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Flexible Plasmonic Sensors

Daniel Shir*,

Electrical Engineering Department, University of California, Los Angeles, CA 90095 USA

Zachary S. Ballard*, and

Electrical Engineering Department, University of California, Los Angeles, CA 90095 USA

Aydogan Ozcan

Electrical Engineering, Bioengineering and Surgery Departments, and the California NanoSystems Institute (CNSI) at the University of California, Los Angeles, CA 90095 USA

Daniel Shir: dshir@g.ucla.edu; Zachary S. Ballard: zballard@g.ucla.edu; Aydogan Ozcan: ozcan@ucla.edu

Abstract

Mechanical flexibility and the advent of scalable, low-cost, and high-throughput fabrication techniques have enabled numerous potential applications for plasmonic sensors. Sensitive and sophisticated biochemical measurements can now be performed through the use of flexible plasmonic sensors integrated into existing medical and industrial devices or sample collection units. More robust sensing schemes and practical techniques must be further investigated to fully realize the potentials of flexible plasmonics as a framework for designing low-cost, embedded and integrated sensors for medical, environmental, and industrial applications.

Index Terms

Flexible Plasmonics; Local Surface Plasmon Resonance (LSPR) sensing; Polydimethylsiloxane (PDMS); Surface Plasmon Resonance (SPR) sensing; Surface Enhanced Raman Spectroscopy (SERS)

I. Introduction

The field of plasmonics deals with engineering the resonant behavior of electron oscillations which occur at a metal and dielectric interface. The plasmonic resonance produces a strong electro-magnetic field in the near field of a given metal/dielectric interface. The magnitude, spectral location, and bandwidth of such resonances are very sensitive to metal/dielectric interface properties as well as geometry (i.e., structure). Therefore, when specifically targeted molecules are brought into close proximity of a metal/dielectric interface, they alter the local permittivity leading to changes in the enhanced near field, which can be detected through e.g., spectral shifts in the resonance as in the case of Local Surface Plasmon Resonance (LSPR) or Surface Plasmon Resonance (SPR) sensing. Specifically, SPR sensing has become a gold standard technology for studying the adsorption of target biomolecules onto a given surface. For example, SPR has been shown to be sensitive to changes as small

* Authors contributed equally.

as 10^{-7} in bulk refractive index units (RIU) [1]. The success of these sensing techniques has resulted in the routine incorporation of dedicated SPR instruments into laboratory settings for the purposes of biochemical detection. The strong plasmonic near field can also be utilized to dramatically enhance fluorescence signal or Raman scattering, leading to for example Surface Enhanced Raman Spectroscopy (SERS) [2]–[5]. SERS has been attracting a great amount of attention mainly due to its high sensitivity, demonstrating detection down a single molecule level [6],[7]. This technique measures the shift in frequency of photons scattered inelastically by molecules undergoing transitions in their vibrational modes. This inelastic scattering process only occurs for an extremely small fraction of photon interactions, therefore SERS leverages the near field effects of plasmonic resonances to enhance this scattering, enabling enhancement factors as high as 10^{10} [3]. However, despite these impressive achievements, SERS still faces some challenges in reproducibility of the engineered enhancement factors, leading to signal inconsistencies among different substrates. Additionally, SERS might suffer from issues of specificity in its application to real samples [6]–[8].

Various assays based on plasmonic nanoparticles have been successfully utilized in sensing applications in medicine and environmental monitoring, among others, due to their robust and simple colorimetric read out [2], [9]–[13]. Additionally, engineered sub-wavelength plasmonic nanostructures which support strong, concentrated near field modes and less stringent momentum matching requirements for resonant coupling have been showcased as powerful substrates for both LSRP and SERS [13]–[15]. These plasmonic nano-structures have traditionally been fabricated through standard semiconductor fabrication techniques, which limited such plasmonic designs to mainly rigid Si or SiO₂ substrates [17]. Moreover, these fabrication techniques are generally costly, requiring a clean room with expensive, dedicated equipment and are often inherently low-throughput, by and large limiting their fabrication and use to resource rich laboratories [14], [18]–[20].

However, emerging, low-cost, and scalable fabrication techniques have now enabled plasmonic structures to be fabricated on inexpensive and mechanically flexible substrates such as paper, Polydimethylsiloxane (PDMS), and various polymeric materials [18]–[21]. This recent, exciting trend has now opened the door for a wide range of sensing applications. The mechanical flexibility and unique properties of these substrates can be now exploited for robust and novel sensing schemes. For example, the porous nature of paper can be utilized to absorb liquid samples through capillary forces [22], [23]. When embedded with plasmonic nanoparticles, the paper can subsequently be used for direct SERS detection, therefore acting as a dual purpose sample collection unit and SERS substrate. As another example, PDMS can make conformal contact with rough and nonplanar substrates and thus can act as a stamp-like sample collector or a substrate for direct SERS detection [24]. Additionally, with the exclusion of colloidal lithography, these emerging low-cost high-throughput techniques allow for a diverse array of nanostructures to be packed into a small sensor area. This type of sensor design is therefore capable of multiplexed or multi-channel detection which can lead to higher accuracy and greater capacity for detecting a panel of target biochemicals [20], [25]. These flexible substrates have also been proven to support a wide range of complex nano-structures such as nano-hole arrays, nano-dome arrays, nano-pillars, and bow-tie structures, without significant loss in fidelity, therefore bringing highly sensitive

adsorption measurements to an ensemble of novel applications [20], [26]–[31]. In this Review, we will first discuss flexible plasmonic sensing devices based on paper substrates, followed by discussions of elastomeric material and polymer based devices and applications, and finally provide our conclusions.

II. Cellulose Paper Based Nanoparticle Devices

Paper based NP devices hold some unique advantages. Paper is very inexpensive, environmentally friendly, and biodegradable. It is also compatible with various low-cost, simple, and large scale fabrication techniques such as physical deposition, solution processing, and inkjet or screen printing techniques [22], [23]. The mechanical flexibility of paper based devices is particularly useful when sample collection and transfer are difficult. A sensing device integrated on paper can be used as a swab to collect samples, followed by sample analysis directly on the paper-based device. Eliminating the extra sample retrieval and transfer step is especially beneficial when the samples of interest are at low volume, on non-planar surfaces, or in solution where the paper can efficiently absorb analytes through capillary forces. For example, Yu and White demonstrated efficient sample collection using a paper based flexible plasmonic sensor as a swab to collect analyte molecules such as Rhodamine 6G (R6G), organophosphate malathion, heroin, and cocaine [23]. The sensor in this case was prepared by inkjet printing Ag NPs onto cellulose paper, and is capable of detecting femto-grams of chemicals using SERS. In a separate study, similar NP based sensors were used to detect extremely small concentrations of analytes on the order of fM in μL volumes by controlling the surface hydrophobicity and capillary forces to concentrate the analytes onto the tip of the SERS substrate as shown in Figure 1 [32]. Similar to inkjet printing, screen printing techniques have also been used to print nanoparticle arrays on filter paper for disposable and flexible plasmonic NP sensors [33]. The sensitivity of these SERS based devices mostly relies on the density and aggregation of the nanoparticles, which are closely correlated to the number of screen printing cycles. Arrays of active SERS sensors can be printed on a single substrate to allow analysis of multiple samples in high throughput [32]. However, the major challenge in printing techniques is the high concentration requirement for NP inks. High concentrations of nanoparticles cause aggregation problems but are still necessary to increase the sensitivity of SERS. Additional developments are required to overcome some of these challenges associated with NP inks to enable large scale and high throughput production of flexible plasmonic sensing devices using inkjet and screen printing processes.

In addition to printing techniques, the complex 3D fibrous, porous structures of filter and cellulose paper make them ideal candidates for exploiting solution based processing techniques. Metal NPs can be deposited randomly on a paper substrate by simply dipping the paper into solutions containing the NPs. Lee *et al.* showed detection of trace amounts of chemical contamination on a glass surface by swabbing with a common piece of filter paper coated with gold nano-rods (AuNR) [22], as shown in Figure 2. SERS measurements using this sensor showed detection down to 140 pg of 1,4-Benzenedithiol (1,4-BDT). However, the frequencies of the molecular vibrations in the measured Raman spectra were shifted compared to bulk measurements, likely due to the changes in the molecule when adsorbed onto the sensor. The sensor is fabricated through a “dip-coating” method where the paper

substrate is dipped into nanoparticle solution for a period of time to soak up the nanoparticles. The density, shape, and size of the nanoparticles can be tuned through controlling the composition and solvent of the nanoparticle solution. This technique is attractive not only because of its simplicity, but also its potential for rapid, high throughput production.

The processing time can be reduced to the order of minutes by dispersing nanoparticles in a highly volatile organic solvent with long chain alkylamines or thiols as a stabilizing agent [34], [35]. The use of volatile organic solvents enables rapid drying and high NP densities, making solution based processing methods suitable for large scale production with enhanced SERS sensitivity. Using this dip-coating method, Zheng, G. *et al.* demonstrated a Au nanoparticle coated filter paper based sensor for sensing 1-naphthalenethiol (1-NAT) with a detection limit of 0.1 nM. This sensor also demonstrated real time SERS monitoring of catalytic reactions, converting 4-nitrothiophenol (4-NTP) into 4-aminothiophenol (4-ATP).

Metal ion reduction is another common solution processing method for depositing plasmonic NPs on paper substrates. The synthesis of nanoparticles (e.g., Ag, Au, Pt, Pd) in situ on porous paper substrates can be achieved by first absorbing the metal ions onto paper substrates in metal ion solutions, followed by the reduction of ions to nanoparticles by incubation in NaBH₄ solutions [36], [37]. This type of solution processing technique can be simplified to a single step by sonicating the porous paper in a solution containing metal ions. The metal ions will reduce to metal nanoparticles with the help of the hydroxyl groups on the paper substrate to stabilize the process [38].

Physical vapor deposition is another viable method for fabricating flexible plasmonic NP devices, particularly when combined with laser induced particle formation [39], [40]. Zhang, R. *et al.* showed detection of Rhodamine 6G down to 0.1nM using SERS test strips formed by physical vapor deposition [38]. This type of technique can produce a wide range of particle sizes and densities. By controlling the laser illumination, it is possible to produce NP patterns that can then be used for e.g., colorimetric sensing of biomolecules. The precise control over the formation of the nanoparticle sensors however, comes at the cost of expensive, bulky, and sophisticated equipment such as high power lasers and sputter deposition machines. The processing cost, therefore, is usually relatively high to produce flexible NP sensors at a large scale.

III. PDMS, Polymer, and Elastomer Substrates

Conventional direct-write lithography, colloidal lithography, and soft lithography have all been developed to fabricate a wide range of nanostructures on flexible substrates such as PDMS, polyethylene terephthalate (PET), and low-density poly-ethylene (LDPE)[19], [20], [41], [42]. However, it is the fabrication techniques which are both high-throughput and low-cost that can truly pave the way for cheap and robust plasmonic sensors with a wide range of applications. Such techniques include replica molding, colloidal self-assembly, and nano-stencil lithography, and thus will be the main focus of this section [18], [19].

Mechanically flexible plasmonic sensors can make intimate contact to curved surfaces, wrap around non-planar objects, and be used as efficient sample collection tools such as medical swabs or sweat patches. Thus far, one of the most actively explored device applications for these flexible plasmonic sensors has been SERS based sensing, despite some of the challenges in its reproducibility. However, as these sensors and their read-out schemes progress, the integration of these sensing substrates into biomedical or industrial devices remains quite promising. Although LSPR based sensors have not yet been widely adopted in laboratory settings as a standardized sensing platform, their rigorously tested capability of measuring selective protein and particle concentrations offers unique sensing opportunities for certain applications. Studies into further improving and validating the reliability, reproducibility, and specificity of LSPR sensors are ongoing, and have already paved the way for commercially available sensing systems [43], [44]. Additionally, as most of these flexible polymer substrates are also optically transparent, they can be incorporated into basic colorimetric sensors with a simple and robust transmission or reflection read-out, while still retaining the ability to be multiplexed with proper surface chemistry [45]–[47]. Flexible substrates have also recently demonstrated the ability to dynamically tune plasmonic resonances, allowing for a new class of adaptable sensing devices[48]–[50].

A. Fabrication Overview: Large-area, Low-cost Production

1) Nanoparticle (NP) Based Flexible Plasmonic Devices—PDMS is one of the most commonly used substrates for flexible electronics and photonics. PDMS is flexible, non-toxic, inert, nonflammable, and most importantly, it's optically transparent across a broad spectrum, making it ideal for applications in sensing [51]. The low surface energy and mechanically flexible nature of PDMS allows it to make conformal contact to irregular and curved surfaces, which can be useful when analysis on non-planar objects is required [52]. NP sensors on PDMS substrates can make conformal contact to a non-planar surface enabling SERS measurements to be made directly [24]. PDMS based sensors are also useful in pressure or displacement sensing as will be described in the following sections.

The key component in developing flexible plasmonic sensing devices based on PDMS substrates is the physical integration of NPs into PDMS. Several promising methods have been developed for this purpose. One of the most commonly used methods is to bind metal NPs to PDMS via electrostatic or chemical forces. In this case, the PDMS surface is usually functionalized with amine or thiol chemistry to enhance the binding strength. These binding chemistries can immobilize NPs on a PDMS substrate for both SERS and refractive index detection on non-planar substrates. Alternatively, NPs can be assembled on planar rigid substrates such as glass or a silicon wafer and then transferred onto PDMS substrate by curing PDMS precursors over pre-assembled NP layers, thus embedding the NPs into the flexible PDMS substrate. These types of techniques are compatible with conventional methods of preparing closely-packed NP arrays such as photolithography, and thus enable additional flexibility and control in NP array pattern formation on the PDMS substrate.

2) Nanostructure (NS) Based Flexible Plasmonic Devices—Traditional semiconductor fabrication methods such as Electron Beam Lithography (EBL), Focused Ion Beam (FIB) milling, or photo/interference lithography have long been the dominating

methods for patterning substrates with complex nanostructures. However, in the field of flexible plasmonic sensors, these conventional techniques are utilized sparingly due to high-cost and/or low-throughput [18], [19]. They additionally require a clean room with sophisticated equipment, trained personnel, and potentially harmful chemicals. Therefore these techniques are by and large restricted to produce costly but high-quality sensing substrates which demand care, thorough cleaning protocols, and are thus mostly fit for use in laboratory settings.

Direct-write techniques are however often employed to produce primary ‘master’ structures for molding and imprinting, or shadow masks for metal deposition. After the fabrication of this primary structure, lower cost and convenient techniques can be performed. For example, one advantage of PDMS, polymer, and elastomer substrates is their ability to replicate the inverse geometry of the ‘master’ with high fidelity. This replica stamp can then be used to produce multiple copies of the master through an imprint or molding process at a fraction of the ‘master’ fabrication cost, thus enabling a low-cost, high-throughput alternative fabrication method known as soft lithography. This type of production permits a new class of low cost and disposable sensors that are suitable for applications that require one-time-use. With high-quality nanostructures and sharp plasmonic resonances, these sensors can be used for sample collection, SERS, and general biomedical sensing [19], [20]. Soft lithography, in the context of patterning plasmonic NS, is a process where a master (typically silicon) is initially patterned using conventional direct write techniques with either the desired final NS or the complimentary relief structure. This first and crucial step in this process must be performed in a clean room, and requires the production of a mask with the desired nano-pattern. This requirement does demand a relatively high fixed cost, for each sensor design. However, once the silicon master is fabricated, it can be used repeatedly for a long period of time (on the order of years with proper care). The entirety of the soft lithography can then take place outside of the clean room in a conventional wet lab. Here, the master is used as a mold for imprinting a target liquid precursor with high viscoelasticity such as hard PDMS (h-PDMS), a UV-curable or thermally-curable polymer, or even a polycarbonate (PC) sheet [18], [19]. The polymer structures can be backed by a flexible substrate such as PET, or cellulose acetate (a typical over-head transparency) [53]. Upon curing, the polymer layer can be peeled from the master, coming away with the desired nanostructure.. Additionally, there exists a solvent-assisted micromolding (SAMIM) process where a solvent is used to soften the target polymer and allow for imprinting [19], [54]. When the solvent evaporates, the polymer solidifies in the form of the desired nanostructure, whereupon it is peeled from the stamp. From here, traditional metal deposition techniques such as Electron Beam Evaporation, sputter coating, or even electroless deposition can be used to deposit metals which support surface plasmons such as Au or Ag with a Cr or Ti adhesion layer [55].

Soft lithography is both low-cost and high-throughput, without sacrificing resolution or capacity for highly-multiplexed sensor designs. It therefore enables the mass production of plasmonic sensors, which, as result of their low cost and flexibility, now have the potential of being incorporated into disposable medical equipment as one-time-use LSPR sensors or SERS substrates. Recently, this replica molding method was scaled-up to produce 2000 ft rolls of nano-hole array structures embossed onto flexible PET [20]. In this case, a secondary Ni master stamp was used to thermally imprint the nano-hole array into the PET

roll at a reported rate of 100 ft/min with a nanostructure yield exceeding 99%. This study further proposed a fully integrated flexible sensor system design with stacked organic LEDs (OLEDs), microfluidics, and imprinted nano-hole array plasmonic structures which could similarly be produced in high-volumes at low costs. Furthermore, this roll-to-roll type of fabrication allows for multichannel sensor design, where many different NS can be packed tightly on the same sensor area. It should be noted however, that the contact nature of the replica molding process is more prone to defects as compared to the non-contact photolithography process, leading to broader resonances and increased sensor to sensor variability. Therefore attention and effort must also be focused towards developing more robust read-out schemes with self-referencing and adequate tolerances [47].

Another fabrication technique which merits discussion is Nano-Stencil Lithography (NSL). Though not explicitly a soft-lithography process, NSL shares the same low-cost, high throughput advantages as the previously discussed replica molding method.

This one-step process requires a template with the desired NS that is used as a shadow mask or 'stencil' for depositing the desired metal onto a wide range non-conventional, non-planar, polymer or elastomer substrates [41], [57]. Asku *et al.* demonstrated NSL as a viable production technique for printing plasmonic NS on PDMS, parylene-based polymers, and even conventional food wrap plastics [41]. Bow-tie structures and nano-rod structures with 100 nm structural dimensions were fabricated and transferred to nonplanar surfaces such as optical fibers for remote sensing applications. NSL does however have a few important disadvantages. It is inherently a lower resolution technique (± 10 nm) due to the shadowing effect caused by the non-zero stencil-substrate gap. Additionally after the evaporated metal particles pass through the stencil, they diffuse outwards, leading to a halo-like edge effect around the well-defined structure [41]. Another limitation of NSL is that it is restricted to mostly planar nanostructures due to the line-of-sight shadow mask process. Therefore 3-D and quasi 3-D structures, which have been demonstrated to exhibit unique and information-rich multi-resonant sensor behavior are out of reach of NSL [26], [58].

Hybrid methods based on colloidal lithography (CL) have also been investigated for creating NS on flexible substrates [29], [59], [60]. For example, Knoblen *et al.* fabricated Au islands on polymer nanopillars, through random colloidal assembly on a gold thin film, followed by Ar ion milling, and an oxygen plasma step [29]. The resulting structure, backed by a flexible polyethersulfone (PES) foil, allows for a decrease in the spatial overlap between the plasmonic near-field and the dielectric substrate. Therefore, the effective refractive index is more suitable for high-sensitivity refractive index sensing based on the LSPR shift. These Au island structures demonstrated a sensitivity of 200 nm/RIU, but can theoretically be optimized to achieve even higher sensitivity, rivalling that of the best plasmonic NS-based designs. Shen *et al.* also developed a silver 'nano-mouth' array on a PDMS substrate through a multi-step process. Silica particles are deposited onto a polystyrene (PS) substrate which is subsequently heated, thus trapping the particles [59]. These particles are then removed by an HF etching step, leaving behind hemispherical relief pockets. The patterned substrate then undergoes a two-step shadow silver deposition process. PDMS is molded into the silver NS, and then a lift-off process comes away with the nano-mouth array on the PDMS substrate. The resulting structure demonstrated a remarkably high ~ 1000 nm/RIU sensitivity due to the

deeply sub-wavelength ‘mouth-like’ slit in the NS, and further exhibited dynamic tunability of the LSPR resonance which will be discussed in a later section. Although these CL hybrid methods are capable of producing exotic NS with high bulk RI sensitivities, they generally involve more processing steps compared to soft-lithography based methods. This multi-step processing does, however, allow for greater control over the dimensions and geometry of the resulting NS based on the size and concentration of particles initially used, or the time of the etching, ion milling, and oxygen plasma steps [46], [60]. However, the main disadvantage of these CL methods is their inability to produce multiplexed or multi-channel sensor designs with a variety of NS packed closely on the same substrate [18].

B. SERS with Flexible Plasmonic Nanostructures

SERS has been one of the most successful applications of the near field enhancement created by plasmonic nanostructures, enabling Raman scattering enhancement factors as high as 10^{10} [3], [61]. Although SERS has been widely used as a technique for molecular and chemical sensing, it has been mostly restricted to rigid surfaces. Cunningham *et al.* demonstrated a flexible SERS sensor in series with an intravenous (IV) tube and Raman scope for verifying and measuring drug delivery concentration, achieving a limit of detection (L.O.D) of 700 ng/mL, far below a typical clinically administered dose [58]. Though not explicitly demonstrated during this study, the flexible nature of the plasmonic nano-dome array (PNA) SERS substrate could enable direct integration of SERS substrate onto the IV tubes, IV bags, or syringes. Furthermore these PNA structures are made through the low-cost, high throughput replica molding process discussed in the previous section and are therefore scalable to roll-to-roll mass production [28].

In a recent effort to showcase the advantages of mechanically flexible sensors, Shiohara *et al.* showed the detection of pesticides on fruit skin using PDMS and NPs as a SERS substrate [24]. In this case, the SERS substrate consisted of Au nanostars immobilized on APTES functionalized PDMS. The SERS substrate was then brought into contact with the curved surface of an apple for SERS measurements, as shown in Fig. 5. This type of application coupled with its low-cost and scalable production could allow for faster and more effective food quality monitoring, where one-time use sensors can be used as stickers and read using a portable SERS read-out instrument.

Flexible substrates also play a key role in Stamping Surface-enhanced Raman Spectroscopy (S-SERS) [25], [62]–[64]. In this technique, a PDMS thin film is used as a molecular carrier substrate by first collecting the desired fluid sample on the PDMS film and allowing this sample to dry. Upon drying, the PDMS thin film can be stamped into the SERS substrate, thus forcing the detectable molecules in close contact with the plasmonic hot-spots on the surface enhanced substrate. Li *et al.* demonstrated the use of S-SERS for the detection of creatinine, an abundant protein found in urine, the concentration of which has been associated with renal disease and kidney problems [62]. Using nano-porous gold disk plasmonic substrates, a limit of detection approaching that of commercial creatinine kits (13.2 nM and 0.68 mg/dl in water and urine, respectively) was achieved via S-SERS. For this application, the mechanical flexibility of the molecular carrier substrate has two important advantages. First, it allows for conformal contact with the SERS substrate,

creating an ideal ‘sandwich’ to best utilize the near field enhancement of the plasmonic design. Second, the flexibility also allows for an alternative, streamlined, and convenient means of sample collection such as patch based sample collectors for sweat, or other ‘stick and peel’ based sample collectors integrated into existing medical devices such as swabs, syringes, or even endoscopes.

C. Dynamically Tunable Flexible Plasmonic Structures

Another exciting aspect of flexible plasmonic nanostructures is the dynamic spectral tunability of the LSPR locations through mechanical stress and strain. Other methods have also been shown in the literature for tuning SERS and LSPR substrates using e.g., electrical, magnetic, and thermal mechanisms; however mechanical stress and strain remain quite attractive, especially for various practical applications [50], [65]–[67]. Elastically flexible substrates with the appropriate plasmonic structures can be stretched uniformly to change the geometry of the surface structures. This geometrical alteration, whether it is elongation of the periodicity, or changes in the effective lattice arrangement can have significant impact on the LSPR as these resonant effects are due to confinement of the coupled electromagnetic fields into well-defined sub-wavelength geometries [50], [68].

For example, Millyard *et al.* achieved a highly tunable LSPR by depositing closely-packed arrays of 20 nm Au NPs onto PDMS via solution processing techniques [68]. The LSPR of such devices is highly dependent on the inter-particle separation of the Au NPs. As a result, resonant shifts of more than 40% can be achieved by stretching the substrate with 20% strain. Kang *et al.* demonstrated real-time tunability with plasmonic cap arrays on a PDMS substrate, fabricated by spin coating colloidal silica particles onto a gold surface and then transferring them to a PDMS substrate through a mold-and-peel process [48]. These embedded silica beads are then surface modified to capture much smaller gold nanoparticles, resulting in a LSPR nanostructure with the ability to alter the arrangement of the embedded colloidal patterns through mechanical stress and strain. For example, the hexagonal arrangement of particles at 0% strain is transformed into distinctly parallel arrays of particle chains at 30% strain. This alteration in the nanostructure geometry can shift the plasmonic resonance over a 40 nm range, and allows for dynamic tuning of the SERS enhancement factor up to 3 times the enhancement factor of the substrate at 0% strain, which can be very useful for optimizing the SERS signal based on e.g., the analyte concentration. As another example, Park *et al.* demonstrated, both experimentally and theoretically, the tunability of Au heptamer clusters on a PDMS substrate [49]. Fabricated through an EBL and lift-off process, the Au heptamer clusters exhibited a sharp Fano resonance in the optical regime that was demonstrated to shift over a 34 nm range with up to 30% strain. Furthermore, Park *et al.* observed the activation of certain optical modes using appropriate strain, which opens an interesting avenue of dynamically tunable resonance sensing. Many other plasmonic nanostructures are, at least in theory, capable of dynamic tuning through mechanical stress and strain. However, to fully realize the potential of such real-time tunable plasmonic structures, new and more elastic substrates must be explored to allow maximum contraction and extension among nanostructure features. Toward this end, NSL has recently been utilized to explore such substrates. Low-density poly-ethylene (LDPE), a polymer with high elasticity, was patterned with gold nano-rods through NSL enabling a remarkable 160 nm

red-shift of the plasmonic resonance upon stretching [38]. Plasmonic triangles in a bow-tie configuration (Fig. 6) have also been fabricated, and show promise for tunability due to the strong gap dependence of the plasmonic hot-spot created by the opposing sharp corners of the bow-tie.

In addition to dynamic tuning of the resonance behavior, the mechanical flexibility of these sensor substrates can also be used to build powerful sensors for various stimuli. For example, Rankin *et al.* developed a pressure sensitive device consisting of silver NPs on PDMS, an air gap, and a underlying conductor [69]. When pressure is applied on the PDMS, the distance between Ag NPs and the bottom conductor is reduced, leading to changes in optical coupling between the NPs and the conductor plane. This change in optical coupling leads to a distinct color alteration from its original state, and therefore enables the detection of pressure that is applied onto the sensor surface. These types of devices are in general very sensitive to any distortions to the elastomeric substrate. As a result, a wide range of sensors can be constructed by engineering the response of the elastomeric substrate to different external stimuli, such as force, pH, moisture, and various chemicals, solvents, etc.

IV. Conclusions and Outlook

Taken together, low-cost and high-throughput fabrication techniques have now enabled a new class of cost-effective and mass-produceable flexible plasmonic sensors which hold great potential for device integration and novel sensing schemes. By fabricating metallic nano-structures and nano-particle assemblies onto substrates such as paper, PDMS, and elastic polymers, strong plasmonic near-field enhancements can be utilized in various applications, including point of care medicine, food safety, and environmental monitoring. To name some successful examples, flexible plasmonic sensors have already been demonstrated as useful and practical tools for drug monitoring, food quality screening, and rapid swab-based trace chemical detection, among others. Therefore these sensors have massive potential as fabrication techniques continue to improve, and as more robust, versatile and cost-effective read-out devices are developed. Both LSPR and SERS can now be fully realized within the context of existing medical and industrial devices as stick and peel sensors, embedded sensors for point-of-care diagnosis, and as dual-purpose sample collection and sensing substrates.

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Biographies

Daniel Shir received his Ph.D. degree in Materials Science and Engineering from University of Illinois at Urbana-Champaign in 2010. After graduating he worked as a senior process development engineer at Intel Corp. for developing the next generation semiconductor processing technology. He joined Prof. Ozcan's research group as a post-doctoral scholar to work on flexible, low cost, and field portable plasmonic sensors. His research interests include novel nanofabrication methods, nano-plasmonics and optical imaging techniques, as well as biosensing applications based on plasmonic sensors.

Zachary S. Ballard received his B.S. degree in Engineering Physics from Brown University in 2013. After graduating he was a visiting researcher at the Max Planck Institute for the Science of Light in Erlangen, Germany where he worked with free-space couple micro-resonators for biosensing applications. He is currently an NSF Fellow and pursuing a Ph.D. degree in the Electrical Engineering Department at the University of California, Los Angeles. His work aims to develop robust imaging and sensing platforms for point-of-care diagnostics applications.

Aydogan Ozcan received his Ph.D. degree at Stanford University Electrical Engineering Department. After a short post-doctoral fellowship at Stanford University, he was appointed as a research faculty at Harvard Medical School, Wellman Center for Photomedicine in 2006. Dr. Ozcan joined UCLA in the summer of 2007 as an Assistant Professor, and was promoted to Associate and Full Professor ranks in 2011 and 2013, respectively. He is

currently the Chancellor's Professor at UCLA and an HHMI Professor with the Howard Hughes Medical Institute, leading the Bio- and Nano-Photonics Laboratory at UCLA Electrical Engineering and Bioengineering Departments, and is also the Associate Director of the California NanoSystems Institute (CNSI) at UCLA.

Dr. Ozcan holds 31 issued patents (all of which are licensed) and more than 20 pending patent applications for his inventions in nanoscopy, wide-field imaging, lensless imaging, nonlinear optics, fiber optics, and optical coherence tomography. Dr. Ozcan gave more than 250 invited talks and is also the author of one book, the co-author of more than 400 peer reviewed research articles in major scientific journals and conferences. In addition, Dr. Ozcan is the founder and a member of the Board of Directors of Holomic LLC.

Prof. Ozcan received several major awards including the 2011 Presidential Early Career Award for Scientists and Engineers (PECASE), which is the highest honor bestowed by the United States government on science and engineering professionals in the early stages of their independent research careers. Dr. Ozcan received this prestigious award for developing innovative optical technologies and signal processing approaches that have the potential to make a significant impact in biological science and medicine; addressing public health needs in less developed countries; and service to the optical science community including mentoring and support for underserved minority undergraduate and graduate students. Dr. Ozcan also received the 2015 UCLA Postdoctoral Scholars Mentoring Award for his commitment to training and mentoring of postdoctoral researchers.

In addition to these, Dr. Ozcan received the 2013 SPIE BioPhotonics Technology Innovator Award, the 2011 Army Research Office (ARO) Young Investigator Award, 2011 SPIE Early Career Achievement Award, the 2010 NSF CAREER Award, the 2009 NIH Director's New Innovator Award, the 2009 Office of Naval Research (ONR) Young Investigator Award, the 2009 IEEE Photonics Society Young Investigator Award and the MIT's Technology Review TR35 Award for his seminal contributions to near-field and on-chip imaging, and telemedicine based diagnostics.

Prof. Ozcan is also the recipient of the 2013 and 2015 Microscopy Today Innovation Awards, 2012 Popular Science Brilliant 10 Award, 2012 National Academy of Engineering (NAE) The Grainger Foundation Frontiers of Engineering Award, 2011 Innovators Challenge Award presented by the Rockefeller Foundation and mHealth Alliance, the 2010 National Geographic Emerging Explorer Award, the 2010 Bill & Melinda Gates Foundation Grand Challenges Award, the 2010 Popular Mechanics Breakthrough Award, the 2010 Netexplorateur Award given by the Netexplorateur Observatory & Forum in France, the 2011 Regional Health Care Innovation Challenge Award given by The von Liebig Center at UCSD, the 2010 PopTech Science and Public Leaders Fellowship, the 2009 Wireless Innovation Award organized by the Vodafone Americas Foundation as well as the 2008 Okawa Foundation Award, given by the Okawa Foundation in Japan.

Prof. Ozcan was selected as one of the top 10 innovators by the U.S. Department of State, USAID, NASA, and NIKE as part of the LAUNCH: Health Forum organized in 2010. He also received the 2012 World Technology Award on Health and Medicine, which is

presented by the World Technology Network in association with TIME, CNN, AAAS, Science, Technology Review, Fortune, Kurzweil and Accelerosity.

Dr. Ozcan is elected Fellow of SPIE and OSA, and is a Lifetime Member of AAAS.

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Fig. 1.

(a) Silver nanoparticles can be printed onto paper. (b) A surface is swabbed with the SERS-active surface. (c) Lateral flow concentration can be achieved by placing the swab in a solvent. (d) SERS detection is performed using a fiber optic Raman probe [32]. Reprinted (adapted) with permission from [24]. Copyright (2010) American Chemical Society

Fig. 2.

(a) Images of the AuNR solutions and the target filter paper before and after exposure; (b) photograph showing the SERS substrate being swabbed on a surface to collect target analytes; (c) SERS spectra from AuNR loaded paper showing different amounts of 1,4-BDT. Reprinted (adapted) with permission from [14]. Copyright (2010) American Chemical Society.

Fig. 3.
Diagram of basic replica molding processes [56].

Fig. 4. (a) Plasmonic nano-dome array structure on polymer sheet substrate; (b) SEM of PNA structures with inset showing inter-cap separation distance (15–20 nm); (c) prototype SERS substrate with IV tube inlet and outlet for serial drug monitoring; (d) experimental set up during SERS drug monitoring [58].

Fig. 5.

Application of flexible SERS substrate for measuring pesticides through conformal contact with the skin of an apple and subsequent spectroscopic read-out. Reproduced (“Adapted” or “in part”) from [24] with permission of The Royal Society of Chemistry.

Fig. 6.

(a) Example of a Silicon stencil mask with a bow-tie pattern; (b) the one-step fabrication process in NSL; (c) surface profile of plasmonic bow-tie structure fabricated through NSL; (d) visualization of induced mechanical strain; (e) illustration of large area fabrication (f) and flexibility [41].