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Low levels of medical residues in environmental, industrial and domestic water systems is a growing concern. The biosensor industry is trying to accommodate the need of sensitive and specific sensor systems capable of ultra-low level detection of medical residues. In this PhD project a surface enhanced Raman spectroscopy (SERS) sensor for the female sex hormone 17β-estradiol was attempted. It is commonly used in contraceptive pills from where it finds its way through waste water treatment plants and into the environment. The SERS substrate was fabricated in a cleanroom facility using techniques well known from the electronics industry. The substrate consisted of silver or gold covered silicon nanopillars. The nanopillars were chemically functionalised with a DNA aptamer specific towards 17β-estradiol using thiol chemistry. At first, an entire functionalisation protocol was carried out to detect Estradiol Glow, which is fluorescently labelled 17β-estradiol. It was shown that Estradiol Glow exhibit very strong Raman activity and was such ideal for initial test. Since a large amount of data was gathered for this experiment it was necessary to develop an algorithm capable of analysing large data sets. Non-negative Matrix Factorization (NMF) was utilised to effectively improve the detection limit of the system by one order of magnitude.

Due to issues relating to the functionalisation protocol it was secondly investigated whether the aptamer was properly immobilised on the nanopillar surface. By hybridisation to a labelled complementary strand it was proven that aptamer was indeed immobilised. It was also found that stronger binding to the gold covered nanopillars could be obtained by a short treatment in reactive O2 plasma. Likewise it was found that the addition of a detergent to the washing buffer had a great influence on the unspecific binding to the nanopillars.

A thorough study of the parameters influencing the degree of functionalisation was then conducted. By utilizing a developed peak-fitting model it was possible to directly inspect the interplay between DNA aptamer and 6-mercaptop-1-hexanol (MCH) used for blocking unspecific binding to gold. By inspecting the spectra of the molecules and their combination it was possible to observe attachment of DNA aptamer and MCH. Displacement/removal of DNA aptamer was also observed for high concentrations of MCH.

The final study was an attempt to detect pure 17β-estradiol using the developed functionalisation parameters. Unfortunately the inherent weak Raman signal of 17β-estradiol proved to faint for direct detection. Therefore Estradiol Glow was employed, however without success. Despite several attempts with varying degree of stringency successful detection was never accomplished.

In conclusion, this PhD project successfully characterised the chemical functionalisation parameters needed for generic SERS aptasensor development using only the Raman signals of the molecules. The SERS substrate was successfully fabricated repeatedly and showed great enhancement of Raman signals. Two analysis methods (NMF and peak-fitting) was developed in collaboration with DTU Compute in order to accomodate for the large amount of data gathered throughout the project. This work displays the complexity in SERS aptasensor development, which is needed for sensitive and selective capture of medical residues.

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