Metamaterial Biological Sensors

H. Altug[1], S. Aksu[2], A. E. Cetin[1], R. Adato[1], A. Artar[1], G. Shvets[3,] C. Wu[3,] A.B. Khanikaev[3] and N. Arju[3]

[1]Department of Electrical and Computer Engineering
Boston University, 8 St. Mary's St. Boston, MA, 02215, USA
Fax: +1-617-358-4769; email: bu.edu
[2] Material Science and Engineering Division
Boston University, 8 St. Mary's St. Boston, MA, 02215, USA
[3] Physics Department,
The University of Texas at Austin, Austin, Texas 78712, USA

Abstract

Sensing of proteins and identification of their interactions is fundamental to our understanding of cell lar biology and could greatly contribute to early diagnosis and treatment of diseases. We will demonstrate plasmonic metamaterials can be used to realize advanced spectroscopy tools that can extract structural and functional information of proteins.

1. Introduction

Sensing of proteins and identification of their interactions is fundamental to our understanding of cellular biology and could greatly contribute to early diagnosis of complex diseases and as well as to the discovery of most effective drugs. Current toolkit for biosensing & spectroscopy is comprised predominantly of fluorescence, label free techniques and vibrational spectroscopy methods.

Fluorescence is one of the most popular techniques as it is sensitive & versatile. But there are some fundamental problems associated with it. Firstly, it relies on using fluorescent labels. Labels often sterically interfere with molecular binding interactions and lead to inaccurate measurements. Secondly, photo-bleaching and quenching of labels also cause further limitations for real-time and quantitative. To get around these issues, various label-free sensing techniques have been introduced, such as optical resonator based nanosensors relying on detection of resonance wavelength shifts. When a molecule sticks to the sensor surface the local refractive index increases, which results in red-shifting of the resonance wavelength. The nice feature here is that aside from having to capture the molecule, there's no label. And, most importantly, the frequency change is easily read out via a peak shift that can be directly and quantitatively related to a mass accumulation or height change in a molecular film.

Another label-free optical detection method is based on Vibrational Spectroscopy. These are based on the fact that every molecular bond has a set of vibrational modes associated with it. In the case of infrared spectrum, these modes directly result in absorption at specific frequencies. So the absorption in the IR gives spectra gives signal that is intrinsic to the most fundamental part of the sample – its molecular structure. This information is so desirable due to the fact that in biology, the theme of structure being intimately related to function is very important. This is especially true for proteins, which are critical because they are the primary machinery of living organisms. Structural information is important to a number of applications and fields, from fundamental biophysical questions to drug discovery. Unfortunately, most of these studies are limited to relatively large quantities of protein. Generally

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films a few um thick are needed due to sensitivity limitations. Fundamentally, this is because Beer's law governs the signal due to some absorbing molecule, so that it is reduced with path length to the point where it can be negligible for monolayers or single molecules. In order to overcome these fundamental challenges we exploit field enhancements offered by plasmonic metamaterials. In this talk we will present our most recent results on metamaterial based sensors.

2. Multifunctional Spectroscopy of Proteins with Asymmetric Metametarials

In the first part of the talk, we will present our detection method based on Fano-Resonant Asymmetric Metamaterials (Fig 1a). We will show that resonance of this specially designed plasmonic metamaterial is affected by the binding of protein molecules. In particular, the real and imaginary part of the refractive index results in spectroscopic perturbation in the form of resonance shift and absorption, respectively. By analyzing these changes both on and away from resonance frequency, we will show that one can extract both layer thickness and oscillator strengths of the protein vibrational mode. In combination, we will show that the measurements can be used to infer orientation of the protein at the sensor surface.

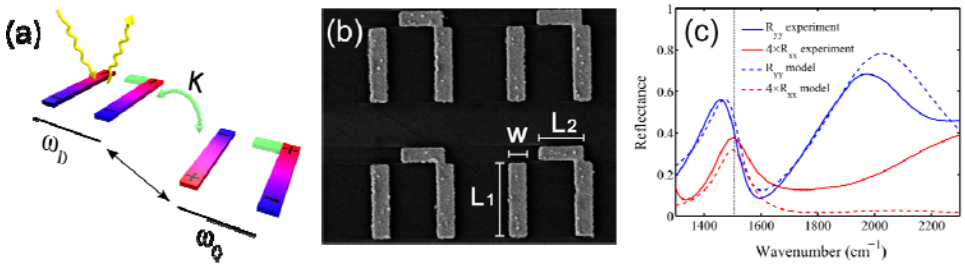

Fig. 1: Fano-Resonant Asymmetric Metamaterials (a) schematic drawing of the structure (b) SEM images of fabricated structure (c) spectral response of the structures.

The antenna design relies on the concepts of plasmon hybridization and Fano resonances. The geometry and principle of the nano-structure are shown in Fig.1. The pair of the two vertically oriented rods forms the hybridized pair, forming in and out of phase dipolar and quadrupolar modes respectively. The horizontal coupler element (shown in green) has two important roles. Firstly, it couples the quadrapole mode and dipole mode. This means that, the quadrapole mode which supports high near-field enhancements can be easily excited with far-field radiation, via its coupling to the intermediate dipole state. In the far-field spectra, this interference between the dipole and quadrapole pathways results in a Fano resonance (blue curve). Fano profile means that any slight shift in the quandrapole resonance will generate a significant differential reflectivity. Secondly, for light polarized along the horizontal, it directly couples the quadrapole mode to the far-field. This is important because it for vertical polarization, the Fano interference makes it impossible to precisely locate the quadrupole resonance frequency. The lorentzian profile (red curve) for x-polarization allows us to pinpoint it exactly so that we can match it to the vibrational resonances.

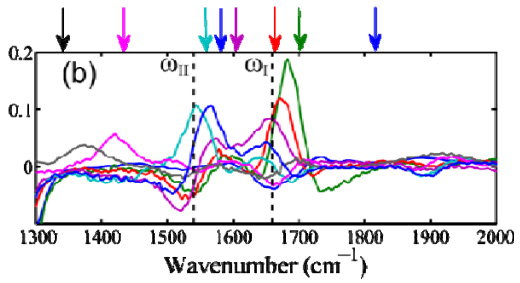

Fig. 2: Scanning the plasmonic resonance through the absorption bands of the protein with arrays of Fano-Resonant Asymmetric Metamaterials.

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In the talk, we will describe the principle behind our sensing mechanism using Fano-Resonant Asymmetric Metamaterials. We will show that by scanning the resonance of the metamaterial through the absorption bands of the protein, we can probe the oscillator strengths of the protein vibrational modes (Fig. 2) as well as obtain additional information including protein height and orientation.

3. Interaction of metallic gaps and molecules at sub-10 nm length scales

In the second part of the talk, we will present our newest results on interaction of biomolecules and plasmonics gaps at length scale below 10 nm. Depending on the molecular weight the size of a human protein could range widely. Antibodies, which are an important protein class of our immune system, could be significantly taller than 10nm, while some proteins could be as small as a few nm. Recent plasmon mediated biosensing studies are concentrated on formidable challenge of fabricating very closely spaced dimers for sensing proteins, even at sub-nanometer23. Although such tiny gaps offer unique advantages for fundamental studies on nano-photonics, spectroscopy applications bring up the following questions: What happens when the gaps are smaller than the molecules to be detected? How does a molecule spatially position inside a relatively smaller or bigger gap? How would molecules interact with evanescently decaying enhanced fields inside the gap and how would these affect overall spectroscopic responses? In this talk, we will answer these untouched questions and experimentally demonstrate spectral and spatial interaction of different size proteins with antennas having a variety of gap distances.

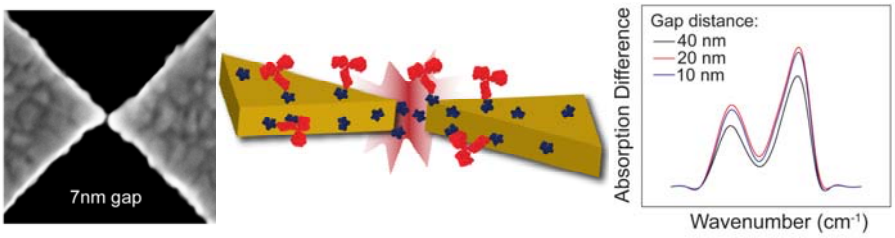

Fig. 3: Interaction of metallic gaps and molecules at sub-10 nm length scales and its effect on spectroscopic signal of protein biomolecules

4. Conclusion

In conclusion, we will show that tailored plasmonic nano-antennas operating at mid-IR frequencies hold a great amount of promise providing a great deal of structural information of biomolecules. In particular, we will demonstrate a platform that combines quantitative measurements of protein layer thickness with the probing of vibrational bands in a single chip. In addition, we will also show how spectroscopic molecular signatures scale when the length of plasmonic gaps approaches to that of biomolecules.

References

[1] Wu et al, Nature Materials Vol. 11, pp 69-75, 2012.
[2] Aksu et al, Submitted February 2012.

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