Miniaturized Surface Plasmon Resonance based Sensor System

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Abstract: We describe the miniaturization of the Surface Plasmon Resonance (SPR) technology which mainly finds its applications in pharmaceutical screening and biotechnology so far. SPR spectroscopy is a label-free, non-destructive and highly sensitive measurement principle detecting changes in the refractive index in striking distance to a gold surface. A transfer of this technology to a miniaturized sensor will broaden the range of possible applications. A promising feature which is included in the miniaturized system is the angle-dependent recording of the SPR signals without moving parts. Commercial SPR assays are mainly working with a small number of sensing spots. In contrast, the SPR imaging system shown here will allow to use an array of many sensing spots. In combination with chemical receptors designed as an artificial nose, the simultaneous detection of many analytes is envisioned for future applications.

1 INTRODUCTION

Surface Plasmon Resonance (SPR) technology is label free, non-destructive and highly sensitive (Schasfoort, 2017). Due to these properties, SPR is an attractive measurement principle for chemical sensors (Homola, 2003). Nevertheless, there are some drawbacks limiting its applications so far: Classical measurement setups are mainly designed for being used in laboratories and therefore they are very expensive. The high temperature sensitivity and the need of trained personal for its operation impede reliable in-field sensing. Motivated by this we developed a miniaturized sensor system, which is able to operate automated in a wide range of temperature.

The system is based on an imaging read-out principle enabling a large number of sensor spots on a small area for addressed parallel online detection. The individual sensing spot can be designed and chemically functionalized as an artificial nose enabling the identification of several analytes in a complex matrix without labelling. In classical SPR setups a laser is used as light source, which is replaced by a modified light emitting diode. While using a semiconductor laser to illuminate a surface one will get speckles. If it comes to very small sensing spots, speckles will ruin your sensing signal. Light, generated by a LED does not exhibit speckles due to the missing coherence.

2 PRINCIPLE

While a thin gold film is irradiated by light, typically the entire light will be reflected (Figure 1). However, if the light is p-polarised and the angle of incidence is altered, one can see a narrow dip in the intensity of the reflected light. This dip is indicating that at this certain angle of incidence (SPR angle) surface plasmons are excited. The SPR angle mainly depends on the refractive index in close proximity to the gold film which is deposited on coupler, usually a glass prism. Therefore, the refractive index on one side of the gold is constant, which means that any variations in the chemical composition – and therefore in the refractive index – next to the other side of the gold film is determining the position of the SPR-angle. Selectivity to a special molecule of interest is generated by a chemical functionalization of the gold

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film by recognition elements (Wolfbeis and Homola, 2010).

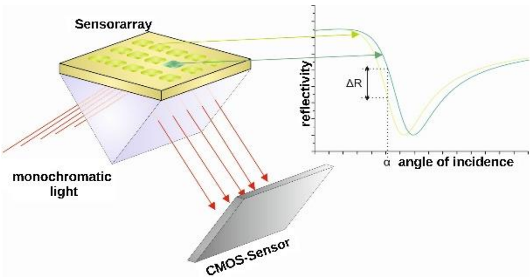

Figure 1: SPR-Sensor principle; the reflecting gold film consists of several region of interests (ROI); the diagram shows the signal response (ΔR) which is caused by a change of the refractive index in close proximity to each Sensor Spot.

3 SYSTEM SETUP

Figure 2 shows a sketch of the sensor setup.

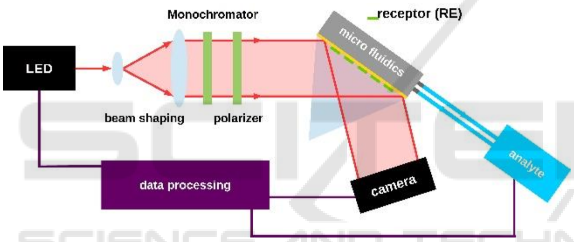

Figure 2: System-Setup, consisting of: 660 nm LED based light source, beam shaping elements, a sensitive area with receptors as well as microfluidics, a camera detection system and a data processing unit.

Lasers are known for generating speckles, which are very annoying in case of SPR imaging as a homogeneous lighting of the whole sensing area is desired. The replacement of the laser by a LED for illumination overcomes this issue. LED light is very broadband compared to laser light and it is non-polarised. Therefore, a notch filter and a polarizer was integrated into the system. Furthermore, the beam is tailored and collimated. The modified beam illuminates a thin gold film which is on top of a glass prism, which consists of 100 sensing spots at an area of 15 x 15 mm. The reflected light is collected by a 2D-camera system, which records the spatial change of the intensity of the reflected light beam.

In order to ensure the homogeneous and constant supply of the analytes in a thin laminar flow over the entire gold surface, a microfluidic system was developed (Figure 3). The microfluidics is 3D-printed with stainless steel. The seal between the microfluidic unit and the prism is made of silicone and has a high of 700 µm. The high of the seal decreases depending on the applied pressure between prism and microfluidic unit. Micro piezo membrane pumps generate the analyte flow. A Tygon hose with an inner diameter of 1 mm connects the individual components of the microfluidic unit.

The temperature next to the sensing area is monitored by PT1000 sensing elements which can be also included cavities which are suitable for.

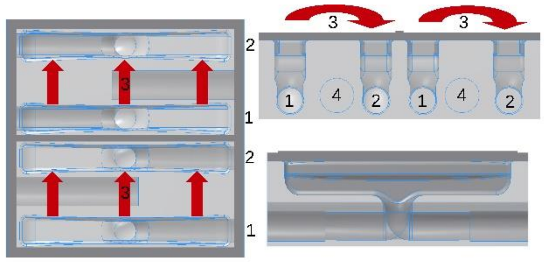

Figure 3: Top view left and side views right. The inlet (1) and outlet (2) of the microfluidic chip is designed to provide a constant flow rate (3) at the entire gold surface of the sensor array. For precise temperature control, the chip has cavities (4) between every inlet and outlet for PT1000 sensors.

The SPR-system can detect changes in the range of $5 \cdot 10^{-6}$ refractive index units (RIU). However, the refractive index of water is very sensitive to temperature fluctuations (Abbate, 1978). Thus, it is obvious that the temperature of the setup needs to be controlled. Here we solved the temperature issue by a sensor packaging consisting of a temperature isolation on both, the inside and the outside. The outside of the housing is covered with a reflective aluminium layer to prevent heating from ambient influences, e.g. by sunlight. The overall thickness of the isolation is 20 mm with a thermal conductivity coefficient of $0.04\ W \cdot m^{-1} \cdot K^{-1}$. To balance the remaining heat flux and the heat which is generated by the components inside the housing a 70 W Peltier element is integrated into the setup.

This configuration was designed for an application in field, operating at temperature ranges from 253K to 323 K. A temperature stabilization of at least +/- 0.25 K for a change of more than 20 K in temperature can be easily achieved. To save cooling capacity, electronics, which are generating large amount of heat, such as thermoelectric driver, computing unit and LED- driver, are housed separately from the sensor-unit.

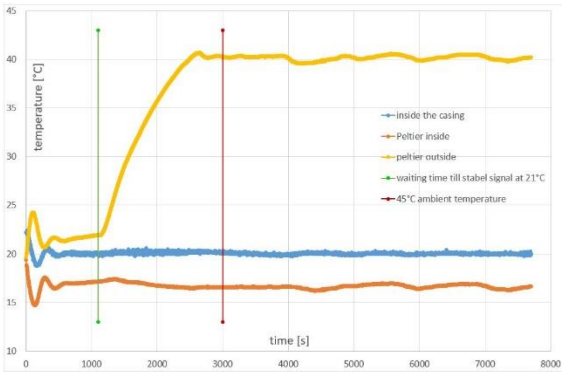

Figure 4: Temperature measurement over time shows the engaging of the sensor system at room temperature (294.6 K) until green line. Between the green and red line the system was heated to 318 K. The blue curve shows the temperature inside the system, in yellow the temperature on the outer side of the housing and in orange the temperature of the peltier at the inner side of the housing is displayed. The graph demonstrates that the current configuration is suitable to avoid disturbance by temperature fluctuations.

4 SYSTEM PERFORMANCE

One should assess the performance of the system from three different aspects. The first aspect is the RIU-resolution. The second aspect is the SPR-angle range, and the third aspect is the spatial resolution and the number of Regions of Interest (ROI) which comes with this aspect. Beside these considerations, the overall recognition sensitivity for a particular substance is crucial. This sensitivity can be improved by graphene-nanostructures, which we showed in (Genslein et al. 2016). For further comparison to other systems please see Ref. (Schasfoort, 2017).

4.1 Refractive Index Unit Resolution

To proof the resolution in refractive index sensing, deionized water and water which contains a defined amount of sodium chloride were applied as analyte. In this way, the refractive index was raised in two steps from 1.3330 to 1.3336. We are able to resolve this step with 140 digits in the SPR signal recorded by the digital camera.

This leads us to a sensitivity of $5{\cdot}10^{-6}$ RIU per digit. While summing up 100 measurements for one value we get a standard deviation of $1.4{\cdot}10^{-6}$ RIU. Since we are using a 12-bit camera, the resolution can be enhanced by the factor of four by switching to a 14-bit model.

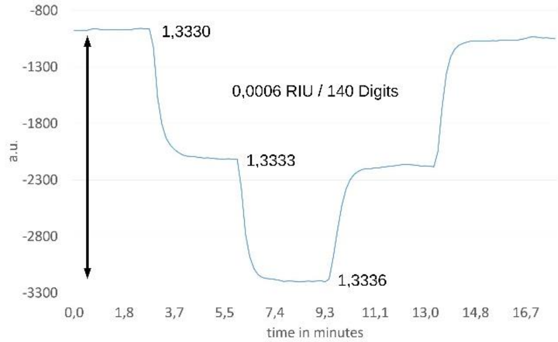

Figure 5: Resolution in refractive index measurements. The refractive index next to the sensor surface was adjusted by changing the analyte from deionized water analyte to aqueous solutions of different concentrations of sodium chloride. One digit of the intensity read out by the camera image equals a change in the refractive index of $5{\cdot}10^{-6}$.

4.2 SPR-Angle Range

Our setup is able to perform a motionless angle scan.

We have different SPR-angles on one single sensor chip at the same time.

The SPR-angle incident changes by 1° per 4 mm in x-direction. The value of °/mm depends on the type of light source.

If the spreading of the °/mm is getting higher, the size of the ROI had to be reduced, otherwise the RIU-resolution will decrease.

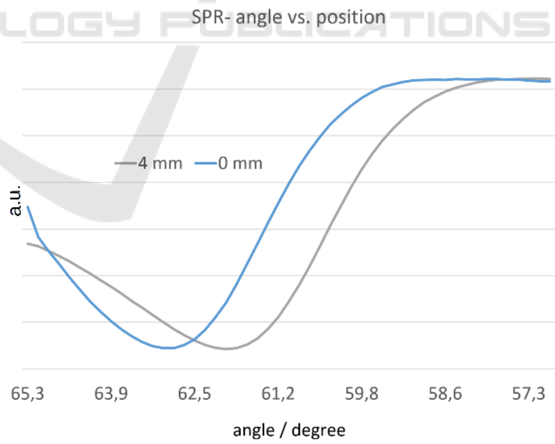

Figure 6: SPR- angle vs. position of ROI. The curve in grey is shifted by 4 mm in x direction on the sensor surface with respect to the curve in blue, this leads to an SPR-angle shift of 1°.

The refractive index of different recognition elements may vary. Therefore, the spreading of the SPR-angle can be used to place every recognition element at its optimum SPR- angle. While a reference area and its recognition elements always had to be placed in the same position in x-direction.

4.3 Spatial Resolution

The setup contains a 2-megapixel camera. In combination with the optical lens system we have depicted 400.000 pixels within an area of 10 mm x 10 mm. Therefore, every pixel depicts an area of 16 µm x 16 µm at the sensing area. In order to reduce noise we determined the area of a region of interest to 10 pixel x 10 pixel. Hence the minimum size of a recognition element is approximately 160 µm x 160 µm. The size of the recognition element can easily be reduced by changing the lens system or by switching to a high-resolution camera system. With a chip size of 2 x 2 cm – which is a common size in commercial devices – about 100 sensing spots can be already achieved with this miniaturized SPR set-up.

5 CONCLUSION

The miniaturized SPR sensor which is described here consists of core part of about 15 cm x 10 cm x 5 cm in size. It also includes the computing unit and it can work in a standard lab environment. The fully equipped system has a size of 25 cm x 30 cm x 25 cm which allows in-field applications at temperatures ranging from 253 K to 318 K. The work is still in progress; hence the size of the system will still be decreased and the temperature operation range will still be expanded. The current RIU resolution is $5 \cdot 10^{-6}$ which is already outstanding for miniaturized system. The RIU resolution will improve significant by introducing software algorithms and a more efficient camera system. Because of the spreading of the spr-angle, the system can be equipped with a wide range of receptors. The investigated system has a range of 4 °, which can be altered by a change of the light source. The overall sensitivity towards individual chemical analytes will be improved using nanostructures on top of the gold surface (Genslein et al. 2017).

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