Title:

Development of nanophotonic biosensor platform towards on-chip liquid biopsy

Abstract:

As a non-invasive approach, a liquid biopsy allows physicians to diagnose, prognosis, and monitor disease at an early stage using body fluidics sample of patients. While many technologies have been developed and validated in research laboratories, there has also been a push to expand these technologies into other clinical settings and as point-of-care devices.

Liquid biopsy has the advantage of a label-free approach, meaning that they are not harm the cell’s viability through binding to the surface protein. The label-free technologies often integrate with on-chip design by using microfluidics to manipulate the individual cells for downstream analysis. Since the microfluidic approach can short the diffusion length, label-free sensors often with the rapid assay, which is better than the gold standard analytical methods, such as ELISA, western blot for proteins.

Optical label-free biosensors serve as a powerful detection tool to analyze biomolecular interactions and have been widely used in pharmaceutical drug discovery and biochemical sensing. Label-free detection generally involves a transducer capable of directly measuring some physical property of the chemical compound, DNA molecule, peptide, protein, virus, or cell and removes experimental uncertainty induced by the effect of the label on molecular conformation, so it greatly simplifies the time and effort required for assay development.

Currently, existing optical label-free biosensor suffer from three limitations. The detection sensitivity, molecules mass transfer, and throughput. The goal of this dissertation is to propose and develop a novel and efficient modality able to overcome these limitations and challenges through three aspects.

First, to increase the sensor detection sensitivity, we investigate the optical bound states in the continuum (BIC) of slotted high-contrast grating (sHCG) structures. The sHCG support BICs and high-Q resonant modes. The slot position can be utilized to tune the linewidth of the high-Q resonances. Then, in order to overcome the mass-transfer limitation and reduce the assay time, we propose a lateral flow-through optical biosensor for rapid detection of biomarkers. The biosensor is fabricated based on the silicon-on-insulator technology and based on the high-contrast grating. Finally, we develop a high-throughput exosome vesicles (EVs) detection assay using a label-free microarray. The EV microarray was fabricated on a photonic crystal (PC) biosensor surface. The hyperspectral imaging approached was implemented to quantify the antibody and EV absorptions on the PC-based microarray. The label-free EV microarray enables low-cost, rapid, and high-throughput characterization of macrophage.

Accomplishing this aim will lead to enhanced detection sensitivity and reduced assay time, for high-throughput molecular profiling of exosomes vesicles.