest molecules play an essential role in forming the host-guest complexation. A glutamic acid molecule contains two hydrophobic $-(CH_2)$ groups and

one hydrophilic $-(\text{COOH})$ group. The interaction between glutamic acids and β -CDs are based on the association between the $-(\text{CH}_2)$ groups and the interior cavity of β -CD [267]. However, due to the mismatch between sizes of $-(\text{CH}_2)$ group and β -CD cavity, although the inclusion complexation of glutamic acid and β -CD can be formed, it would be much weaker compared with the tightly fitted cholesterol. Similarly, a cysteine molecule has only one hydrophobic $-(\text{CH}_2)$ group, the interaction between cysteine and β -CD would be even weaker than glutamic acid. The lactone ring in ascorbic acid and the benzene ring in dopamine can also be housed by the CD cavity [268–270]. However, their sizes most tightly fit with α -CD cavity but a bit loosely fit with β -CD cavity [271]. Moreover, the concentrations of ascorbic acid and dopamine in human serum are much lower than that of cholesterol. Especially for dopamine, although the host-guest interaction with CD has been adopted for dopamine sensing [268], its concentration is lower by 10^6 in human serum. Therefore it has negligible interference to realistic cholesterol detection.

Figure 6-14. An interference study with the existence of common substances in human serum. The concentrations of interfering substances are added based on the realistic proportions in human serum.

6.4 Summary

For the first time, we investigate the highly integrated LSPR biosensing potential of β -CD-capped AuNPs synthesized in a facial and eco-friendly way where β -CDs function

as reducing and stabilizing agents as well as selective biointerface. The synthesis of β -CD-capped AuNPs is a one-step process that realizes not only the formation of uniform nanoparticles but also the functionalization of biorecognition layer. Benefited from the very thin thickness of β -CD layer which is even comparable to 2D materials and the highly efficient molecular recognition capability, the β -CD-capped AuNPs based fiber-optic biosensor achieves ultralow LOD as well as specific recognition of cholesterol molecules. Given that CD can house a variety of guest molecules, our proposed highly integrated and biocompatible plasmonic sensing platform can be versatile in various biosensing scenarios.

Chapter 7 Highly-Birefringent MOF Based SPR Sensor

MOFs are recognized by their fine arrangement of air holes in the cladding region extended along the entire fiber length. Gas or liquid analyte can be infiltrated into the cladding air holes around fiber core and approaches to the strong evanescent field of guided mode due to the small core dimension. Meanwhile, the interaction between the evanescent field and the infiltrated analyte can extend along the entire fiber length. This unique feature realizes exceptional excitation of surface plasmons when coating plasmonic materials on the inner walls of cladding air holes. Several structures of MOF have been proposed previously for plasmonic sensing. However, as discussed in Section 2.3.4, phase birefringence exists in most designs of MOF based SPR sensors due to the structural asymmetry in two orthogonal polarization directions in pursuit of higher sensitivities by enhancing the light-matter interaction. Birefringence leads to the separation of resonant wavelengths corresponding to two orthogonal polarizations. Generally, the output of an SPR sensor is obtained by monitoring the resonant dip of the polarization that excites the strongest SPP. However, external perturbations or inaccurate input polarization would mix unwanted polarization, thus result in an output which is the superposition of two resonant dips of orthogonal polarizations. The resultant resonant wavelength is thereby divergent from that of wanted polarization, hence the accuracy of SPR sensor is compromised. To address such issue, we propose to use a so-called polarization-maintaining MOF that introduces a phase birefringence large enough to suppress the impact of polarization crosstalk on sensor output, meanwhile achieving a promising sensitivity.

In this chapter, we design a highly-birefringent MOF and numerically analyze its SPR sensing performance. Section 7.1 introduces the configuration and working principle of our proposed highly-birefringent MOF. Section 7.2 discusses how the phase birefringence impacts the output accuracy of MOF based SPR sensor. Section 7.3 analyzes what parameters in MOF structure can impact the performance of SPR sensing.

7.1 Configuration and Principle

The SPR sensor we proposed is a near-panda MOF as shown in Figure 7-2 (a). It consists of three rings of photonic-crystal arranged cladding air holes. The two central air holes in lateral direction are enlarged so that their diameters are 2.5 times larger than those of the others. The diameters of the enlarged holes and normal holes are $d_1 = 1.75 \mu\text{m}$ and $d_2 = 4.38 \mu\text{m}$, respectively. The pitch of photonic crystal is $3.94 \mu\text{m}$. Thin gold layers are coated on the inner walls of two enlarged holes, in which analyte will be infiltrated. The SPR behavior of our proposed sensor is numerically analyzed by COMSOL, that employs the finite element method (FEM) to mesh the constructed geometry into different sizes of triangular elements [272]. In our calculation, we use very dense mesh at the boundaries of gold layers which are quite thin compared with the fiber dimension. The maximum and minimum element sizes are set to be $0.05 \mu\text{m}$ and 0.45 nm respectively. The remaining part of geometry is meshed with the fine mesh that is predefined by COMSOL. A portion of the mesh is shown in Figure 7-1, where the two blue lines are the boundaries of gold layer. At the boundary of constructed fiber geometry, we add a $3\text{-}\mu\text{m}$ thick perfectly matched layer (PML) to avoid the reflection interference.

Figure 7-1. Mesh sizes around the boundaries of gold layer in numerical model.

Figure 7-2. (a) Schematic drawing of the proposed MOF structure; (b) x-polarized and (c) y-polarized core mode pattern calculated by FEM.

The fiber material is fused silica, of which the refractive index can be calculated by the Sellmeier equation. The optical property of gold is characterized by an improved Drude-Lorentz model [273]. Figure 7-2 (b) and (c) show the x-polarized and y-polarized core mode pattern respectively. It can be seen that SPP is only excited by the polarization of which the direction is perpendicular to the surface of thin metal film, which is expected based on the SPR theories explained in Section 2.3.2.

According to Equation (24), SPR is excited when achieving the phase matching condition, at which the real part of the effective index of core mode equals to that of the surface plasmon (SP) mode. We use the eigenmode analysis of COMSOL to get the effective indices at each wavelength. Figure 7-3 plots both the real part and the imaginary part of the effective refractive index of the x-polarized core mode, which primarily excites SPP, and the real part of effective index of surface plasmon (SP) mode. The intersection of the red line and the black line in Figure 7-3 indicates the phase matching point, which corresponds to the highest attenuation on the transmission spectrum. The resonant wavelength is $\sim 600 \text{ nm}$, since the effective index of SP mode is closed to that of bordering analyte, e.g. 1.33, which is much lower than a silica

Figure 7-3. Effective indices of core mode and surface plasmon mode with refractive index of analyte of 1.33 and gold layer thickness of 70 nm.

fiber [125]. Hence the phase matching condition can only be satisfied at ~ 600 nm where the mode indices are ~ 1.45 . Based on Equation (30), the core mode attenuation is a function of the imaginary part of core mode effective index. We use the wavelength

Figure 7-4. Changes of core mode transmission loss when refractive index of analyte increases from 1.33 to 1.34.

interrogation that follows the shift of resonant wavelength at which the core mode loss is highest to calculate the sensitivity of SPR sensor. Figure 7-4 shows the variation of attenuation spectrum when the analyte refractive index increases from 1.33 to 1.34. The resonant peak undergoes a redshift from 604 nm to 617 nm. We can also observe a considerable enhancement of the peak transmission loss.

7.2 Phase Birefringence and Sensing Accuracy

Considering a conventional solid core PCF with hexagonal-lattice arranged cladding holes. The diameter of the air holes is the same with that of the normal air holes in our proposed sensor, $1.75\ \mu\text{m}$ and the pitch is also $3.94\ \mu\text{m}$. Thin gold films are coated on the inner walls of first-ring air holes. As shown in Figure 7-5, SPP can be excited by both x- and y- polarized core mode since the thin gold layers coated on the inner walls of air holes are cylindrical. To investigate how the birefringence in fiber structure influences the divergence between the resonant dips corresponding to two orthogonal polarizations thereby offset the sensor output, we intentionally introduce birefringence by gradually enlarging the diameters of the two central holes in lateral direction. The thickness of thin gold layers is 50 nm and the refractive index of infiltrated analyte is set to be 1.38, since it is a typical refractive index of cytoplasm [274–276] and several types of proteins [277,278].

Figure 7-5. Mode patterns of (a) x- and (b) y-polarized core mode in conventional PCF with 50 nm gold layers and analyte refractive index of 1.38.

Figure 7-6 (a) shows the loss spectra of the SPR sensor when the ratio of the normal holes diameter d_1 and the enlarged holes diameter d_2 is 0.95. When $d_1/d_2 = 0.95$, a small phase birefringence of $\sim 2 \times 10^{-5}$ is introduced. The resonant wavelengths corresponding to x- and y-polarized core modes are 642.66 nm and 641.19 nm, respectively. There is not much difference between the peak losses of the two resonant dips. The overall resonant wavelength is 641.99 nm, which drifts 0.67 nm from that of

Figure 7-6. Loss spectra of MOF based SPR sensors when (a) $d_1/d_2=0.95$ (b) $d_1/d_2=0.4$ with analyte refractive index of 1.38.

the x-polarized mode. Therefore, the existence of the unwanted y-polarization would cause an offset of 0.67 nm that considerably compromises the accuracy of SPR sensor. On the other hand, Figure 7-6 (b) shows the loss spectra of our proposed high-birefringent MOF, i.e. $d_1/d_2 = 0.4$. It can be seen that the high birefringence significantly enlarges the difference between the intensities of the peak losses corresponding to the two orthogonal polarizations. SPP is mainly excited by x-polarized core mode as shown in Figure 7-2 (b). Hence the overall attenuation spectrum is predominated by that of x-polarized core mode. As a result, although the resonant wavelengths of x- and y-polarized modes are more divergent, the resonant wavelength offset is suppressed to be as small as 0.06 nm. The phase birefringence of $d_1/d_2 = 0.4$ is as large as $\sim 4.2 \times 10^{-4}$.

Figure 7-7. The relation between phase birefringence and the resonant wavelength offset.

The offset of the resonant wavelength of overall attenuation spectrum from that of x-polarized core mode is determined by phase birefringence. As the two central holes in lateral direction expanding, the wavelength offset experiences a rise and fall along

with the increasing phase birefringence. As shown in Figure 7-7, the wavelength offset increases to be as high as 18.89 nm when d_1/d_2 varies from 0.9 to 0.65, meanwhile the phase birefringence increases from $\sim 4 \times 10^{-5}$ to $\sim 1 \times 10^{-4}$. As the central holes dimension keeps increasing, the wavelength offset suddenly drops and tends towards 0 after the phase birefringence exceeds $\sim 4 \times 10^{-4}$. The resonant wavelengths of x- and y-polarized core modes are more and more separated as the phase birefringence increases. When the birefringence is relatively small, the overall resonant wavelength is drifted away from that of x-polarized core mode since the relative magnitude between two polarizations is not significant. The influence of y-polarized mode on the overall spectrum is considerable. After the birefringence exceeds a threshold, i.e. $\sim 2 \times 10^{-4}$, the wavelength offset is effectively reduced since the intensity of peak loss of y-polarized mode is much smaller than that of x-polarized mode. Even though the two resonant wavelengths keep drifting apart, the overall resonant wavelength quickly shifts back towards that of x-polarized core modes. That is the reason why the offset suddenly drops after $d_1/d_2 = 0.65$. Our proposed sensor provides a phase birefringence as high as $\sim 4.2 \times 10^{-4}$, which can suppress the wavelength offset to be extremely small.

7.3 Influencing Factors on SPR Behavior

We also investigate how the thickness of gold layer influences the SPR behaviors. Figure 7-8 (a) plots the loss spectra of our proposed sensor when the gold thickness is 50 nm, 60 nm, 70 nm and 100 nm. The thickening of gold layer shifts the resonance peak towards longer wavelengths, meanwhile significantly reduces its intensity especially when the thickness increases from 50 nm to 60 nm. Similar phenomenon has been reported in [279,280]. The decrease of peak loss intensity is due to the reduction of the penetration of electric field through the gold layer. The redshift of resonant wavelength along with gold layer thickening can be explained by Equation (24), that $\Delta\beta$ decreases as the metal layer thickness increases. Thereby the phase matching condition is satisfied at a longer wavelength, at which the mode effective indices are smaller. Although the intensity of SPP is highly dependent on the gold layer thickness, the sensitivity of our proposed SPR sensor is weakly affected. Figure 7-8 (b) compares the sensitivities when the gold thickness is 50 nm, 60 nm, 70 nm and 100 nm. We can

see that the resonant wavelength shifts can be fit into polynomial curves. The larger the analyte refractive index, the high the sensitivity is. According to Equation (25), the denominator consists of two terms with opposite signs, since $dn_p/d\lambda$, the material dispersion is negative. The second term slightly increases with increasing wavelength, hence the sensitivity is dominated by the first term of denominator. Hence the sensitivity is higher at longer wavelength, which corresponds to larger analyte

Figure 7-8. (a) Loss spectra and (b) Sensitivity curves of proposed SPR sensor when gold thickness is 50, 60, 70 and 100 nm respectively.

refractive index. Also, the parameters in Equation (25) are weekly affected by the thickness of gold layer. That explains why the sensitivity curves of 50 nm, 60 nm, 70 nm and 100 nm are nearly parallel. Within a relatively small refractive index range, the sensitivity can be considered to be linear. Within analyte refractive index of 1.37-1.38, the sensitivity of 50 nm, 60 nm, 70 nm and 100 nm are 3000, 3000, 3100 and 3100 nm/RIU respectively.

Besides effectively suppressing the impact of polarization crosstalk, the expanding of the two central holes also promotes the sensitivity of SPR sensor. Figure 7-9 compares the sensitivities of different central holes dimensions of $d_1/d_2 = 0.4$, $d_1/d_2 = 0.5$, $d_1/d_2 = 0.6$ and $d_1/d_2 = 1.0$. It shows that the more expanded central holes provide higher sensitivity, especially at relatively high refractive index range. Within refractive index of 1.37-1.38, the sensitivities corresponding to $d_1/d_2 = 1.0$, 0.6, 0.5 and 0.4 are 1900, 2500, 2800 and 3000 nm/RIU respectively. The improvement of sensitivity is due to the expanded interaction area between the guided light in fiber core and the infiltrated analyte in the enlarged holes. Also, the expanding of two central holes leads to a small lateral dimension of fiber, thus enhances the SPP intensity. Therefore compared with other hexagonal latticed non-birefringent PCF, our proposed sensor also shows advantages in sensitivity [160–162].

Figure 7-9. Sensitivity curves when $d_1/d_2 = 1.0$, 0.6, 0.5 and 0.4 respectively.

7.4 Summary

For the first time we investigate the relation between the phase birefringence and the resonant wavelength offset. Our results show that a phase birefringence higher than 4×10^{-4} can effectively suppress the wavelength offset caused by polarization crosstalk. Large phase birefringence can be introduced by expanding the two central holes in lateral direction. The proposed sensor could be easily fabricated by the stack-and-draw process and infiltrated with analyte in the enlarged microfluidic channels. Meanwhile, it also provides a sensitivity as high as 3100 nm/RIU.

Chapter 8 Summary and Future Work

8.1 Summary and Discussion

In this thesis, we integrate recent emerging functional nanomaterials with various fiber-optic platforms and explore their potentials in highly integrated and highly sensitive biosensing applications. We also analyze the proper designs of optical fiber structures to optimize the light-matter interaction meanwhile improve the measurement accuracy.

The first contribution is to develop a highly sensitive optical fiber based magnetic field sensor. Inspired by the emergence of magnetic nanoparticles enhanced biosensing schemes, optical fiber based accurate measurement of magnetic field strength responded by magnetic nanoparticles would pave the path to realize highly-integrated and all-fiber optomagnetic biosensing system. In this work, the fiber-optic magnetic field sensor is constructed by coating an LPG with magnetic fluid which possesses remarkable optomagnetic properties. When the magnetic-fluid-coated LPG is subjected to external magnetic field, the magnetic fluid undergoes phase transitions thereby varies the surrounding refractive index of LPG. Benefited from the acute response of LPG to the change of ambient medium, our proposed magnetic field sensor provides a sensitivity as high as 0.154 dB/Gauss, which is superior in the state-of-the-art fiber-optic magnetic field sensors.

The second contribution is to demonstrate a side-polished optical fiber based biosensing platform integrated with a graphene-on-gold hybrid plasmonic structure. In this work, we first carry out numerical analysis and found that depositing single-layer graphene on thin gold film effectively enhances the SPP strength as well as the plasmonic sensing performance. Then we experimentally verify that additional layer of graphene effectively improves the bulk refractive index sensitivity of conventional fiber-optic SPR sensor. Besides the SPP enhancement, the graphene sheet also serves as surface functionalization that stably adsorbs ssDNA molecules. The proposed biosensing platform provides a LOD of ssDNA as low as 1 pM. As a comparison, we

also conduct ssDNA detection using bare thin gold film coated side-polished fiber and find that LOD degrades to 1 nM, proving the huge prospect of integrating 2D materials with conventional SPR biosensor in achieving highly sensitive, highly integrated, miniaturized and flexible biosensors.

The third contribution is to explore the potentials of 2D TMOs in highly integrated plasmonic biosensing for the first time. We fabricate and characterize electron-rich 2D α -MoO_{3-x} nanoflakes with strong plasmon resonance in NIR range. Integrated with a microfiber, the α -MoO_{3-x} nanoflakes show good affinity to negatively charged protein molecules and promising plasmonic biosensing capability. A low LOD of BSA of 1 pg/mL is achieved. In addition, the Drude model parameters of quasi-metallic α -MoO_{3-x} are deduced via eigenmode analysis. Based on the deduced Drude model parameters, we carry out simulation and prove that the α -MoO_{3-x} nano-layer on microfiber surface strongly absorbs and confines the electric field, leading to improved biosensing capability.

The fourth contribution is to investigate the LSPR biosensing performance of β -CD-capped AuNPs in highly integrated fiber-optic device. We realize completely green synthesis of monodisperse β -CD-capped AuNPs. β -CDs serve as both reducing and capping agent during the synthesis process. The host-guest interaction between the β -CD cavities on AuNPs surface and the cholesterol molecules facilitates highly efficient immobilization of target cholesterol molecules. Meanwhile, the β -CD cavities with height less than 1 nm enables strong plasmon-matter interaction even comparable with 2D materials. Therefore, our proposed β -CD-capped AuNPs and microfiber based biosensing device achieves a LOD of cholesterol as low as 5 aM, meaning extremely low consumption of clinical samples in practical applications. Moreover, we conduct interference study and verify that common substances in human serum hardly interfere with the cholesterol detection.

The fifth contribution is to design a highly birefringent MOF that can effectively suppress the SPR sensing inaccuracy caused by polarization crosstalk. We carry out numerical analysis to figure out the relation between phase birefringence and SPR sensing output. It is shown that commonly existed phase birefringence in MOF based SPR sensor designs would induce considerable sensing offset. If the

birefringence is intentionally enlarged to beyond $\sim 2 \times 10^{-4}$, the sensing offset can be significantly reduced. Our proposed MOF based SPR sensor possesses a phase birefringence as high as $\sim 4.2 \times 10^{-4}$, which effectively suppresses the measurement offset to be negligible. Meanwhile, it provides a sensitivity of 3100 nm/RIU, which is comparable to those of the state-of-the-art MOF based SPR sensors.

8.2 Future Work

In the future work, we plan to fulfill following experiments:

1) *Synthesis of various morphologies of macrocyclic supramolecules modified AuNPs for biosensing.* In our work presented in Chapter 6, we synthesized monodisperse spherical AuNPs in an eco-friendly and facile way. Other morphologies of AuNPs such as gold nanorods and nanostars have not been synthesized by such eco-friendly and facile method. Gold nanorods and nanostars possess unique advantages in enhancing plasmon-matter interaction. The hotspots between two self-assembled gold nanorods and the intense field enhancement at sharp tips of gold nanostars facilitate more acute biomolecule detection. We plan to achieve facile synthesis of various gold nanostructures with macrocyclic supramolecules function as both reducing and capping agent. Not only CDs, other macrocyclic supramolecules such as pillar[n]arene, calix[n]arene and cucurbit[n]uril can also be explored for synthesizing biocompatible AuNPs without introducing harsh reagents. Different morphologies of AuNPs capped with a series of macrocyclic supramolecules can target for numerous guest biomolecules. Coupled with flexible optical fibers, we can achieve a versatile biosensing platform with high degree of integration, high sensitivity, good biocompatibility and numerous selective biomolecular recognitions.

2) *Green synthesis and biosensing of 2D plasmonic TMOs.* Our synthesis of MoO_{3-x} nanoflakes shown in Chapter 5 is realized by introducing strong reagent NaBH_4 , which degrades the biocompatibility of the biosensing device. A very recent research has reported the possibility of inducing and tuning the plasmonic properties of MoO_{3-x} nanoflakes in NIR range by employing ascorbic acid as a reducing agent [281]. We plan to explore the feasibility of synthesizing not only MoO_{3-x}

nanoflakes but also other few-layer TMOs (e.g. WO_3) in a mild environment, thus achieving biocompatible biosensing platforms. Moreover, the tunable plasmon resonance of 2D TMOs is an indicator of the concentration of mild reducing agents such as ascorbic acid. We will try to discover more kinds of proper biomolecules functioning as both reducing agent and target analyte that can be detected via tuning the plasmonic properties of 2D TMOs.

Publications

Journals

- **N.M.Y. Zhang**, K. Li, T. Zhang, P.P. Shum, Z. Wang, Z. Wang, N. Zhang, J. Zhang, T. Wu and L. Wei, “Electron-Rich Two-Dimensional Molybdenum Trioxides for Highly Integrated Plasmonic Biosensing,” *ACS Photonics* 5(2), (2018).

- **N.M.Y. Zhang**, K. Li, P.P. Shum, X. Yu, S. Zeng, Z. Wu, Q.J. Wang, K.T. Yong and L. Wei, “Hybrid Graphene/Gold Plasmonic Fiber-Optic Biosensor,” *Advanced Materials Technologies*, 2(2), (2017).

- **N.M.Y. Zhang**, D.J.J. Hu, Shum, Z. Wu, K. Li, T. Huang and L. Wei, “Design and analysis of surface plasmon resonance sensor based on high-birefringent microstructured optical fiber,” *Journal of Optics*, 18(6), 065005, (2016).

- **N.M.Y. Zhang**, X. Dong, P.P. Shum, D.J.J. Hu, H. Su, W. S. Lew and L. Wei, “Magnetic Field Sensor Based on Magnetic-Fluid-Coated Long-Period Fiber Grating,” *Journal of Optics*, 17(6), 065402 (2015).

- K. Li, N. Zhang, T. Zhang, Z. Wang, M. Chen, T. Wu, S. Ma, **N.M.Y. Zhang**, J. Zhang, U.S. Dinish, P.P. Shum, M. Olivo and L. Wei, “Ultra-flexible, conformal, and nano-patterned photonic surfaces via polymer cold-drawing,” *Journal of Materials Chemistry C* (2018).

- K. Li, **N.M.Y. Zhang**, N. Zhang, T. Zhang, G. Liu and L. Wei, “Spectral characteristics and ultrahigh sensitivity near the dispersion turning point of optical microfiber couplers,” *Journal of Lightwave Technology* PP(99), (2018).

- K. Li, N. Zhang, **N.M.Y. Zhang**, G. Liu, T. Zhang and L. Wei, “Ultrasensitive measurement of gas refractive index using an optical nanofiber coupler,” *Optics letters*, 43(4), (2018).

- J. Zhang, K. Li, T. Zhang, P.J.S Buenconsejo, M. Chen, Z. Wang, **N.M.Y. Zhang**, Z. Wang, and L. Wei, “Laser-Induced In-Fiber Fluid Dynamical Instabilities for Precise and Scalable Fabrication of Spherical Particles,” *Advanced Functional Materials*, 27(43), (2017).
- N. Zhang, G. Humbert, Z. Wu, K. Li, P.P. Shum, **N.M.Y. Zhang**, Y. Cui, J.L. Auguste, X.Q. Dinh and L. Wei, “In-line optofluidic refractive index sensing in a side-channel photonic crystal fiber,” *Optics Express*, 24(24), 27674-27682, (2016).
- K. Li, T. Zhang, G. Liu, N. Zhang, **N.M.Y. Zhang** and L. Wei, “Ultrasensitive optical microfiber coupler based sensors operating near the turning point of effective group index difference,” *Applied Physics Letters*, 109(10), 101101, (2016).
- K. Li, T. Zhang, N. Zhang, **N.M.Y. Zhang**, J. Zhang, T. Wu, S. Ma, J. Wu, M. Chen, Y. He and L. Wei, “Integrated liquid crystal photonic bandgap fiber devices,” *Frontiers of Optoelectronics*, 9(3), 466-482, (2016).

Conferences

- **N.M.Y. Zhang**, K. Li, T. Zhang, P. Shum, Z. Wang, Z. Wang, N. Zhang, J. Zhang, T. Wu and L. Wei, “Layered Molybdenum Trioxides as Two-Dimensional Plasmonic Material for Highly Integrated and Flexible Biosensing,” Accepted by *MRS Spring Meeting & Exhibit*, Materials Research Society, (2018).
- **N.M.Y. Zhang**, K.Li, P.P. Shum, X.Yu, S.Zeng, Z.Wu, Q. J. Wang, K.T. Yong and L. Wei, “Graphene Enhanced Surface Plasmon Resonance Fiber-Optic Biosensor,” In *CLEO: Science and Innovations* (SM4P-4), Optical Society of America (2016).
- **N.M.Y. Zhang**, D.J.J. Hu, P.P. Shum, Z. Wu, K. Li, T. Huang and L. Wei, “High-Birefringent Microstructured Optical Fiber Based Surface Plasmon Resonance Sensor,” In *CLEO: Applications and Technology* (JTU5A-116), Optical Society of America (2016).

- **N.M.Y. Zhang**, X. Dong, P.P. Shum, D.J.J. Hu, H. Su, W. S. Lew and L. Wei, “Highly Sensitive Magnetic Field Sensor Using Long-Period Fiber Grating,” In *Conference on Lasers and Electro-Optics/Pacific Rim (CLEO-PR)*, 27F2_3, Optical Society of America (2015).
- J. Zhang, K. Li, **N.M.Y. Zhang**, T. Zhang and L. Wei, “High-Q silicon microsphere whispering gallery mode resonator fabricated by laser induced in-fiber capillary instability,” In *Conference on Lasers and Electro-Optics/Pacific Rim (CLEO-PR)*, IEEE (2017).
- N. Zhang, G. Humbert, K. Li, Z. Wu, **N.M.Y. Zhang**, P.P. Shum, Y. Cui, J.L. Auguste, X.Q. Dinh and L. Wei, “In-Line Optofluidic Sensor Based on a Long-Period Grating in a Side-Channel Photonic Crystal Fiber,” In *CLEO: Science and Innovations (SM2P-2)*, Optical Society of America (2016).
- K. Li, T. Zhang, G. Liu, N. Zhang, **N.M.Y. Zhang** and L. Wei, “Extraordinary sensitivity in optical microfiber based refractive index sensors near the turning point of turning point of effective group index difference,” In *Asia Communications and Photonics Conference (AF1B-5)*, Optical Society of America (2016).

References

1. D. Dey and T. Goswami, "Optical biosensors: A revolution towards quantum nanoscale electronics device fabrication," *J. Biomed. Biotechnol.* **2011**, (2011).
2. A. Ricciardi, A. Crescitelli, P. Vaiano, G. Quero, M. Consales, M. Pisco, E. Esposito, and A. Cusano, "Lab-on-fiber technology: a new vision for chemical and biological sensing," *Analyst* **140**, 8068–8079 (2015).
3. A. François, Y. Zhi, and A. Meldrum, "Whispering gallery mode devices for sensing and biosensing," in *Springer Series in Materials Science* (2015), Vol. 229, pp. 237–288.
4. A. J. Haes and R. P. Van Duyne, "A unified view of propagating and localized surface plasmon resonance biosensors," *Anal. Bioanal. Chem.* **379**, 920–930 (2004).
5. Y. Yanase, T. Hiragun, K. Ishii, T. Kawaguchi, T. Yanase, M. Kawai, K. Sakamoto, and M. Hide, "Surface plasmon resonance for cell-based clinical diagnosis.," *Sensors (Basel)*. **14**, 4948–59 (2014).
6. G. A. Lopez, M. C. Estevez, M. Soler, and L. M. Lechuga, "Recent advances in nanoplasmonic biosensors: Applications and lab-on-a-chip integration," *Nanophotonics* **6**, 123–136 (2017).
7. T. Schuster, N. Neumanna, and C. Schäffer, "Miniaturized fiber-optic surface-plasmon-resonance sensor 7753_474," *21st Int. Conf. Opt. Fiber Sensors* (2011).
8. S. Roh, T. Chung, and B. Lee, "Overview of the characteristics of micro- and nano-structured surface plasmon resonance sensors," *Sensors* **11**, 1565–1588 (2011).
9. R. K. Verma and B. D. Gupta, "Theoretical modelling of a bi-dimensional U-shaped surface plasmon resonance based fibre optic sensor for sensitivity enhancement," *J. Phys. D-Applied Phys.* **41**, (2008).
10. A. Cusano, *Lab-on-Fiber Technology* (Springer Series in Surface Sciences 56,

- 2015).
11. H.-Y. Lin, C.-H. Huang, C.-C. Huang, Y.-C. Liu, and L.-K. Chau, "Multiple resonance fiber-optic sensor with time division multiplexing for multianalyte detection," *Opt. Lett.* **37**, 3969 (2012).
 12. Y. Peng, J. Hou, Z. Huang, and Q. Lu, "Temperature sensor based on surface plasmon resonance within selectively coated photonic crystal fiber," *Applied Opt.* **51**, 6361–6367 (2012).
 13. A. Hassani and M. Skorobogatiy, "Photonic crystal fiber-based plasmonic sensors for the detection of biolayer thickness," *J. Opt. Soc. Am. B* **26**, 1550 (2009).
 14. Y. Zhang, C. Zhou, L. Xia, X. Yu, and D. Liu, "Wagon wheel fiber based multichannel plasmonic sensor," *Opt. Express* **19**, 22863–73 (2011).
 15. S. Zeng, D. Baillargeat, H.-P. Ho, and K.-T. Yong, "Nanomaterials enhanced surface plasmon resonance for biological and chemical sensing applications," *Chem. Soc. Rev.* **43**, 3426 (2014).
 16. X. Luo, T. Qiu, W. Lu, and Z. Ni, "Plasmons in graphene: Recent progress and applications," *Mater. Sci. Eng. R Reports* **74**, 351–376 (2013).
 17. D. Rodrigo, O. Limaj, D. Janner, D. Etezadi, F. J. García De Abajo, V. Pruneri, and H. Altug, "Mid-infrared plasmonic biosensing with graphene," *Science* (80-.). **349**, 165–168 (2015).
 18. L. Ju, B. Geng, J. Horng, C. Girit, M. Martin, Z. Hao, H. A. Bechtel, X. Liang, A. Zettl, Y. R. Shen, and F. Wang, "Graphene plasmonics for tunable terahertz metamaterials," *Nat. Nanotechnol.* **6**, 630–634 (2011).
 19. F. H. L. Koppens, D. E. Chang, and F. J. García De Abajo, "Graphene plasmonics: A platform for strong light-matter interactions," *Nano Lett.* **11**, 3370–3377 (2011).
 20. D. Rodrigo, O. Limaj, D. Janner, D. Etezadi, F. J. Garcia de Abajo, V. Pruneri, and H. Altug, "Mid-infrared plasmonic biosensing with graphene," *Science*

- (80-). **349**, 165–168 (2015).
21. E. Faridi, M. Moradi, N. Ansari, A. H. B. Ghasemi, A. Afshar, and S. M. Mohseni, "Au/NiFe/M(Au, MoS₂, graphene) trilayer magnetoplasmonics DNA-hybridized sensors with high record of sensitivity," *J. Biomed. Opt.* **22**, (2017).
 22. S. H. El-Gohary, N.-H. Kim, and K. M. Byun, "Optical determination of thick graphene layer number based on surface plasmon resonance," *J. Nanophotonics* **7**, 073799 (2013).
 23. L. Wu, H. S. Chu, W. S. Koh, and E. P. Li, "Highly sensitive graphene biosensors based on surface plasmon resonance," *Opt. Express* **18**, 14395–14400 (2010).
 24. P. K. Maharana and R. Jha, "Chalcogenide prism and graphene multilayer based surface plasmon resonance affinity biosensor for high performance," *Sensors Actuators, B Chem.* **169**, 161–166 (2012).
 25. N. F. Chiu, S. Y. Fan, C. Du Yang, and T. Y. Huang, "Carboxyl-functionalized graphene oxide composites as SPR biosensors with enhanced sensitivity for immunoaffinity detection," *Biosens. Bioelectron.* **89**, 370–376 (2017).
 26. B. Meshginqalam, H. Toloue, M. T. Ahmadi, A. Sabatyan, A. Centeno, and R. Ismail, "Graphene embedded surface plasmon resonance based sensor prediction model," *Opt. Quantum Electron.* **48**, (2016).
 27. H. Zhang, Y. Sun, S. Gao, J. Zhang, H. Zhang, and D. Song, "A novel graphene oxide-based surface plasmon resonance biosensor for immunoassay," *Small* **9**, 2537–2540 (2013).
 28. Y. Ryu, S. Moon, Y. Oh, Y. Kim, T. Lee, D. H. Kim, and D. Kim, "Effect of coupled graphene oxide on the sensitivity of surface plasmon resonance detection," *Appl. Opt.* **53**, 1419 (2014).
 29. Y. V. Stebunov, O. A. Aftenieva, A. V. Arsenin, and V. S. Volkov, "Highly Sensitive and Selective Sensor Chips with Graphene-Oxide Linking Layer," *ACS Appl. Mater. Interfaces* **7**, 21727–21734 (2015).

30. J. B. Maurya, Y. K. Prajapati, V. Singh, and J. P. Saini, "Sensitivity enhancement of surface plasmon resonance sensor based on graphene-MoS₂ hybrid structure with TiO₂-SiO₂ composite layer," *Appl. Phys. a-Materials Sci. Process.* **121**, 525–533 (2015).
31. S. Zeng, S. Hu, J. Xia, T. Anderson, X.-Q. Dinh, X.-M. Meng, P. Coquet, and K.-T. Yong, "Graphene–MoS₂ hybrid nanostructures enhanced surface plasmon resonance biosensors," *Sensors Actuators B Chem.* **207**, 801–810 (2015).
32. J. B. Maurya, Y. K. Prajapati, V. Singh, J. P. Saini, and R. Tripathi, "Performance of graphene–MoS₂ based surface plasmon resonance sensor using Silicon layer," *Opt. Quantum Electron.* **47**, 3599–3611 (2015).
33. K. Manthiram and A. P. Alivisatos, "Tunable localized surface plasmon resonances in tungsten oxide nanocrystals," *J. Am. Chem. Soc.* **134**, 3995–3998 (2012).
34. H. Cheng, M. Wen, X. Ma, Y. Kuwahara, K. Mori, Y. Dai, B. Huang, and H. Yamashita, "Hydrogen Doped Metal Oxide Semiconductors with Exceptional and Tunable Localized Surface Plasmon Resonances," *J. Am. Chem. Soc.* **138**, 9316–9324 (2016).
35. H. Cheng, T. Kamegawa, K. Mori, and H. Yamashita, "Surfactant-free nonaqueous synthesis of plasmonic molybdenum oxide nanosheets with enhanced catalytic activity for hydrogen generation from ammonia borane under visible light," *Angew. Chemie - Int. Ed.* **53**, 2910–2914 (2014).
36. M. M. Y. A. Alsaif, S. Balendhran, M. R. Field, K. Latham, W. Wlodarski, J. Z. Ou, and K. Kalantar-Zadeh, "Two dimensional α -MoO₃ nanoflakes obtained using solvent-assisted grinding and sonication method: Application for H₂ gas sensing," *Sensors Actuators, B Chem.* **192**, 196–204 (2014).
37. M. M. Y. A. Alsaif, M. R. Field, T. Daeneke, A. F. Chrimes, W. Zhang, B. J. Carey, K. J. Berean, S. Walia, J. Van Embden, B. Zhang, K. Latham, K. Kalantar-Zadeh, and J. Z. Ou, "Exfoliation solvent dependent plasmon resonances in two-dimensional sub-stoichiometric molybdenum oxide nanoflakes," *ACS Appl. Mater. Interfaces* **8**, 3482–3493 (2016).

38. W. Liu, Q. Xu, W. Cui, C. Zhu, and Y. Qi, "CO₂-Assisted Fabrication of Two-Dimensional Amorphous Molybdenum Oxide Nanosheets for Enhanced Plasmon Resonances," *Angew. Chemie - Int. Ed.* **56**, 1600–1604 (2017).
39. H. Cheng, X. Qian, Y. Kuwahara, K. Mori, and H. Yamashita, "A Plasmonic Molybdenum Oxide Hybrid with Reversible Tunability for Visible-Light-Enhanced Catalytic Reactions," *Adv. Mater.* **27**, 4616–4621 (2015).
40. E. G. Lee, K. M. Park, J. Y. Jeong, S. H. Lee, J. E. Baek, H. W. Lee, J. K. Jung, and B. H. Chung, "Carbon nanotube-assisted enhancement of surface plasmon resonance signal," *Anal. Biochem.* **408**, 206–211 (2011).
41. C. M. Cobley, J. Chen, E. C. Cho, L. V. Wang, and Y. Xia, "Gold nanostructures: A class of multifunctional materials for biomedical applications," *Chem. Soc. Rev.* **40**, 44–56 (2011).
42. X. Ma and Y. Zhao, "Biomedical Applications of Supramolecular Systems Based on Host-Guest Interactions," *Chem. Rev.* **115**, 7794–7839 (2015).
43. P. F. Andrade, A. F. de Faria, D. S. da Silva, J. A. Bonacin, and M. do C. Goncalves, "Structural and morphological investigations of beta-cyclodextrin-coated silver nanoparticles.," *Colloids Surf. B. Biointerfaces* **118**, 289–297 (2014).
44. D. Wen, W. Liu, A. K. Herrmann, D. Haubold, M. Holzschuh, F. Simon, and A. Eychmüller, "Simple and Sensitive Colorimetric Detection of Dopamine Based on Assembly of Cyclodextrin-Modified Au Nanoparticles," *Small* **12**, 2439–2442 (2016).
45. S. Pande, S. K. Ghosh, S. Praharaj, S. Panigrahi, S. Basu, S. Jana, A. Pal, T. Tsukuda, and T. Pal, "Synthesis of normal and inverted gold-silver core-shell architectures in β -cyclodextrin and their applications in SERS," *J. Phys. Chem. C* **111**, 10806–10813 (2007).
46. H. Li, D. X. Chen, Y. L. Sun, Y. B. Zheng, L. L. Tan, P. S. Weiss, and Y. W. Yang, "Viologen-mediated assembly of and sensing with carboxylatopillar[5]arene- modified gold nanoparticles," *J. Am. Chem. Soc.* **135**,

- 1570–1576 (2013).
47. T. Huang, F. Meng, and L. Qi, "Facile Synthesis and One-Dimensional Assembly of Cyclodextrin-Capped Gold Nanoparticles and Their Applications in Catalysis and Surface-Enhanced Raman Scattering," *J. Phys. Chem. C* **113**, 13636–13642 (2009).
 48. T. Premkumar and K. E. Geckeler, "Facile synthesis of silver nanoparticles using unmodified cyclodextrin and their surface-enhanced Raman scattering activity," *New J. Chem.* **38**, 2847 (2014).
 49. V. I. Bhoi, S. Kumar, and C. N. Murthy, "Cyclodextrin encapsulated monometallic and inverted core–shell bimetallic nanoparticles as efficient free radical scavengers," *New J. Chem.* **40**, 1396–1402 (2016).
 50. J. R. Lakkakula, D. Divakaran, M. Thakur, M. K. Kumawat, and R. Srivastava, "Cyclodextrin-stabilized Gold nanoclusters for bioimaging and selective label-free intracellular sensing of Co^{2+} ions," *Sensors Actuators, B Chem.* **262**, 270–281 (2018).
 51. Y. Teramura, Y. Arima, and H. Iwata, "Surface plasmon resonance-based highly sensitive immunosensing for brain natriuretic peptide using nanobeads for signal amplification," *Anal. Biochem.* **357**, 208–215 (2006).
 52. S. Krishnan, V. Mani, D. Wasalathanthri, C. V. Kumar, and J. F. Rusling, "Attomolar detection of a cancer biomarker protein in serum by surface plasmon resonance using superparamagnetic particle labels," *Angew. Chemie - Int. Ed.* **50**, 1175–1178 (2011).
 53. Y. Wang, W. Knoll, and J. Dostalek, "Bacterial pathogen surface plasmon resonance biosensor advanced by long range surface plasmons and magnetic nanoparticle assays," *Anal. Chem.* **84**, 8345–8350 (2012).
 54. D. M. Bruls, T. H. Evers, J. a H. Kahlman, P. J. W. van Lankvelt, M. Ovsyanko, E. G. M. Pelssers, J. J. H. B. Schleipen, F. K. de Theije, C. a Verschuren, T. van der Wijk, J. B. a van Zon, W. U. Dittmer, a H. J. Immink, J. H. Nieuwenhuis, and M. W. J. Prins, "Rapid integrated biosensor for multiplexed immunoassays

- based on actuated magnetic nanoparticles.," *Lab Chip* **9**, 3504–3510 (2009).
55. R. Gao, Y. Jiang, and S. Abdelaziz, "All-fiber magnetic field sensors based on magnetic fluid-filled photonic crystal fibers.," *Opt. Lett.* **38**, 1539–41 (2013).
 56. W. Lin, Y. Miao, H. Zhang, B. Liu, Y. Liu, and B. Song, "Fiber-optic in-line magnetic field sensor based on the magnetic fluid and multimode interference effects," *Appl. Phys. Lett.* **103**, (2013).
 57. J. Zheng, X. Dong, P. Zu, J. Ji, H. Su, and P. Ping Shum, "Intensity-modulated magnetic field sensor based on magnetic fluid and optical fiber gratings," *Appl. Phys. Lett.* **103**, 1–5 (2013).
 58. Y. Miao, J. Wu, W. Lin, K. Zhang, Y. Yuan, B. Song, H. Zhang, B. Liu, and J. Yao, "Magnetic field tunability of optical microfiber taper integrated with ferrofluid," *Opt. Express* **21**, 29914–29920 (2013).
 59. J. M. P. Coelho, C. Silva, M. Nespereira, M. Abreu, and J. Rebordão, "Writing of Long Period Fiber Gratings Using CO₂ Laser Radiation," *Adv. Opt. Fiber Technol. Fundam. Opt. Phenom. Appl.* (2015).
 60. S. W. James and R. P. Tatam, "Optical fibre long-period grating sensors: characteristics and application," *Meas. Sci. Technol.* **14**, R49–R61 (2003).
 61. R. Hou, Z. Ghassemlooy, A. Hassan, C. Lu, and K. P. Dowker, "Modelling of long-period fibre grating response to refractive index higher than that of cladding," *Meas. Sci. Technol.* **12**, 1709–1713 (2001).
 62. J. H. Chong, P. Shum, H. Haryono, A. Yohana, M. K. Rao, C. Lu, and Y. Zhu, "Measurements of refractive index sensitivity using long-period grating refractometer," *Opt. Commun.* **229**, 65–69 (2004).
 63. V. Bhatia and a M. Vengsarkar, "Optical fiber long-period grating sensors.," *Opt. Lett.* **21**, 692–694 (1996).
 64. B. H. Lee, Y. Liu, S. B. Lee, S. S. Choi, and J. N. Jang, "Displacements of the resonant peaks of a long-period fiber grating induced by a change of ambient refractive index.," *Opt. Lett.* **22**, 1769–1771 (1997).

65. H. Young-Geun, "Dependence of the Refractive Index of a Coating on a Long-Period Fiber Grating on the Initial Coupling Strength," *J. Korean Phys. Soc.* **55**, 2621 (2009).
66. S. W. J. and R. P. Tatam, "Optical fibre long-period grating sensors: characteristics and application," *Meas. Sci. Technol.* **14**, R49 (2003).
67. M. Jung, J. Koo, J. Park, Y.-W. Song, Y. M. Jhon, K. Lee, S. Lee, and J. H. Lee, "Mode-locked pulse generation from an all-fiberized, Tm-Ho-codoped fiber laser incorporating a graphene oxide-deposited side-polished fiber," *Opt. Express* **21**, 20062 (2013).
68. Y. W. Song, S. Y. Jang, W. S. Han, and M. K. Bae, "Graphene mode-lockers for fiber lasers functioned with evanescent field interaction," *Appl. Phys. Lett.* **96**, (2010).
69. J. Lee, J. Koo, P. Debnath, Y.-W. Song, and J. H. Lee, "A Q -switched, mode-locked fiber laser using a graphene oxide-based polarization sensitive saturable absorber," *Laser Phys. Lett.* **10**, 035103 (2013).
70. S. G. Lee, J. P. Sokoloff, B. P. McGinnis, and H. Sasabe, "Fabrication of a side-polished fiber polarizer with a birefringent polymer overlay," *Opt. Lett.* **22**, 606–608 (1997).
71. Q. Bao, H. Zhang, B. Wang, Z. Ni, C. H. Y. X. Lim, Y. Wang, D. Y. Tang, and K. P. Loh, "Broadband graphene polarizer," *Nat. Photonics* **5**, 411–415 (2011).
72. R. Slavík, J. Homola, J. Tyroky, and E. Brynda, "Novel spectral fiber optic sensor based on surface plasmon resonance," *Sensors Actuators, B Chem.* **74**, 106–111 (2001).
73. W. G. Jung, S. W. Kim, K. T. Kim, E. S. Kim, and S. W. Kang, "High-sensitivity temperature sensor using a side-polished single-mode fiber covered with the polymer planar waveguide," *IEEE Photonics Technol. Lett.* **13**, 1209–1211 (2001).
74. A. O. Dikovska, P. A. Atanasov, A. T. Andreev, B. S. Zafirova, E. I. Karakoleva, and T. R. Stoyanchov, "ZnO thin film on side polished optical fiber for gas

- sensing applications," *Appl. Surf. Sci.* **254**, 1087–1090 (2007).
75. M. Yang, H. Liu, D. Zhang, and X. Tong, "Hydrogen sensing performance comparison of Pd layer and Pd/WO₃ composite thin film coated on side-polished single- and multimode fibers," *Sensors Actuators, B Chem.* **149**, 161–164 (2010).
 76. H.-Y. Lin, W.-H. Tsai, Y.-C. Tsao, and B.-C. Sheu, "Side-polished multimode fiber biosensor based on surface plasmon resonance with halogen light.," *Appl. Opt.* **46**, 800–806 (2007).
 77. J. Dai, M. Yang, Y. Chen, K. Cao, H. Liao, and P. Zhang, "Side-polished fiber Bragg grating hydrogen sensor with WO₃-Pd composite film as sensing materials.," *Opt. Express* **19**, 6141–6148 (2011).
 78. H. S. Jang, K. N. Park, J. P. Kim, S. J. Sim, O. J. Kwon, Y.-G. Han, and K. S. Lee, "Sensitive DNA biosensor based on a long-period grating formed on the side-polished fiber surface," *Opt. Express* **17**, 3855–3860 (2009).
 79. J. Tang, J. Zhou, J. Guan, S. Long, J. Yu, H. Guan, H. Lu, Y. Luo, J. Zhang, and Z. Chen, "Fabrication of Side-Polished Single Mode-Multimode-Single Mode Fiber and Its Characteristics of Refractive Index Sensing," *IEEE J. Sel. Top. Quantum Electron.* **23**, (2017).
 80. M. R. R. Khan, B.-H. Kang, S.-W. Lee, S.-H. Kim, S.-H. Yeom, S.-H. Lee, and S.-W. Kang, "Fiber-optic multi-sensor array for detection of low concentration volatile organic compounds," *Opt. Express* **21**, 20119 (2013).
 81. S. K. Liaw, J. Y. Chiu, and S. M. Tseng, "Precision side-polished fibers with a long interaction length," *Japanese J. Appl. Physics, Part 2 Lett.* **36**, (1997).
 82. M. R. R. Khan, B. H. Kang, S. H. Yeom, D. H. Kwon, and S. W. Kang, "Fiber-optic pulse width modulation sensor for low concentration VOC gas," *Sensors Actuators, B Chem.* **188**, 689–696 (2013).
 83. S.-M. Tseng and C.-L. Chen, "Side-polished fibers," *Appl. Opt.* **31**, 3438 (1992).
 84. W. Cao and Y. Duan, "Optical fiber-based evanescent ammonia sensor," *Sensors*

- Actuators, *B Chem.* **110**, 252–259 (2005).
85. X. Wu and L. Tong, "Optical microfibers and nanofibers," *Nanophotonics* **2**, 407–428 (2013).
 86. T. A. Birks, I. Gris-Sánchez, S. Yerolatsitis, S. G. Leon-Saval, and R. R. Thomson, "The photonic lantern," *Adv. Opt. Photonics* **7**, 107 (2015).
 87. R. Garcia-Fernandez, W. Alt, F. Bruse, C. Dan, K. Karapetyan, O. Rehband, A. Stiebeiner, U. Wiedemann, D. Meschede, and A. Rauschenbeutel, "Optical nanofibers and spectroscopy," *Appl. Phys. B Lasers Opt.* **105**, 3–15 (2011).
 88. J. D. Love, W. M. Henry, W. J. Stewart, R. J. Black, S. Lacroix, and F. Gonthier, "Tapered single-mode fibres and devices. I. Adiabaticity criteria," *Optoelectron. IEE Proc. J* **138**, 343–354 (1991).
 89. M. I. Zibaii, H. Latifi, Z. Saeedian, and Z. Chenari, "Nonadiabatic tapered optical fiber sensor for measurement of antimicrobial activity of silver nanoparticles against *Escherichia coli*," *J. Photochem. Photobiol. B Biol.* **135**, 55–64 (2014).
 90. P. Lu, J. Harris, X. Wang, G. Lin, L. Chen, and X. Bao, "Tapered-fiber-based refractive index sensor at an air/solution interface.," *Appl. Opt.* **51**, 7368–73 (2012).
 91. W. Bin Ji, H. H. Liu, S. C. Tjin, K. K. Chow, and A. Lim, "Ultrahigh sensitivity refractive index sensor based on optical microfiber," *IEEE Photonics Technol. Lett.* **24**, 1872–1874 (2012).
 92. T. A. Birks and Y. W. Li, "The Shape of Fiber Tapers," *J. Light. Technol.* **10**, 432–438 (1992).
 93. H. G. Cha, C. W. Kim, S. W. Kang, B. K. Kim, and Y. S. Kang, "Preparation and Characterization of the Magnetic Fluid of Trimethoxyhexadecylsilane-Coated Fe₃O₄ Nanoparticles," *J. Phys. Chem. C* **114**, 9802–9807 (2010).
 94. S. Odenbach, "Ferrofluids - Magnetically controlled suspensions," in *Colloids and Surfaces A: Physicochemical and Engineering Aspects* (2003), Vol. 217, pp.

- 171–178.
95. A. Weddemann, I. Ennen, A. Regtmeier, C. Albon, A. Wolff, K. Eckstädt, N. Mill, M. K. H. Peter, J. Mattay, C. Plattner, N. Sewald, and A. Hütten, "Review and outlook: From single nanoparticles to self-assembled monolayers and granular GMR sensors," *Beilstein J. Nanotechnol.* **75** (2010).
 96. D. Jin and H. Kim, "Magnetization of magnetite ferrofluid studied by using a magnetic balance," *Bull. Korean Chem. Soc.* **34**, 1715–1721 (2013).
 97. A. Skumiel, A. Józefczak, T. Hornowski, and M. Labowski, "The influence of the concentration of ferroparticles in a ferrofluid on its magnetic and acoustic properties," *J. Phys. D. Appl. Phys.* **36**, 3120 (2003).
 98. X. Fang, Y. Xuan, and Q. Li, "Theoretical investigation of the extinction coefficient of magnetic fluid," *J. Nanoparticle Res.* **15**, (2013).
 99. D. Heinrich, A. R. Goñi, and C. Thomsen, "Dynamics of magnetic-field-induced clustering in ionic ferrofluids from Raman scattering," *J. Chem. Phys.* **126**, (2007).
 100. M. F. Islam, K. H. Lin, D. Lacoste, T. C. Lubensky, and A. G. Yodh, "Field-induced structures in miscible ferrofluid suspensions with and without latex spheres," *Phys. Rev. E* **67**, 21402 (2003).
 101. S. Y. Yang, H. E. Horng, C. Y. Hong, and H. C. Yang, "Structures, optical properties and potentially electro-optical applications of magnetic fluid films," *Tamkang J. Sci. Eng.* **5**, 85–93 (2002).
 102. M. F. Islam, K. H. Lin, D. Lacoste, T. C. Lubensky, and A. G. Yodh, "Field-induced structures in miscible ferrofluid suspensions with and without latex spheres," *Phys. Rev. E - Stat. Physics, Plasmas, Fluids, Relat. Interdiscip. Top.* **67**, 8 (2003).
 103. Y. F. Chen, S. Y. Yang, W. S. Tse, H. E. Horng, C. Y. Hong, and H. C. Yang, "Thermal effect on the field-dependent refractive index of the magnetic fluid film," *Appl. Phys. Lett.* **82**, 3481–3483 (2003).

104. L. X. Chen, X. G. Huang, J. H. Zhu, G. C. Li, and S. Lan, "Fiber magnetic-field sensor based on nanoparticle magnetic fluid and Fresnel reflection," *Opt Lett* **36**, 2761–2763 (2011).
105. S. Y. Yang, Y. F. Chen, H. E. Horng, C. Y. Hong, W. S. Tse, and H. C. Yang, "Magnetically-modulated refractive index of magnetic fluid films," *Appl. Phys. Lett.* **81**, 4931–4933 (2002).
106. C. Y. Hong, H. E. Horng, and S. Y. Yang, "Tunable refractive index of magnetic fluids and its applications," in *Physica Status Solidi C: Conferences* (2004), Vol. 1, pp. 1604–1609.
107. H. Wang, S. Pu, N. Wang, S. Dong, and J. Huang, "Magnetic field sensing based on singlemode-multimode-singlemode fiber structures using magnetic fluids as cladding," *Opt. Lett.* **38**, 3765–8 (2013).
108. Y. Chen, Q. Han, T. Liu, X. Lan, and H. Xiao, "Optical fiber magnetic field sensor based on single-mode-multimode-single-mode structure and magnetic fluid.," *Opt. Lett.* **38**, 3999–4001 (2013).
109. J. Lenz and S. Edelstein, "Magnetic sensors and their applications," *Sensors Journal, IEEE* **6**, 631–649 (2006).
110. H. Eren and J. G. Webster, *Measurement, Instrumentation, and Sensors Handbook: Electromagnetic, Optical, Radiation, Chemical, and Biomedical Measurement* (CRC Press, 2014).
111. V. Kravljaca and S. E. Lyshevski, "Measuring spatiotemporal magnetic fields by hall effect sensors with post-processing solutions," in *2017 IEEE 37th International Conference on Electronics and Nanotechnology, ELNANO 2017 - Proceedings* (2017), pp. 61–66.
112. S. Tumanski, "Modern Magnetic Field Sensors – A Review," *PRZEGLĄD ELEKTROTECHNICZNY* **10**, (2013).
113. P. Ripka and M. Janošek, "Advances in magnetic field sensors," in *IEEE Sensors Journal* (2010).

114. Z. Wang, "Analysis of optical response of long period fiber gratings to nm-thick thin-film coatings," *Opt. Express* **13**, 2808–2813 (2005).
115. T. Liu, X. Chen, Z. Di, J. Zhang, X. Li, and J. Chen, "Tunable magneto-optical wavelength filter of long-period fiber grating with magnetic fluids," *Appl. Phys. Lett.* **91**, 2005–2008 (2007).
116. A. H. P. Ho, D. Kim, and M. G. Somekh, *Handbook of Photonics for Biomedical Engineering* (2017).
117. M. Li, S. K. Cushing, and N. Wu, "Plasmon-enhanced optical sensors: a review," *Analyst* **140**, 386–406 (2015).
118. G. R. Parkins, W. E. Lawrence, and R. W. Christy, "Intraband optical conductivity (T) of Cu, Ag, and Au: Contribution from electron-electron scattering," *Phys. Rev. B* **23**, 6408–6416 (1981).
119. S. A. Maier, *Plasmonics: Fundamentals and Applications* (2007).
120. J. M. Luther, P. K. Jain, T. Ewers, and A. P. Alivisatos, "Localized surface plasmon resonances arising from free carriers in doped quantum dots," *Nat. Mater.* **10**, 361–366 (2011).
121. A. V. Andrade-Neto, "Dielectric function for free electron gas: comparison between Drude and Lindhard models Função dielétrica de um gás de elétrons: comparação entre os modelos de Drude e de Lindhard," *Rev. Bras. Ensino Física* **39**, (2017).
122. F. Wooten, "Optical Properties of Solids," *Am. J. Phys.* **70**, 1269 (2002).
123. Y. Zhao, Z. Deng, and J. Li, "Photonic crystal fiber based surface plasmon resonance chemical sensors," *Sensors Actuators B Chem.* **202**, 557–567 (2014).
124. J. Jana, M. Ganguly, and T. Pal, "Enlightening surface plasmon resonance effect of metal nanoparticles for practical spectroscopic application," *RSC Adv.* **6**, 86174–86211 (2016).
125. B. Gauvreau, A. Hassani, M. Fassi Fehri, A. Kabashin, and M. a Skorobogatiy, "Photonic bandgap fiber-based Surface Plasmon Resonance sensors.," *Opt.*

- Express **15**, 11413–11426 (2007).
126. B. D. Gupta and R. K. Verma, "Surface plasmon resonance-based fiber optic sensors: Principle, probe designs, and some applications," *J. Sensors* **2009**, (2009).
 127. J. Homola, "On the sensitivity of surface plasmon resonance sensors with spectral interrogation," *Sensors Actuators B Chem.* **41**, 207–211 (1997).
 128. K. M. Mayer and J. H. Hafner, "Localized surface plasmon resonance sensors," *Chem. Rev.* **111**, 3828–3857 (2011).
 129. S. Peiris, J. McMurtrie, and H.-Y. Zhu, "Metal nanoparticle photocatalysts: emerging processes for green organic synthesis," *Catal. Sci. Technol.* **6**, 320–338 (2016).
 130. L. Guo, J. A. Jackman, H. H. Yang, P. Chen, N. J. Cho, and D. H. Kim, "Strategies for enhancing the sensitivity of plasmonic nanosensors," *Nano Today* **10**, 213–239 (2015).
 131. P. Zhao, N. Li, and D. Astruc, "State of the art in gold nanoparticle synthesis," *Coord. Chem. Rev.* **257**, 638–665 (2013).
 132. J. Turkevich, P. C. Stevenson, and J. Hillier, "A study of the nucleation and growth processes in the synthesis of colloidal gold," *Discuss. Faraday Soc.* **11**, 55–75 (1951).
 133. V. Mody, R. Siwale, A. Singh, and H. Mody, "Introduction to metallic nanoparticles," *J. Pharm. Bioallied Sci.* **2**, 282 (2010).
 134. M. Wang, P. Wang, J. Zhang, H. Hou, C. Li, and Y. Jin, "Pd/Ag nanosheet as a plasmonic sensing platform for sensitive assessment of hydrogen evolution reaction in colloid solutions," *Nano Res.* **11**, 2093–2103 (2018).
 135. F. Qadami, A. Molaeirad, M. Alijanianzadeh, A. Azizi, and N. Kamali, "Localized Surface Plasmon Resonance (LSPR)-Based Nanobiosensor for Methamphetamine Measurement," *Plasmonics* (2018).
 136. J. Kim, S. Y. Oh, S. Shukla, S. B. Hong, N. S. Heo, V. K. Bajpai, H. S. Chun,

- C. H. Jo, B. G. Choi, Y. S. Huh, and Y. K. Han, "Heteroassembled gold nanoparticles with sandwich-immunoassay LSPR chip format for rapid and sensitive detection of hepatitis B virus surface antigen (HBsAg)," *Biosens. Bioelectron.* **107**, 118–122 (2018).
137. Y.-T. Long and C. Jing, *Localized Surface Plasmon Resonance Based Nanobiosensors*. (2014).
138. J. A. Jackman, A. Rahim Ferhan, and N.-J. Cho, "Nanoplasmonic sensors for biointerfacial science," *Chem. Soc. Rev.* **46**, 3615–3660 (2017).
139. G. Liang, Z. Zhao, Y. Wei, K. Liu, W. Hou, and Y. Duan, "Plasma enhanced label-free immunoassay for alpha-fetoprotein based on a U-bend fiber-optic LSPR biosensor," *RSC Adv.* **5**, 23990–23998 (2015).
140. R. Dutta, R. Bharadwaj, S. Mukherji, and T. Kundu, "Study of localized surface-plasmon-resonance-based optical fiber sensor," *Appl. Opt.* **50**, E138 (2011).
141. H.-Y. Lin, C.-H. Huang, G.-L. Cheng, N.-K. Chen, and H.-C. Chui, "Tapered optical fiber sensor based on localized surface plasmon resonance.," *Opt. Express* **20**, 21693–701 (2012).
142. S. Link and M. A. El-Sayed, "Size and Temperature Dependence of the Plasmon Absorption of Colloidal Gold Nanoparticles," *J. Phys. Chem. B* **103**, 4212–4217 (1999).
143. E. K. Akowuah, T. Gorman, H. Ademgil, S. Haxha, G. K. Robinson, and J. V. Oliver, "Numerical analysis of a photonic crystal fiber for biosensing applications," *IEEE J. Quantum Electron.* **48**, 1403–1410 (2012).
144. X. Yu, Y. Zhang, S. Pan, P. Shum, M. Yan, Y. Leviatan, and C. Li, "A selectively coated photonic crystal fiber based surface plasmon resonance sensor," *J. Opt.* **12**, 015005 (2009).
145. Z. Tan, X. Li, Y. Chen, and P. Fan, "Improving the Sensitivity of Fiber Surface Plasmon Resonance Sensor by Filling Liquid in a Hollow Core Photonic Crystal Fiber," *Plasmonics* **9**, 167–173 (2014).

146. C. Caucheteur, T. Guo, and J. Albert, "Review of plasmonic fiber optic biochemical sensors: improving the limit of detection," *Anal. Bioanal. Chem.* **407**, 3883–3897 (2015).
147. T. Schuster, N. Neumann, and C. Schäffer, "Miniaturized fiber-optic surface-plasmon-resonance sensor," 77530W (2011).
148. C. Caucheteur, Y. Shevchenko, L.-Y. Shao, M. Wuilpart, and J. Albert, "High resolution interrogation of tilted fiber grating SPR sensors from polarization properties measurement.," *Opt. Express* **19**, 1656–1664 (2011).
149. M. D. Baiad, M. Gagné, W.-J. Madore, E. De Montigny, N. Godbout, C. Boudoux, and R. Kashyap, "Surface plasmon resonance sensor interrogation with a double-clad fiber coupler and cladding modes excited by a tilted fiber Bragg grating.," *Opt. Lett.* **38**, 4911–4 (2013).
150. D. J. Gentleman and K. S. Booksh, "Determining salinity using a multimode fiber optic surface plasmon resonance dip-probe," *Talanta* **68**, 504–515 (2006).
151. J. Pollet, F. Delport, D. T. Thi, M. Weversy, and J. Lammertyn, "Aptamer-Based Surface Plasmon Resonance Probe," in *Proceedings of IEEE Sensors* (2008), pp. 1187–1190.
152. S. K. Srivastava, R. Verma, and B. D. Gupta, "Surface plasmon resonance based fiber optic sensor for the detection of low water content in ethanol," *Sensors Actuators, B Chem.* **153**, 194–198 (2011).
153. T. Allsop, R. Neal, C. Mou, P. Brown, S. Rehman, K. Kalli, D. J. Webb, D. Mapps, and I. Bennion, "Multilayered coated infra-red surface plasmon resonance fibre sensors for aqueous chemical sensing," *Opt. Fiber Technol.* **15**, 477–482 (2009).
154. C. Te Huang, C. P. Jen, T. C. Chao, W. Te Wu, W. Y. Li, and L. K. Chau, "A novel design of grooved fibers for fiber-optic localized plasmon resonance biosensors," *Sensors* **9**, 6456–6470 (2009).
155. J. H. Ahn, T. Y. Seong, W. M. Kim, T. S. Lee, I. Kim, and K.-S. Lee, "Fiber-optic waveguide coupled surface plasmon resonance sensor," *Opt. Express* **20**,

- 21729 (2012).
156. M.-C. Navarrete, N. Díaz-Herrera, A. González-Cano, and Ó. Esteban, "Surface plasmon resonance in the visible region in sensors based on tapered optical fibers," *Sensors Actuators B Chem.* **190**, 881–885 (2014).
 157. T. Wieduwilt, K. Kirsch, J. Dellith, R. Willsch, and H. Bartelt, "Optical Fiber Micro-Taper with Circular Symmetric Gold Coating for Sensor Applications Based on Surface Plasmon Resonance," *Plasmonics* **8**, 545–554 (2013).
 158. S. K. Srivastava, V. Arora, S. Sapra, and B. D. Gupta, "Localized Surface Plasmon Resonance-Based Fiber Optic U-Shaped Biosensor for the Detection of Blood Glucose," *Plasmonics* **7**, 261–268 (2012).
 159. Y. Zhao, Z. Deng, and J. Li, "Photonic crystal fiber based surface plasmon resonance chemical sensors," *Sensors Actuators B Chem.* **202**, 557–567 (2014).
 160. L. Zheng, X. Zhang, X. Ren, J. Gao, L. Shi, X. Liu, Q. Wang, and Y. Huang, "Surface plasmon resonance sensors based on Ag-metalized nanolayer in microstructured optical fibers," *Opt. Laser Technol.* **43**, 960–964 (2011).
 161. W. Wei, X. Zhang, X. Guo, L. Zheng, J. Gao, W. Shi, Q. Wang, Y. Huang, and X. Ren, "Refractive index sensors based on Ag-metalized nanolayer in microstructured optical fibers," *Optik (Stuttg.)* **123**, 1167–1170 (2012).
 162. P. Bing, J. Yao, Y. Lu, and Z. Li, "A surface-plasmon-resonance sensor based on photonic-crystal-fiber with large size microfluidic channels," *Opt. Appl.* **42**, 493–501 (2012).
 163. B. Doherty, A. Csáki, M. Thiele, M. Zeisberger, A. Schwuchow, J. Kobelke, W. Fritzsche, and M. A. Schmidt, "Nanoparticle functionalised small-core suspended-core fibre – a novel platform for efficient sensing," *Biomed. Opt. Express* **8**, 790 (2017).
 164. A. A. Rifat, R. Ahmed, A. K. Yetisen, H. Butt, A. Sabouri, G. A. Mahdiraji, S. H. Yun, and F. R. M. Adikan, "Photonic crystal fiber based plasmonic sensors," *Sensors Actuators, B Chem.* **243**, 311–325 (2017).

165. A. Hassani and M. Skorobogatiy, "Design criteria for microstructured-optical-fiber-based surface-plasmon-resonance sensors," *J. Opt. Soc. Am. B* **24**, 1423 (2007).
166. A. Hassani and M. Skorobogatiy, "Photonic crystal fiber-based plasmonic sensors for the detection of biolayer thickness," *J. Opt. Soc. Am. B* **26**, 1550 (2009).
167. E. K. Akowuah, T. Gorman, H. Ademgil, and S. Haxha, "A highly sensitive photonic crystal fibre (PCF) surface plasmon resonance (SPR) sensor based on a bimetallic structure of gold and silver," *Proc. 2012 IEEE 4th Int. Conf. Adapt. Sci. Technol. ICAST 2012* 121–125 (2012).
168. N. Luan and J. Yao, "Surface Plasmon Resonance Sensor Based On Exposed-Core Microstructured Optical Fiber Placed With A Silver Wire," *IEEE Photonics J.* **8**, 1–8 (2016).
169. X. Yang, Y. Lu, M. Wang, and J. Yao, "SPR Sensor Based on Exposed-Core Grapefruit Fiber with Bimetallic Structure," *IEEE Photonics Technol. Lett.* **28**, 649–652 (2016).
170. M. Erdmanis, D. Viegas, M. Hautakorpi, S. Novotny, J. L. Santos, and H. Ludvigsen, "Comprehensive numerical analysis of a surface-plasmon-resonance sensor based on an H-shaped optical fiber," *Opt. Express* **19**, 13980–13988 (2011).
171. H.-Y. Lin, Y.-C. Tsao, W.-H. Tsai, Y.-W. Yang, T.-R. Yan, and B.-C. Sheu, "Development and application of side-polished fiber immunosensor based on surface plasmon resonance for the detection of *Legionella pneumophila* with halogens light and 850nm-LED," *Sensors Actuators A Phys.* **138**, 299–305 (2007).
172. R. Slavík, J. Homola, and E. Brynda, "A miniature fiber optic surface plasmon resonance sensor for fast detection of Staphylococcal enterotoxin B.," *Biosens. Bioelectron.* **17**, 591–595 (2002).
173. J. Pollet, F. Delport, K. P. F. Janssen, D. T. Tran, J. Wouters, T. Verbiest, and J.

- Lammertyn, "Fast and accurate peanut allergen detection with nanobead enhanced optical fiber SPR biosensor," *Talanta* **83**, 1436–1441 (2011).
174. L. Lipoprotein, R. Verma, S. K. Srivastava, and B. D. Gupta, "Surface-Plasmon-Resonance-Based Fiber-Optic Sensor for the Detection," *IEEE Sens. J.* **12**, 3460–3466 (2012).
175. Y. Shevchenko, T. J. Francis, D. A. D. Blair, R. Walsh, M. C. Derosa, and J. Albert, "In situ biosensing with a surface plasmon resonance fiber grating aptasensor," *Anal. Chem.* **83**, 7027–7034 (2011).
176. V. Voisin, J. Pilate, P. Damman, P. Mégret, and C. Caucheteur, "Highly sensitive detection of molecular interactions with plasmonic optical fiber grating sensors," *Biosens. Bioelectron.* **51**, 249–254 (2014).
177. B. Sciacca, A. François, P. Hoffmann, and T. M. Monroe, "Multiplexing of radiative-surface plasmon resonance for the detection of gastric cancer biomarkers in a single optical fiber," *Sensors Actuators, B Chem.* **183**, 454–458 (2013).
178. A. J. Mieszawska, W. J. M. Mulder, Z. A. Fayad, and D. P. Cormode, "Multifunctional gold nanoparticles for diagnosis and therapy of disease," *Mol. Pharm.* **10**, 831–847 (2013).
179. S. Tadepalli, Z. Kuang, Q. Jiang, K.-K. Liu, M. A. Fisher, J. J. Morrissey, E. D. Kharasch, J. M. Slocik, R. R. Naik, and S. Singamaneni, "Peptide Functionalized Gold Nanorods for the Sensitive Detection of a Cardiac Biomarker Using Plasmonic Paper Devices.," *Sci. Rep.* **5**, 16206 (2015).
180. M. Oliverio, S. Perotto, G. C. Messina, L. Lovato, and F. De Angelis, "Chemical Functionalization of Plasmonic Surface Biosensors: A Tutorial Review on Issues, Strategies, and Costs," *ACS Appl. Mater. Interfaces* **9**, 29394–29411 (2017).
181. O. R. Bolduc and J. F. Masson, "Advances in surface plasmon resonance sensing with nanoparticles and thin films: Nanomaterials, surface chemistry, and hybrid plasmonic techniques," *Anal. Chem.* **83**, 8057–8062 (2011).

182. S. Tadepalli, Z. Kuang, Q. Jiang, K. K. Liu, M. A. Fisher, J. J. Morrissey, E. D. Kharasch, J. M. Slocik, R. R. Naik, and S. Singamaneni, "Peptide Functionalized Gold Nanorods for the Sensitive Detection of a Cardiac Biomarker Using Plasmonic Paper Devices," *Sci. Rep.* **5**, (2015).
183. F. Ruffino, G. Meli, and M. G. Grimaldi, "Nanoscale electrical characteristics of metal (Au, Pd)-graphene-metal (Cu) contacts," *Solid State Commun.* **225**, 1–6 (2016).
184. Y. Liu, X. Dong, and P. Chen, "Biological and chemical sensors based on graphene materials," *Chem. Soc. Rev.* **41**, 2283 (2012).
185. M. Zhou, Z. Liu, W. Ming, Z. Wang, and F. Liu, "Sd2 Graphene: Kagome Band in a Hexagonal Lattice," *Phys. Rev. Lett.* **113**, (2014).
186. G. Lu, K. Yu, Z. Wen, and J. Chen, "Semiconducting graphene: Converting graphene from semimetal to semiconductor," *Nanoscale* **5**, 1353–1368 (2013).
187. J. A. Kim, T. Hwang, S. R. Dugasani, R. Amin, A. Kulkarni, S. H. Park, and T. Kim, "Graphene based fiber optic surface plasmon resonance for bio-chemical sensor applications," *Sensors Actuators, B Chem.* **187**, 426–433 (2013).
188. M. Bruna and S. Borini, "Optical constants of graphene layers in the visible range," *Appl. Phys. Lett.* **94**, (2009).
189. Y. Zhao, X. Li, X. Zhou, and Y. Zhang, "Review on the graphene based optical fiber chemical and biological sensors," *Sensors Actuators B Chem.* **231**, 324–340 (2016).
190. G.-D. J.S. and J. Perruisseau-Carrier, "Microwave to THz properties of graphene and potential antenna applications," *2012 Int. Symp. Antennas Propag.* 239–242 (2012).
191. G. W. Hanson, "Dyadic Green's functions and guided surface waves for a surface conductivity model of graphene," *J. Appl. Phys.* **103**, (2008).
192. K. Nagashio and A. Toriumi, "Density-of-states limited contact resistance in graphene field-effect transistors," *Jpn. J. Appl. Phys.* **50**, (2011).

193. G. Giovannetti, P. A. Khomyakov, G. Brocks, V. M. Karpan, J. Van Den Brink, and P. J. Kelly, "Doping graphene with metal contacts," *Phys. Rev. Lett.* **101**, (2008).
194. P. A. Khomyakov, G. Giovannetti, P. C. Rusu, G. Brocks, J. Van Den Brink, and P. J. Kelly, "First-principles study of the interaction and charge transfer between graphene and metals," *Phys. Rev. B - Condens. Matter Mater. Phys.* **79**, 1–12 (2009).
195. S. Zeng, K. V. Sreekanth, J. Shang, T. Yu, C. K. Chen, F. Yin, D. Baillargeat, P. Coquet, H. P. Ho, A. V. Kabashin, and K. T. Yong, "Graphene-Gold Metasurface Architectures for Ultrasensitive Plasmonic Biosensing," *Adv. Mater.* **27**, 6163–6169 (2015).
196. S. Zeng, K. V. Sreekanth, J. Shang, T. Yu, C. K. Chen, F. Yin, D. Baillargeat, P. Coquet, H. P. Ho, A. V. Kabashin, and K. T. Yong, "Graphene-Gold Metasurface Architectures for Ultrasensitive Plasmonic Biosensing," *Adv. Mater.* **27**, 6163–6169 (2015).
197. O. Salihoglu, S. Balci, and C. Kocabas, "Plasmon-polaritons on graphene-metal surface and their use in biosensors," *Appl. Phys. Lett.* **100**, (2012).
198. T. Xue, S. Yu, X. Zhang, X. Zhang, L. Wang, Q. Bao, C. Chen, W. Zheng, and X. Cui, "R6G molecule induced modulation of the optical properties of reduced graphene oxide nanosheets for use in ultrasensitive SPR sensing," *Sci. Rep.* **6**, (2016).
199. B. Song, D. Li, W. Qi, M. Elstner, C. Fan, and H. Fang, "Graphene on Au(111): A highly conductive material with excellent adsorption properties for high-resolution bio/nanodetection and identification," *ChemPhysChem* **11**, 585–589 (2010).
200. S. Tadepalli, Z. Kuang, Q. Jiang, K.-K. Liu, M. A. Fisher, J. J. Morrissey, E. D. Kharasch, J. M. Slocik, R. R. Naik, and S. Singamaneni, "Peptide Functionalized Gold Nanorods for the Sensitive Detection of a Cardiac Biomarker Using Plasmonic Paper Devices.," *Sci. Rep.* **5**, 16206 (2015).

201. M. M. Y. A. Alsaif, K. Latham, M. R. Field, D. D. Yao, N. V. Medhekar, G. A. Beane, R. B. Kaner, S. P. Russo, J. Z. Ou, and K. Kalantar-Zadeh, "Tunable plasmon resonances in two-dimensional molybdenum oxide nanoflakes," *Adv. Mater.* **26**, 3931–3937 (2014).
202. W. Liu, Q. Xu, W. Cui, C. Zhu, and Y. Qi, "Surface Plasmon Resonance Very Important Paper CO₂-Assisted Fabrication of Two-Dimensional Amorphous Molybdenum Oxide Nanosheets for Enhanced Plasmon Resonances Angewandte," **450052**, 1600–1604 (2017).
203. S. D. Lounis, E. L. Runnerstrom, A. Llordés, and D. J. Milliron, "Defect chemistry and Plasmon physics of colloidal metal oxide Nanocrystals," *J. Phys. Chem. Lett.* **5**, 1564–1574 (2014).
204. M. M. Y. A. Alsaif, S. Balendhran, M. R. Field, K. Latham, W. Wlodarski, J. Z. Ou, and K. Kalantar-Zadeh, "Two dimensional α -MoO₃ nanoflakes obtained using solvent-assisted grinding and sonication method: Application for H₂ gas sensing," *Sensors Actuators, B Chem.* **192**, 196–204 (2014).
205. K. Kazuto, W. Ryota, Y. Shinji, H. Yoshiyuki, S. Shigehiko, and Y. Mitsuaki, "Characteristics of MoO₃ films grown by molecular beam epitaxy," *Jpn. J. Appl. Phys.* **53**, 05FJ02 (2014).
206. J. Z. Ou, J. L. Campbell, D. Yao, W. Wlodarski, and K. Kalantar-Zadeh, "In situ Raman spectroscopy of H₂ gas interaction with layered MoO₃," *J. Phys. Chem. C* **115**, 10757–10763 (2011).
207. K. Kalantar-Zadeh, J. Tang, M. Wang, K. L. Wang, A. Shailos, K. Galatsis, R. Kojima, V. Strong, A. Lech, W. Wlodarski, and R. B. Kaner, "Synthesis of nanometre-thick MoO₃ sheets," *Nanoscale* **2**, 429–433 (2010).
208. K. Kalantar-zadeh, J. Z. Ou, T. Daeneke, A. Mitchell, T. Sasaki, and M. S. Fuhrer, "Two dimensional and layered transition metal oxides," *Appl. Mater. Today* **5**, 73–89 (2016).
209. M. B. Sreedhara, H. S. S. R. Matte, A. Govindaraj, and C. N. R. Rao, "Synthesis, characterization, and properties of few-layer moO₃," *Chem. - An Asian J.* **8**,

- 2430–2435 (2013).
210. J. Dagar, P. Tyagi, R. Ahmad, R. Singh, O. P. Sinha, C. K. Suman, and R. Srivastava, "Application of 2D-MoO₃ nano-flakes in organic light emitting diodes: effect of semiconductor to metal transition with irradiation," *Rsc Adv.* **5**, 8397–8403 (2015).
 211. M. M. Y. A. Alsaif, A. F. Chrimes, T. Daeneke, S. Balendhran, D. O. Bellisario, Y. Son, M. R. Field, W. Zhang, H. Nili, E. P. Nguyen, K. Latham, J. Van Embden, M. S. Strano, J. Z. Ou, and K. Kalantar-Zadeh, "High-Performance Field Effect Transistors Using Electronic Inks of 2D Molybdenum Oxide Nanoflakes," *Adv. Funct. Mater.* **26**, 91–100 (2016).
 212. S. Balendhran, S. Walia, M. Alsaif, E. P. Nguyen, J. Z. Ou, S. Zhuiykov, S. Sriram, M. Bhaskaran, and K. Kalantar-Zadeh, "Field effect biosensing platform based on 2D α -MoO₃," *ACS Nano* **7**, 9753–9760 (2013).
 213. X. Tan, L. Wang, C. Cheng, X. Yan, B. Shen, and J. Zhang, "Plasmonic MoO₃-x@MoO₃nanosheets for highly sensitive SERS detection through nanoshell-isolated electromagnetic enhancement," *Chem. Commun.* **52**, 2893–2896 (2016).
 214. H. S. Kim, J. B. Cook, H. Lin, J. S. Ko, S. H. Tolbert, V. Ozolins, and B. Dunn, "Oxygen vacancies enhance pseudocapacitive charge storage properties of MoO₃-x," *Nature Materials* (2016).
 215. M. M. Y. A. Alsaif, M. R. Field, B. J. Murdoch, T. Daeneke, K. Latham, A. F. Chrimes, A. S. Zoolfakar, S. P. Russo, J. Z. Ou, and K. Kalantar-Zadeh, "Substoichiometric two-dimensional molybdenum oxide flakes: A plasmonic gas sensing platform," *Nanoscale* **6**, 12780–12791 (2014).
 216. X. K. Hu, Y. T. Qian, Z. T. Song, J. R. Huang, R. Cao, and J. Q. Xiao, "Comparative Study on MoO₃ and HxMoO₃ Nanobelts: Structure and Electric Transport," *Chem. Mater.* **20**, 1527–1533 (2008).
 217. D. H. Qu, Q. C. Wang, Q. W. Zhang, X. Ma, and H. Tian, "Photoresponsive Host-Guest Functional Systems," *Chem. Rev.* **115**, 7543–7588 (2015).
 218. Y. W. Yang, Y. L. Sun, and N. Song, "Switchable host-guest systems on

- surfaces," *Acc. Chem. Res.* **47**, 1950–1960 (2014).
219. H. Li, D.-X. Chen, Y.-L. Sun, Y. B. Zheng, L.-L. Tan, P. S. Weiss, and Y.-W. Yang, "Viologen-mediated assembly of and sensing with carboxylatopillar[5]arene-modified gold nanoparticles.," *J. Am. Chem. Soc.* **135**, 1570–6 (2013).
 220. G. Yu, K. Jie, and F. Huang, "Supramolecular Amphiphiles Based on Host – Guest Molecular Recognition Motifs," *Chem. Rev* **115**, 7240–7303 (2015).
 221. J. Xie, T. Zuo, Z. Huang, L. Huan, Q. Gu, C. Gao, and J. Shao, "Theoretical study of a novel imino bridged pillar[5]arene derivative," *Chem. Phys. Lett.* **662**, 25–30 (2016).
 222. J. Lagona, P. Mukhopadhyay, S. Chakrabarti, and L. Isaacs, "The cucurbit[n]uril family," *Angew Chem Int Ed Engl* **44**, 4844–4870 (2005).
 223. H.-J. Schneider and A. K. Yatsimirsky, "Selectivity in supramolecular host–guest complexes," *Chem. Soc. Rev.* **37**, 263–277 (2008).
 224. E. Christoforides, A. Papaioannou, and K. Bethanis, "Crystal structure of the inclusion complex of cholesterol in β -cyclodextrin and molecular dynamics studies," *Beilstein J. Org. Chem.* **14**, 838–848 (2018).
 225. Y. Yu, C. Chipot, W. Cai, and X. Shao, "Molecular dynamics study of the inclusion of cholesterol into cyclodextrins," *J. Phys. Chem. B* **110**, 6372–6378 (2006).
 226. A. Sánchez, P. Díez, R. Villalonga, P. Martínez-Ruiz, M. Eguílaz, I. Fernández, and J. M. Pingarrón, "Seed-mediated growth of jack-shaped gold nanoparticles from cyclodextrin-coated gold nanospheres," *Dalt. Trans.* **42**, 14309–14314 (2013).
 227. Y. Zhao, Y. Huang, H. Zhu, Q. Zhu, and Y. Xia, "Three-in-One: Sensing, Self-Assembly, and Cascade Catalysis of Cyclodextrin Modified Gold Nanoparticles," *J. Am. Chem. Soc.* **138**, 16645–16654 (2016).
 228. R. Kashyap, *Fiber Bragg Gratings* (1999), Vol. 1.

229. D. J. J. Hu, J. L. Lim, M. Jiang, Y. Wang, F. Luan, P. P. Shum, H. Wei, and W. Tong, "Long period grating cascaded to photonic crystal fiber modal interferometer for simultaneous measurement of temperature and refractive index.," *Opt. Lett.* **37**, 2283–5 (2012).
230. S. Chaubey, P. Joshi, M. Kumar, R. Arya, A. K. Nath, and S. Kher, "Design and development of long-period grating sensors for temperature monitoring," *Sadhana - Acad. Proc. Eng. Sci.* **32**, 513–519 (2007).
231. S. Pu, X. Chen, Y. Chen, Y. Xu, W. Liao, L. Chen, and Y. Xia, "Fiber-optic evanescent field modulator using a magnetic fluid as the cladding," *J. Appl. Phys.* **99**, (2006).
232. Y. Zhao, L. Cai, X. G. Li, and F. C. Meng, "Liquid concentration measurement based on SMS fiber sensor with temperature compensation using an FBG," *Sensors Actuators, B Chem.* **196**, 518–524 (2014).
233. Y. S. Hsu and Y. J. Chiang, "Temperature compensation of optical fiber Bragg grating pressure sensor," *IEEE Photonics Technol. Lett.* **18**, 874–876 (2006).
234. C.-H. Chen, R. O. Reynolds, and A. Kost, "Origin of spectral modal noise in fiber-coupled spectrographs," *Appl. Opt.* **45**, 519 (2006).
235. A. Orth, M. Ploschner, I. S. Maksymov, and B. C. Gibson, "Extended depth of field imaging through multicore optical fibers," *Opt. Express* **26**, 6407–6419 (2018).
236. M. Grabka, B. Wajnchold, S. Pustelny, W. Gawlik, K. Skorupski, and P. Mergo, "Experimental and theoretical study of light propagation in suspended-core optical fiber," *Acta Phys. Pol. A* **118**, (2010).
237. L. Peng, F. Shi, G. Zhou, S. Ge, Z. Hou, and C. Xia, "A Surface Plasmon Biosensor Based on a D-Shaped Microstructured Optical Fiber With Rectangular Lattice," *IEEE Photonics J.* **7**, (2015).
238. Q. Liu, S. Li, H. Li, J. Zi, W. Zhang, Z. Fan, G. An, and Y. Bao, "Broadband Single-Polarization Photonic Crystal Fiber Based on Surface Plasmon Resonance for Polarization Filter," *Plasmonics* **10**, 931–939 (2015).

239. L. Zheng, X. Zhang, X. Ren, Y. Wang, X. Liu, and Y. Huang, "A comparison of Au and Ag metalized layer in Microstructured Optical Fibers for Surface Plasmon Resonance excitation," **7634**, 1–6 (2009).
240. Z. Tan, X. Hao, Y. Shao, Y. Chen, X. Li, and P. Fan, "Phase modulation and structural effects in a D-shaped all-solid photonic crystal fiber surface plasmon resonance sensor," *Opt. Express* (2014).
241. D. L. Mills, "Attenuation of surface polaritons by surface roughness," *Phys. Rev. B* **12**, 4036–4046 (1975).
242. K. M. Byun, S. J. Yoon, and D. Kim, "Effect of surface roughness on the extinction-based localized surface plasmon resonance biosensors.," *Appl. Opt.* **47**, 5886–92 (2008).
243. X. Li, Y. Zhu, W. Cai, M. Borysiak, B. Han, D. Chen, R. D. Piner, L. Colomba, and R. S. Ruoff, "Transfer of large-area graphene films for high-performance transparent conductive electrodes," *Nano Lett.* **9**, 4359–4363 (2009).
244. X. Li, W. Cai, J. An, S. Kim, J. Nah, D. Yang, R. Piner, A. Velamakanni, I. Jung, E. Tutuc, S. K. Banerjee, L. Colombo, and R. S. Ruoff, "Large-area synthesis of high-quality and uniform graphene films on copper foils," *Science* (80-.). **324**, 1312–1314 (2009).
245. S. Bhat, N. Curach, T. Mostyn, G. S. Bains, K. R. Griffiths, and K. R. Emslie, "Comparison of methods for accurate quantification of DNA mass concentration with traceability to the international system of units," *Anal. Chem.* **82**, 7185–7192 (2010).
246. A. Kumar, K. M. Pate, M. A. Moss, D. N. Dean, and V. Rangachari, "Self-propagative replication of A?? oligomers suggests potential transmissibility in Alzheimer disease," *PLoS One* **9**, (2014).
247. S. Singh, A. Kumar, S. Khare, A. Mulchandani, and Rajesh, "Single-walled carbon nanotubes based chemiresistive genosensor for label-free detection of human rheumatic heart disease," *Appl. Phys. Lett.* **105**, (2014).
248. M. Ootsubo, T. Shimizu, R. Tanaka, T. Sawabe, K. Tajima, M. Yoshimizu, Y.

- Ezura, T. Ezaki, and H. Oyaizu, "Oligonucleotide probe for detecting Enterobacteriaceae by in situ hybridization," *J. Appl. Microbiol.* **93**, 60–68 (2002).
249. I. V. Wesley, L. Schroeder-Tucker, A. L. Baetz, F. E. Dewhirst, and B. J. Paster, "Arcobacter-specific and Arcobacter butzleri-specific 16S rRNA-based DNA probes," *J. Clin. Microbiol.* **33**, 1691–1698 (1995).
250. M. M. Y. A. Alsaif, M. R. Field, T. Daeneke, A. F. Chrimes, W. Zhang, B. J. Carey, K. J. Berean, S. Walia, J. Van Embden, B. Zhang, K. Latham, K. Kalantar-Zadeh, and J. Z. Ou, "Exfoliation solvent dependent plasmon resonances in two-dimensional sub-stoichiometric molybdenum oxide nanoflakes," *ACS Appl. Mater. Interfaces* **8**, 3482–3493 (2016).
251. I. Shakir, M. Shahid, H. W. Yang, and D. J. Kang, "Structural and electrochemical characterization of γ -MoO₃ nanorod-based electrochemical energy storage devices," *Electrochim. Acta* **56**, 376–380 (2010).
252. X. Liu, J.-H. Kang, H. Yuan, J. Park, S. J. Kim, Y. Cui, H. Y. Hwang, and M. L. Brongersma, "Electrical tuning of a quantum plasmonic resonance," *Nat. Nanotechnol.* (2017).
253. V. Prabhakaran, B. L. Mehdi, J. J. Ditto, M. H. Engelhard, B. Wang, K. D. D. Gunaratne, D. C. Johnson, N. D. Browning, G. E. Johnson, and J. Laskin, "Rational design of efficient electrode–electrolyte interfaces for solid-state energy storage using ion soft landing," *Nat. Commun.* **7**, 11399 (2016).
254. S. Balendhran, S. Walia, M. Alsaif, E. P. Nguyen, J. Z. Ou, S. Zhuiykov, S. Sriram, M. Bhaskaran, and K. Kalantar-Zadeh, "Field effect biosensing platform based on 2D γ -MoO₃," *ACS Nano* **7**, 9753–9760 (2013).
255. K. D. Vernon-Parry, "Scanning electron microscopy: an introduction," *III-Vs Rev.* **13**, 40–44 (2000).
256. J. Goldstein, D. E. Newbury, D. C. Joy, C. E. Lyman, P. Echlin, E. Lifshin, L. Sawyer, and J. R. Michael, *Scanning Electron Microscopy and X-Ray Microanalysis* (2003), Vol. 44.

257. W. Bin Ji, H. H. Liu, S. C. Tjin, K. K. Chow, and A. Lim, "Ultrahigh sensitivity refractive index sensor based on optical microfiber," *IEEE Photonics Technol. Lett.* **24**, 1872–1874 (2012).
258. W. Bin Ji, Y. C. Tan, B. Lin, S. C. Tjin, and K. K. Chow, "Nonadiabatically tapered microfiber sensor with ultrashort waist," *IEEE Photonics Technol. Lett.* **26**, 2303–2306 (2014).
259. H.-J. Schneider, F. Hacket, V. Rüdiger, and H. Ikeda, "NMR Studies of Cyclodextrins and Cyclodextrin Complexes," *Chem. Rev.* **98**, 1755–1786 (1998).
260. M. Rjeb, A. Labzour, A. Rjeb, S. Sayouri, M. C. El Idrissi, S. Massey, A. Adnot, D. Roy, and C. M. Society, "Contribution To the Study By X-Ray Photoelectron Spectroscopy of the Natural Aging of the Polypropylene," *Moroccan J. Condens. Matter* **5**, 168–172 (2004).
261. M. I. Halawa, F. Wu, T. H. Fereja, B. Lou, and G. Xu, "One-pot green synthesis of supramolecular B-cyclodextrin functionalized gold nanoclusters and their application for highly selective and sensitive fluorescent detection of dopamine," *Sensors Actuators, B Chem.* **254**, 1017–1024 (2018).
262. P. H. Chua, K. G. Neoh, E. T. Kang, and W. Wang, "Surface functionalization of titanium with hyaluronic acid/chitosan polyelectrolyte multilayers and RGD for promoting osteoblast functions and inhibiting bacterial adhesion," *Biomaterials* **29**, 1412–1421 (2008).
263. K. M. Mayer and J. H. Hafner, "Localized surface plasmon resonance sensors," *Chem. Rev.* **111**, 3828–3857 (2011).
264. M. E. Haberland and J. A. Reynolds, "Self-association of Cholesterol in Aqueous Solution," *Proc. Natl. Acad. Sci.* **70**, 2313–2316 (1973).
265. R. Ahmad, N. Tripathy, S. H. Kim, A. Umar, A. Al-Hajry, and Y. B. Hahn, "High performance cholesterol sensor based on ZnO nanotubes grown on Si/Ag electrodes," *Electrochem. commun.* **38**, 4–7 (2014).
266. X. Lin, Y. Ni, and S. Kokot, "Electrochemical cholesterol sensor based on

- cholesterol oxidase and MoS₂-AuNPs modified glassy carbon electrode," *Sensors Actuators, B Chem.* **233**, 100–106 (2016).
267. M. N. Roy, D. Ekka, S. Saha, and M. Chandra Roy, "Host-guest inclusion complexes of α and β -cyclodextrins with α -amino acids," *RSC Adv.* **4**, 42383–42390 (2014).
 268. J. Liu, X. Leng, Y. Xiao, C. Hu, and L. Fu, "3D nitrogen-doped graphene/beta-cyclodextrin: host-guest interactions for electrochemical sensing," *Nanoscale* **7**, 11922–11927 (2015).
 269. P. Monti, G. Rocchitta, S. Marceddu, M. A. Dettori, D. Fabbri, S. Jaoua, Q. Migheli, G. Delogu, and P. A. Serra, "Use of β -cyclodextrin as enhancer of ascorbic acid rejection in permselective films for amperometric biosensor applications," *Talanta* **186**, 53–59 (2018).
 270. S. Saha, A. Roy, K. Roy, and M. N. Roy, "Study to explore the mechanism to form inclusion complexes of β -cyclodextrin with vitamin molecules," *Sci. Rep.* **6**, 35764 (2016).
 271. W. Chen, C. E. Chang, and M. K. Gilson, "Calculation of cyclodextrin binding affinities: Energy, entropy, and implications for drug design," *Biophys. J.* **87**, 3035–3049 (2004).
 272. A. Cucinotta, S. Selleri, L. Vincetti, and M. Zoboli, "Holey fiber analysis through the finite-element method," *IEEE Photonics Technol. Lett.* **14**, 1530–1532 (2002).
 273. A. Vial, A. S. Grimault, D. Macías, D. Barchiesi, and M. Lamy De La Chapelle, "Improved analytical fit of gold dispersion: Application to the modeling of extinction spectra with a finite-difference time-domain method," *Phys. Rev. B - Condens. Matter Mater. Phys.* **71**, (2005).
 274. S. Khan, D. Pierce, and R. D. Vale, "Interactions of the chemotaxis signal protein CheY with bacterial flagellar motors visualized by evanescent wave microscopy," *Curr. Biol.* **10**, 927–930 (2000).
 275. X. J. Liang, A. Q. Liu, C. S. Lim, T. C. Ayi, and P. H. Yap, "Determining

- refractive index of single living cell using an integrated microchip," *Sensors Actuators, A Phys.* **133**, 349–354 (2007).
276. I. Meglinski and A. Doronin, "Monte Carlo Modeling of Photon Migration for the Needs of Biomedical Optics and Biophotonics," 1–72 (2014).
 277. T. T. Nguyen, S. O. Bea, D. M. Kim, W. J. Yoon, J. W. Park, S. S. A. An, and H. Ju, "A regenerative label-free fiber optic sensor using surface plasmon resonance for clinical diagnosis of fibrinogen," *Int. J. Nanomedicine* **10**, 155–163 (2015).
 278. A. Psarouli, A. Salapatas, A. Botsialas, P. S. Petrou, I. Raptis, E. Makarona, G. Jobst, K. Tukkiniemi, M. Sopanen, R. Stoffer, S. E. Kakabakos, and K. Misiakos, "Monolithically integrated broad-band Mach-Zehnder interferometers for highly sensitive label-free detection of biomolecules through dual polarization optics," *Sci. Rep.* **5**, 17600 (2015).
 279. A. Hassani and M. Skorobogatiy, "Design criteria for microstructured-optical-fiber-based surface-plasmon-resonance sensors," *J. Opt. Soc. Am. B* **24**, 1423 (2007).
 280. H. Suzuki, M. Sugimoto, Y. Matsui, and J. Kondoh, "Effects of gold film thickness on spectrum profile and sensitivity of a multimode-optical-fiber SPR sensor," *Sensors Actuators, B Chem.* **132**, 26–33 (2008).
 281. R. Li, H. An, W. Huang, and Y. He, "Molybdenum oxide nanosheets meet ascorbic acid: Tunable surface plasmon resonance and visual colorimetric detection at room temperature," *Sensors Actuators, B Chem.* **259**, 59–63 (2018).
 282. T. Ogoshi, T. A. Yamagishi, and Y. Nakamoto, "Pillar-Shaped Macrocyclic Hosts Pillar[n]arenes: New Key Players for Supramolecular Chemistry," *Chem. Rev.* **116**, 7937–8002 (2016).
 283. J. Zhou, G. Yu, and F. Huang, "Supramolecular chemotherapy based on host-guest molecular recognition: A novel strategy in the battle against cancer with a bright future," *Chem. Soc. Rev.* **46**, 7021–7053 (2017).
 284. Y. Yu, C. Chipot, W. Cai, and X. Shao, "Molecular Dynamics Study of the

Inclusion of Cholesterol into Cyclodextrins," *J. Phys. Chem. B* **110**, 6372–6378 (2006).