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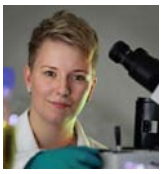


Surface enhanced Raman spectroscopy-based detection of drug permeation in an intestinal cell model

Marlitt Viehrig[1], Kinga Zór[1], Tomas Rindzevicius[1], Michael S. Schmidt[1], Annette Müllertz[1,2], Anja Boisen[1]

[1]*The Danish National Research Foundation and Villum Foundation's Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics (IDUN), Department of Micro- and Nanotechnology, Technical University of Denmark, Kgs. Lyngby, Denmark.*

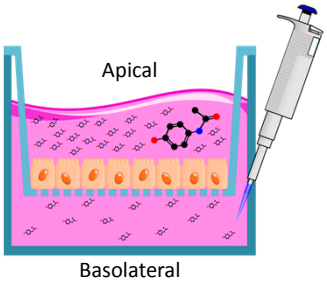
[2]*Department of Pharmacy, University of Copenhagen, Copenhagen, Denmark.*

We present the development of a detection strategy based on surface-enhanced Raman spectroscopy (SERS) sensing in liquids, relevant for biological samples. The SERS substrates, fabricated from free-standing, gold-capped silicon nanopillars are commonly used for the detection of analytes dissolved in organic solvents and dried on the sensor surface. We developed a method where detection can be performed directly in liquid using a model drug acetoaminophene (Paracetamol).

SERS sensing in Cell Models

Intestinal Cell Model - Transwell® Systems

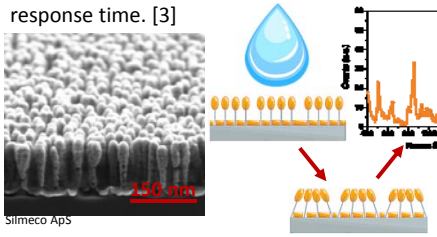
Caco-2 cells, are widely used as *in vitro* intestinal model. [2] Transwell® systems are used in *in vitro* drug permeation studies, where drugs are added to the transport media (e.g. Hanks` balanced salt solution (HBSS)).



Samples are commonly analyzed with robust, but time and resource consuming techniques such as high-performance liquid chromatography. (Bio)sensors based on SERS offer fast, accurate and cost effective alternatives for identifying drug types and concentrations in permeation studies.

SERS Substrates – Gold Capped Nanopillars

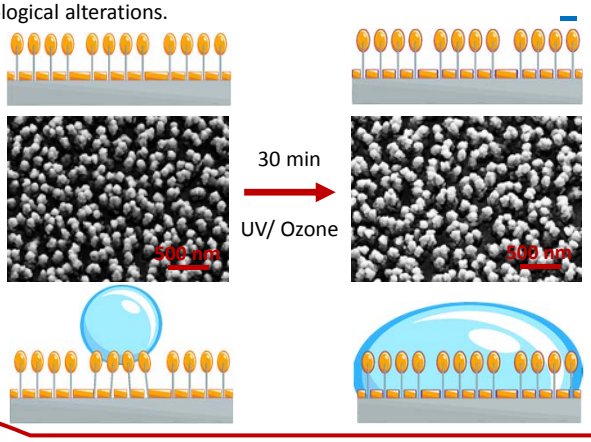
SERS is a powerful analysis technique capable of detecting molecular fingerprints of analytes with high sensitivity and fast response time. [3]

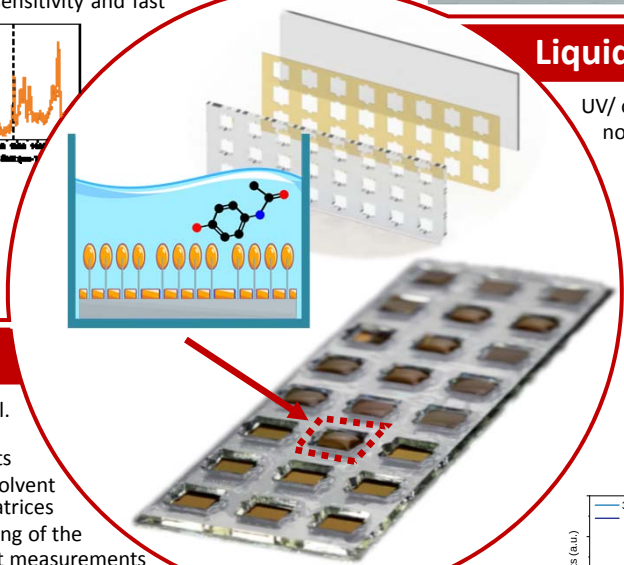


Classical dry droplet SERS sensing using gold-capped Si nanopillars. [4]

Surface Treatment

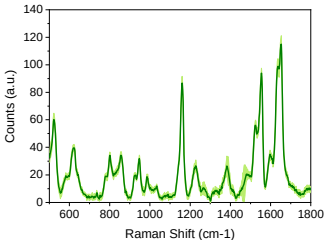
UV/ ozone exposure is commonly utilized as surface treatment and cleaning procedure in a variety of microfabrication processes. It renders the surface of gold-capped nanopillars from hydrophobic to hydrophilic without any morphological alterations.



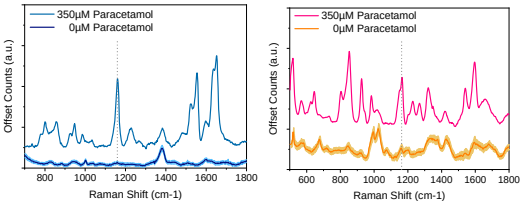


Liquid Measurements

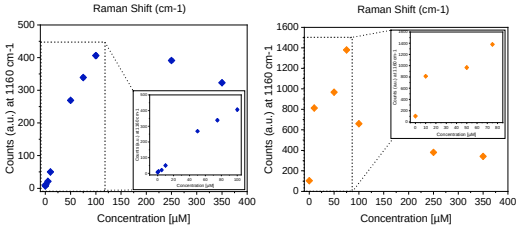
UV/ ozone treatment enabled the development of a novel liquid measurement technique for nanopillar SERS based sensing.



Detection of 350 µM paracetamol in liquid **UV/ Ozone treated** samples.

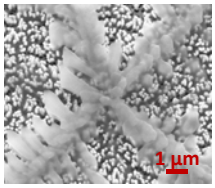


Paracetamol spiked in **MQ** and **HBSS**. Liquid detection of paracetamol in MQ is possible over a linear range of **5–100µM**. Direct liquid measurements in HBSS displayed a linear trend between **5 – 75 µM**.

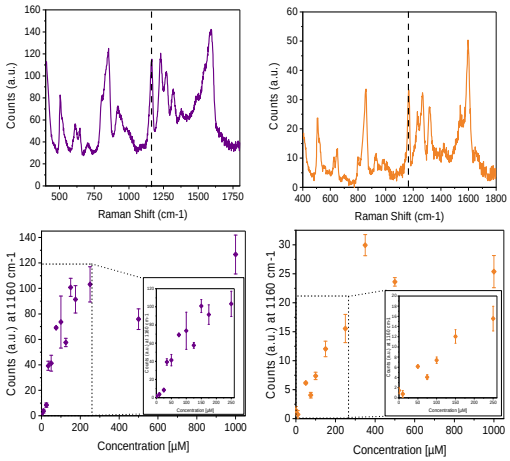


Droplet SERS

Dry droplet SERS-based detection of paracetamol.



Dry droplet measurements are highly influenced by solvent composition. Complex matrices like HBSS can lead to fouling of the sensors. To enable droplet measurements it was necessary to dilute HBSS 1:10 with pure ethanol.



Paracetamol spiked in pure **ethanol** and **HBSS**. Calibration curves were obtained following the characteristic paracetamol peak at 1160 cm^{-1}. We found that Paracetamol dissolved in ethanol can be detected in a linear range between **35 – 200µM**, while when spiked in HBSS and diluted 1:10 with EtOH a linear trend between **50 – 350µM** is observed.

Acknowledgement

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Presenting Author – Marlitt Viehrig

E-Mail: mvie@nanotech.dtu.dk

Phone: +45 45255745