Nanoplasmonics 1:

Capture and Sensing of Virus-like Particles in Plasmonic Nanoholes

The Insplorion XNano II instrument system comes with software specifically designed to analyse and monitor changes in spectra from plasmonic nanostructures. While Insplorion provides nanoplasmonic sensor substrates to customers, it is also possible to use custom made sensors in the instrument. Used in this way, the Insplorion XNano II provides the user with a temperature controlled microfluidic compartment and a means of controllable sample delivery. The Insplorer software can be used to acquire and store real-time spectra which can be subsequently analysed.
In this application note, the Insplorion Instrument has been used to deliver samples and analyse spectra from a gold nanohole array sensor specifically designed to capture virus-like particles.

Introduction

There is a huge interest in the development of molecular detection and characterisation tools for antiviral drug evaluation and viral infection diagnosis. Standard methods for antiviral drug evaluation exhibit some shortcomings, including long incubation times and the need to establish cell culture models. Surface-based measurement platforms could be a promising alternative that enables direct monitoring between captured virus particles and drug candidates.
Plasmonic nanohole substrates are highly interesting platforms for this type of application since they could offer a means of both capturing the virus particles as well as label-free detection of the particles response to drug candidates.

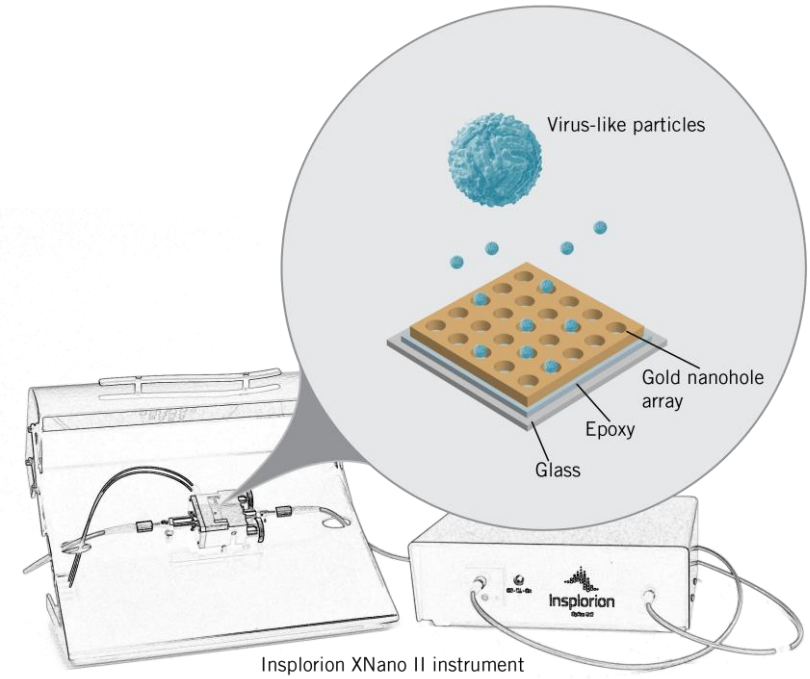

Figure 1: Insplorion XNano II system setup. The inset shows a cartoon of the periodic nanohole array designed to selectively capture virus-like particles inside the nanoholes.

Experimental Procedure

The nanohole arrays where fabricated from a Si template patterned with nanoimprint lithography with circular holes, 600 nm deep, 160 nm in diameter, and with a 500 nm periodicity. A 200 nm thick gold film was evaporated on the Si template and subsequently peeled off using optical epoxy and transferred to a glass support. A cartoon of the thus fabricated array is shown in Figure 1.
To prevent non-specific adsorption of virus particles a self-assembled monolayer of methoxy-polyethylene glycol (mPEG) was formed on the gold surface. Virus like particles where prepared by extrusion of lipid vesicles, 75 nm in diameter consisting of 30 mol% cholesterol and 70 mol% DOPC. A synthetic peptide exhibiting virucial activity (membrane disruption) was used to demonstrate the sensing

Insplorion AB • Medicinaregatan 8A • 413 46 Gothenburg • Sweden
Tel: +46 (0)31 380 26 95
Web: www.insplorion.com
E-mail: info@insplorion.com

capabilities of the nanohole array.

Results

The periodic nanohole array exhibits three distinct transmission peaks attributed to different plasmon modes (Figure 2A). The position of these peaks is highly sensitive to the local dielectric environment. The sensitivities of the plasmon peak positions to bulk refractive index changes was determined by injecting a series of water-glycerol mixtures (Figure 2B). Peak 2 exhibited a bulk refractive index sensitivity of 220 nm/RIU and is chosen in the subsequent graphs for the time-resolved measurements. The nanohole array was functionalised with mPEG to prevent adsorption of virus-like particles to the gold and facilitate capture of particles into the non-functionalised holes. Figure 2C shows the spectral shift over time while flowing a solution of 0.3 mg/mL virus-like particles over the mPEG modified nanohole array. The resulting spectral shift of about 1 nm can be attributed to capture of the virus-like particles as shown in the SEM images. Figure 2D shows the response upon addition of the membrane rupturing peptide. The resulting blue shift of about 0.5 nm is due to rupture and removal of the captured particles.

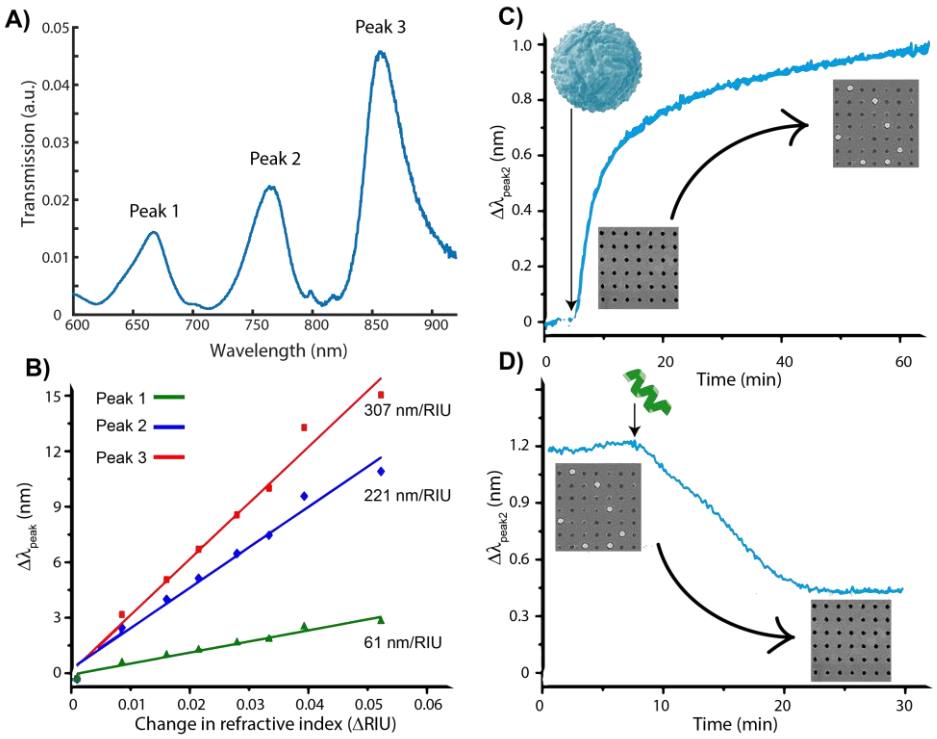

Figure 2: A) Optical transmission spectrum of the gold nanohole array in aqueous buffer. The tree distinct peaks are attributed to different plasmon modes of the nanoholes. The middle peak exhibit the highest sensitivity to bulk refractive index changes and is therefore used in the subsequent plots. **B)** Bulk refractive index sensitivities of the three plasmon peaks. **C)** Shift in position of peak 2 during adsorption of virus-like particles into the nanohole array (Insets show SEM images before and after). **D)** Shift in position of peak 2 during injection of a membrane-disrupting peptide.

Conclusions

The demonstrated platform constitutes a very feasible sensing scheme for capturing virus particles and analysing the effect of antiviral drug candidates. The XNano II instrument system is an efficient tool in the characterization and evaluation of plasmonic nanostructures in general such as the nanohole array studied in this work.

Note

[1] This study was performed in the group of Professor Nam-Joon Cho at the School of Materials Science and Engineering at Nanyang Technological University, Singapore.

Joshua A. Jackman, Eric Linardy, Daehan Yoo, Jeongeun Seo, Wei Beng, Ng, Daniel J. Klemme, Nathan J. Wittenberg, Sang-Hyun Oh, and Nam-Joon Cho. Plasmonic Nanohole Sensor for Capturing Single Virus-Like Particels toward Virucidal Drug Evaluation. *Small* ***2015***. *DOI: 10.1002/smll.201501914*