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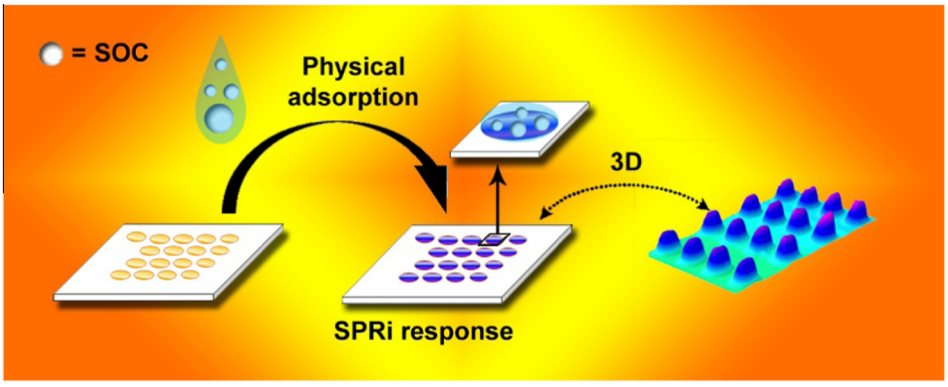
Surface plasmon resonance imaging of gold–small molecule interactions is influenced by refractive index and chemical structures

Zainab H. Al Mubarak [a], Rajagopal Ramesh [b,c], Lin Liu [d], Sadagopan Krishnan [a,*]

[a] Department of Chemistry, Oklahoma State University, Stillwater, OK 74078, United States
[b] Department of Pathology, University of Oklahoma Health Sciences Center, Oklahoma City, OK 73104, United States
[c] Stephenson Cancer Center, University of Oklahoma Health Sciences Center, Oklahoma City, OK 73104, United States
[d] Department of Physiological Sciences, Oklahoma State University, Stillwater, OK 74078, United States

GRAPHICAL ABSTRACT



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ABSTRACT

Hypothesis: We hypothesize that surface plasmon resonance imaging (SPRi) of interactions between small organic compounds and gold is influenced by the refractive index and chemical structures of the compounds.
Experiments: For the first time we imaged the SPR signals upon interaction of a gold surface with seven compounds representing aromatic, cyclic, short chain, and long chain carbon structures using an array format.
Findings: The refractive index and chemical structures of the tested compounds influenced the sensitivity of detection of the SPR microarray imager. Thus, the array methodology presented herein is suitable for studying interactions of small molecules with a gold surface.

1. Introduction

Adsorption of small organic compounds (SOCs) with gold can facilitate catalyzing certain unique chemical reactions and also help understand the nature of electronic (conductivity) and plasmonic properties of gold for sensitive detection of SOCs [1–6].

Abbreviations: SPRi, surface plasmon resonance imaging; SOC, small organic compound; O-DCB, ortho-dichlorobenzene; CyHex-OH, cyclohexanol; Ac, acetone; HCHO, formaldehyde; P-OH, 1-pentanol; Hex-al, hexanal; EtOH, ethanol; RI, refractive index; LOD, limit of detection; ppm, parts per million.

* Corresponding author.
E-mail address: gopan.krishnan@okstate.edu (S. Krishnan).

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The objective of the present investigation was to understand the influence of refractive index (RI) and chemical structures of SOCs on adsorption with gold and on detection by an optical imaging microarray system. Results of this study will help with the development of an innovative analytical platform for disease diagnostics and environmental pollution monitoring based on small molecules.

SPRi is an advanced version of conventional SPR that features array-based detection of pixel intensity changes. SPRi offers relatively better throughput than SPR, and image-based analysis and interpretation of results are technically less challenging for molecular screening and sensing applications [7]. These features translate to decreased assay time and increased analytical precision from several replicate data points available in a single measurement [8–10]. Furthermore, the SPRi technique can be easily scaled up to high density arrays. The simplicity and better throughput of SPRi are also advantageous over methods such as gas chromatography–mass spectrometry [11].

Detecting large biomolecules and macromolecules using SPR sensors poses no problem. The challenge lies in the detection of small molecules due to sensitivity limitations, as small molecules cannot induce sufficient changes in RI upon binding to the SPR sensor surface. In this study, we show that depending on the RIs and chemical structures of compounds one can obtain varying extent of detection capabilities controlled by the type and extent of secondary interactions of small molecules with gold surface plasmons.

The SPR technique using polyethylene glycol drop-coated onto a thin silver film on a prism surface has been used to detect hydrocarbons, aldehydes, and alcohols [12]. Compounds with a greater number of carbon atoms exhibited better sensitivity than their smaller carbon counterparts. In another study, a nanometric polyimide film was exposed to ethanol and SPR was measured to detect its presence [13]. Construction of gold or silver nanoparticles coated on glass slides (so called "localized SPR") and their use for sensing vapors of toluene, n-octane, chlorobenzene, m-xylene, and pentanol with limits of detection (LODs) of a few tens of parts per million (ppm) has also been described [2].

In this study we examined the influence of direct physical adsorption of certain SOCs onto gold surface plasmons on the resulting detection levels by SPRi. Although SPRi has been preferentially used to study large biomolecular interactions (e.g., protein, antigen, and DNA) [14,15], in this study we evaluated the performance characteristics of the gold surface featuring adsorbed small molecules to determine if they could be useful for developing sensing platforms applicable to environmental screening of small molecule exposomes. A future goal is to advance this method for detection of SOCs at clinically and environmentally relevant low levels in complex and real sample matrices, and results of this study provide the basis and fundamental insights needed to move forward [16–18].

2. Experimental

2.1. Chemicals, reagents, and apparatus

Seven SOCs with different RIs and chemical structures were analyzed in this study. Ortho-dichlorobenzene (O-DCB), 1-pentanol (P-OH), ethanol (EtOH), and formaldehyde (HCHO) were purchased from Sigma–Aldrich. Acetone (Ac) was purchased from Pharmaco-AAPER. Cyclohexanol (CyHex-OH) and hexanal (Hex-al) were purchased from Fisher Scientific. All solutions of SOCs were prepared in ultrapure water. All experiments were performed using an SPRimager®II array instrument (GWC Technologies, Madison, WI, USA) at room temperature. Glass chips (18×18 mm^2) coated with 16 gold spots plus a reference spot were used (1 mm spot size, SPR-1000-016). All SPRi difference images (pixel intensities of SOC-adsorbed array spots minus the pixel intensities of water-treated spots containing no SOC) were collected using the software package Digital Optics V++ provided with the instrument. The solubility of O-DCB in water is 140 mg L^{-1} at 25 °C, and the other compounds are reasonably water soluble. The LOD was calculated using the following formula [19]: $\mathrm{LOD} = M_{\mathrm{blank}} + 3S_{\mathrm{blank}}$, where M is the mean of the blank signals (i.e., ultrapure water with no SOC present) and S is the standard deviation of the blank.

2.2. SOC adsorption and detection procedures

SPRi gold array chips were used without any surface modification to adsorb SOCs. On control spots, only ultrapure water with no added SOC was used. The chip was assembled on a SPRi prism layered with an index matching fluid (GWC Technologies) between the prism and chip. Deionized water was added to all gold spots and a reference image was taken. The water was removed and a solution of SOC was spotted on each array spot (~0.5 μL) and adsorbed for 30 min. During adsorption, array chips were covered with a moisturized beaker to avoid drying of SOC solutions. The SOC-treated array spots were rinsed with water before capturing an image using a charge-coupled-device camera built into the SPRi instrument.

The difference between the two images (before and after SOC adsorption) was calculated to obtain the net increase in SPRi pixel intensity caused by the SOC, which is the extent of the height of each array spot in a 3D image representation. In some experiments, both the control water spots and SOC spots were analyzed within a single array chip. Moreover, SPRi array procedure to measure a range of concentrations of an analyte in a single microarray chip was tested using O-DCB in the concentration range of 0–50 ppm. In addition, four compounds, O-DCB, P-OH, HCHO, and Ac, are compared in a single array to demonstrate the multi-analyte detection feature of the SPRi approach for SOCs, which is not available in the conventional SPR that operates either on a single or a dual channel. The average intensity differences and standard deviations for all concentrations were calculated by repeating the measurements three times.

3. Results and discussion

Scheme 1 is a cartoon illustration of the pixel intensity increase when an SOC is adsorbed onto a SPRi gold microarray.

Fig. 1 shows the raw difference image data of the microarray adsorbed with either 50 ppm O-DCB (spots A) or pure water (spots B). The intensity of array spots adsorbed with 50 ppm O-DCB is greater than that of the pure water-adsorbed spots. Good reproducibility across the spots is clearly evident from the image. In the line profile plot presented below the image, the x coordinate position corresponds to the position of the spots along the third row in the difference image. The line profile data show a nearly 10-times pixel intensity increase for the adsorption of 50 ppm O-DCB compared to water.

Fig. 2 shows the 3D representation of SPRi difference images when the chip was exposed to 100, 500, and 1000 ppm concentrations of the HCHO solution. The intensity of microarray spots increased with the increase in concentration of HCHO used for adsorption. The net increase in SPRi pixel intensity (height) with SOC concentration is indicative of the proportionately higher levels of SOC molecules adsorbed on the gold surface.

To demonstrate the ability of SPRi to analyze multiple concentrations of an SOC within one assay, we carried out experiments with various concentrations of O-DCB adsorbed onto spots in one microarray chip. Fig. 3 shows the 3D difference image for various