Surface Enhanced Raman Spectroscopy Biosensor

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Abstract:
We are developing a surface enhanced Raman spectroscopy (SERS) based biosensor to study protein interactions and monitor the concentrations of disease-related proteins. To combat reproducibility of Raman spectra issues, construction of SERS substrates that host surface plasmon modes and that reliably allow molecules of interest to be brought in close contact with the surface plasmon-enhanced field is imperative. We have constructed a microfluidic step channel that forces gold colloid to aggregate at the entrance to a nanochannel via capillary force where the molecules of interest are trapped in the interstices of the particles, where the largest field enhancements occur.

Introduction:
Raman spectroscopy offers an alternative to fluorescence spectroscopy with advantages as follows: lack of photobleaching, wider variety Raman active tags, greater potential for multiplexing due to narrow linewidths of Raman modes, ability to “excite” multiple Raman active dyes with one laser and potential to provide qualitative as well as quantitative information. Surface enhanced Raman spectroscopy (SERS) has expanded the use of Raman spectroscopy; however issues arise with the reproducibility of Raman spectra and configuring ways to analyze the Raman modes for structural and chemical information as well as quantitative information.

Summary of Research:
We are currently developing assays to detect disease-related proteins, such as cardiac biomarkers, which can provide early identification and diagnosis of heart disease. SERS can be a reliable technique to probe proteins over other techniques, such as infrared spectroscopy, circular dichroism, nuclear magnetic resonance spectroscopy, x-ray diffraction, and fluorescence spectroscopy. Experimentation and modeling has shown strong Raman mode enhancements can be found within aggregates of gold nanoparticles due to the excitation of surface plasmons (collective oscillations of conduction band electrons). Therefore, we have created a SERS substrate by trapping 60 nm gold particles at a 40 nm channel and the molecules of interest are allowed to randomly adsorb within the interstices of the gold aggregates at a precise location. We have been able to obtain structural information from disease related and other proteins, such as the β-amyloid protein (a prion protein implicated in the neurotoxicity of Alzheimer’s disease) and the denaturation of proteins.

The device was fabricated on a 500 µm thick polished borosilicate wafer. The microchannel (150 µm × 6 µm deep) was patterned with wet hydrofluoric acid etching and the nanochannel (5 µm × 40 µm × 40 nm deep) was patterned with a reactive ion etching process. This wafer was then bonded to a blank wafer to seal the trenches and create the channels. Inlet holes were created at the ends of the microchannel with a sandblaster and plastic reservoirs were attached over the inlet holes. The protein solutions were loaded into the biosensor through the plastic reservoirs with a syringe and consecutive scans were taken with a Renishaw System 1000 Raman spectrometer coupled to a Leica DMLM microscope with a 50x air objective with a 12 mW, 785 nm diode excitation laser with a 60 second integration time.

References: