Integrated Plasmonic Systems for Ultrasensitive Spectroscopy and Biodetection

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Abstract

Plasmonics, by localizing light to the sub-wavelength volumes and dramatically enhancing local fields, is enabling myriad of exciting opportunities for construction of novel photonic devices and integrated nanophotonic systems. In this talk, I will present our recent work on integrated on-chip plasmonics, nanofluidics, and metamaterials and their applications in ultrasensitive spectroscopy and biodetection.

1. Introduction

Biosensors that can detect and analyze small quantities of molecules (i.e proteins, enzymes) as well as dangerous pathogens (i.e viruses, spores) are very important for clinical applications, biomedical reseach and national defense. For example, screening of large variety of proteins and determination of their functions can enable early diagnostics of complex diseases such as cancer and Alzheimer's as well their treatment by discovering effective drugs. Large-scale study of proteins is significant due to such far-reaching implications, however its realization is challenging due to the limitation of current detection techniques. In human proteome, there are more than 100,000 kinds of proteins[1] and some expressed in few copies. Protein functions have to be deciphered without using labeling techniques since labels interfere with the protein interactions[2]. Unlike deoxyribonucleic acid (DNA) replication with polymerase chain reaction (PCR), there is no equivalent for protein amplification, a major limitation for the identification of low abundant proteins. Similarly, rapid detection and surveillance of infectious pathogens remains to be a challenge for point-of-care applications in public health and national defense. Deliberate release of viruses as a biological warfare agent can cause millions of deaths, if the outbreak is not detected at its onset. Current detection techniques rely on extensive sample processing and require advanced equipment and infrastructure. Furthermore, most common tests (such as flu) are for single pathogens. Rapid, sensitive and multiplexed detection platforms that can screen large variety of biomolecules and bio-agents simultaneously are needed.

Within the last decade, plasmonics and its application for biodetection and spectroscopy has been extensively investigated. Although significant progress has been achieved, many fundamental questions and practical challenges are still remaining to address. For example, for biosensors based on refractive index change, the detection limit depends on both the LSPR sensitivity to the local dielectric environment and the resonance line-width. Narrower line-widths allow smaller shifts to be detected[3,4]. So far, most of the effort has been concentrated on optimizing the nanoparticle geometries to improve the near-field enhancements and to control the resonance frequencies/line-widths[5,6]. Further improvements in plasmon line-widths (lifetimes) and near-field enhancements require innovative approaches such as "*radiative engineering*" of plasmonic losses. Another problem in biosensing applications is the "*size mistmatch*" between the nanoscale optical sensing volumes and the micronscale fluidic circuits utilized for analyte delivery. As a result, performances of the biosensors are often limited in a fluidic environment by the inefficient analyte (mass) transport, instead of their intrinsic detection capabilities[7]. In this talk, we will present some of the unique detection systems that we have developed to address these challenges. We will start

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with an ultra-sensitive, collectively enhanced infrared absorption spectroscopy enabling direct detection of molecular specific signatures of zepto-mole levels of proteins[8,9,10]. To overcome size mismatch problem, we will introduce a novel hybrid biosensing platform merging nanoplasmonics and nanofluidics[11,12,13].

2. Plasmonics and metamaterials for ultrasensitive Mid-IR nanospectroscopy

Infrared absorption spectroscopy is a unique tool for identifying and characterizing molecular bonds[14]. For most organic and inorganic molecules (such as proteins, chemical toxins and gases), vibrational and rotational modes are spectroscopically accessible within the mid-infrared (mid-IR; 3-20 μm) regime of the electromagnetic spectrum. Characteristic vibrational modes are associated with unique IR absorption spectral bands that are bond-specific. Because of that, the IR wavelength range is also known as "finger print" region. However, because of the Beer-Lambert law, its sensitivity has been limited to perform analytical/functional studies on small samples often available from biological specimens. We overcome this limitation by specifically arraying tailored nanorod antennas (Figure 1(a)). With engineered nanorod arrays, radiative losses can be manipulated to create plasmonic excitations with spectrally narrower far-field resonances as shown in Figure 1(b). Furthermore, we can achieve much stronger near-field enhancements than those achievable with an individual nanoantenna (as shown in Figure 1(c)). The additional field enhancements are particularly crucial for enhanced spectroscopy methods.

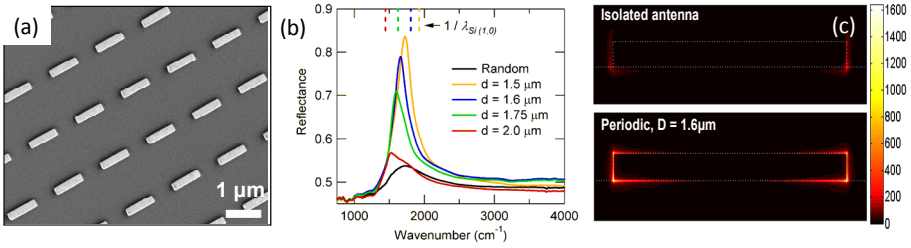

Figure 1 (a) Scanning electron microscope (SEM) images of a periodic array. (b) Reflectance spectra of periodic nanoantenna arrays. All the antennas are 1100 nm long. The wavenumbers corresponding to $1 / \lambda_{Si\,(1,0)}$ for a given periodicity are indicated by the dashed lines at the top of the figure. (c) Cross-sections of the intensity distribution taken through the edge of the rod are shown for periodic (d = 1.6 μm) and isolated antenna.

To demonstrate the effect of plasmonic excitations on engineered arrays for surface enhanced spectroscopy, we applied a 2 nm thin film of silk fibroin protein layer. Atomic force microscopy (AFM) is used to confirm the uniformity and the thickness of the film (Figure. 2a). As shown in Figure 2c, protein absorption bands are clearly noticeable within the optical spectra collected from the protein-coated antenna arrays with 1.6 μm periodicity. Dips in the plasmonic response as a result of the amide I and II absorption bands are indicated in the figure at 1660 and 1537 cm^{-1}, respectively. The signal enhancement was highest with the optimized array (Figure 2d). To quantify the signal enhancement factors we have performed IR reflection absorption spectroscopy (IRRAS) measurements. Our measurements indicate that up to 100,000-fold enhancements of backbone signatures of proteins can be achieved with our engineered plasmonic substrates. As a result, we demonstrated direct detection of absorption signals at zeptomole sensitivity. Currently, we are investigating metamaterials and Fano-resonances in plasmonic hetero-dimers for additional field enhancements and ultrasensitive mid-IR spectroscopy. Experimental and numerical results on these new substrates will be included in the talk.

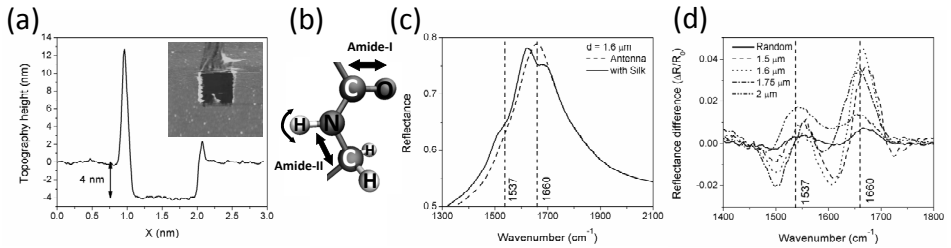

Figure 2. (a) Silk protein film thickness (4 nm) is measured by AFM. (b) Amide-I and II vibrational modes of the protein back bone. (c) Reflectance spectra from the 1.6 μm periodic array before (dashed line) and after coating of 2 nm thick protein film (solid line). (d) Difference absorption spectra of different arrays.

3. Plasmonics nanohole arrays for biosensing and nanofluidics

As we have highlighted in the introduction, in recent years label free bio-sensors combined with innovative signal transduction methods are proposed to push the detection limits down to femto-molar concentrations of analytes[15]. Concurrently, researchers are integrating such sensitive and compact nano-sensors with micro-fluidics for automated sample handling[16]. While micro-fluidics can enable portable and lab-on-a-chip systems, recent calculations indicate that performances of surface biosensors can be seriously limited in a fluidic environment by the inefficient analyte (mass) transport instead of their intrinsic detection capabilities[17]. As the analytes are collected by the functionalized surface, a depletion zone forms around the sensing area where the analyte transport is diffusive. Random nature of the mass transport in the depletion zone severely limits the delivery of the analytes from the convective flow to the sensor surface. At low concentrations, this limitation causes impractically long detection times[17]. Innovative approaches are needed to overcome the mass transport limitations.

Recently, we demonstrated a hybrid biosensing system merging nanoplasmonics and nanofluidics in a single platform[11]. Our system employs suspended plasmonic nanohole arrays sealed in a multi-layered microfluidic chambers (Figure 3). For sensing, we use the extraordinary light transmission effect. At the same time, we utilize the nano-scale openings to actively steer the convective flow to the surface (Fig. 3b). This is contrary to the conventional approach in which the convective flow stream passes over the sensor (Fig. 3a).

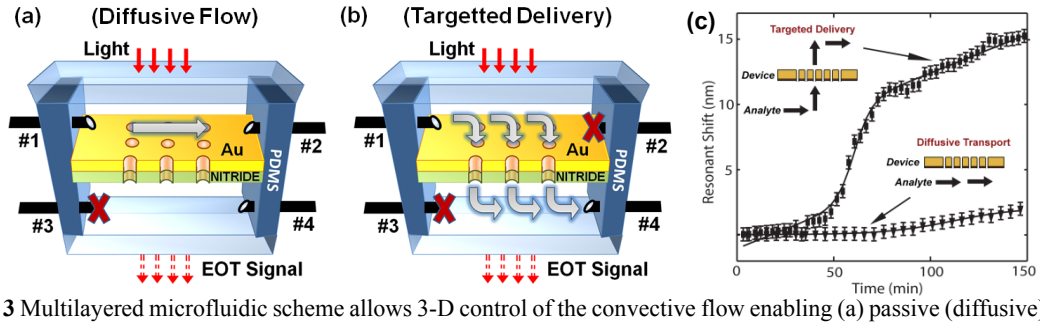

Figure 3 Multilayered microfluidic scheme allows 3-D control of the convective flow enabling (a) passive (diffusive) and (b) active (targeted delivery) transport of the analytes to the sensing surface. (c) Efficiencies of the passive (triangles) and targeted (squares) delivery of the analytes are compared in real time measurements. Solid lines are fit to sigmoid function. 14-fold improvement in mass transport rate constant is observed for the targeted delivery scheme.

To show dramatic improvements in sensor response time by targeted analyte delivery, we performed time dependent spectral measurements (Figure 3c). Initially, both the top and the bottom channels are filled with a low

refractive index liquid, deionized (DI) water ($n_{DI} = 1.333$), The spectrum, obtained once the channels are filled with DI-water, is used as a background for the following measurements. To quantify the analyte transport efficiency of the both delivery schemes, a lower viscosity analyte solution (IPA, $n_{IPA} = 1.377$) with higher refractive index is introduced from the bottom inlet and time-dependent spectral measurements are performed. In the diffusive transport scheme, IPA solution is pumped into the bottom channel and collected from the bottom side while the top outlet is kept open. For targeted delivery of the convective current to the surface, IPA is directed from down-to-top direction by enabling flow between 3→2 (inlets/outlets are numbered as in Figure 3). As shown in Fig. 3c, the directed delivery results in a larger resonance shift compared to the passive one, indicating a much more efficient analyte delivery to the biosensor area. Experimentally observed resonance shifts are (least squares) fitted to a sigmoid function of form $A_b + \left(A_t - A_b\right) \Big/ \left(1 + e^{-k(t-t_0)}\right)$. This is superposed to a linearly increasing background with $C_t\left(t - t_0\right) + C_0$ due to increasing refractive index of the bulk medium in the top channels as IPA concentration increases. The mass transport rate constants are obtained as $k_{pass} = 0.0158\ \text{min}^{-1}$ and $k_{act} = 0.2193\ \text{min}^{-1}$ for the passive and targeted transport schemes, respectively. This corresponds to more than 14-fold improvement in rate constants, which is crucial for enhancing the performance in immunoassay based applications. Recently, we used our platform to perform bio-assays with virus and protein samples. New experimental results from these measurements will be included in the talk.

4. Conclusion

In conclusion, we will present unique integrated on-chip plasmonics and metamaterials systems for demonstration of ultrasensitive nanospectroscopy and novel optofluidic nanobiosensors.

5. References and links

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