RESEARCH ARTICLE | APRIL 02 2021

Industrial view of plasmonic devices made by nanoimprint or injection molding **FREE**

Iris Prinz **록** [[][©] ; Michael J. Haslinger [[][©] ; Michael Mühlberger; Gottfried Reiter; Adrian Prinz; Martina M. Schmidt; Thorsten Schaller; Maria Bauer; Maurizio Musso [[][©] ; Georg Bauer

(Check for updates

J. Appl. Phys. 129, 130902 (2021) https://doi.org/10.1063/5.0039152







Industrial view of plasmonic devices made by nanoimprint or injection molding

Cite as: J. Appl. Phys. 129, 130902 (2021); doi: 10.1063/5.0039152 Submitted: 30 November 2020 · Accepted: 14 March 2021 · Published Online: 2 April 2021



Iris Prinz,^{1,a)} 🝺 Michael J. Haslinger,² 🔟 Michael Mühlberger,² Gottfried Reiter,¹ Adrian Prinz,¹ Martina M. Schmidt,³ Thorsten Schaller,³ Maria Bauer,⁴ Maurizio Musso,⁵ 🝺 and Georg Bauer¹

AFFILIATIONS

¹Stratec Consumables GmbH, Sonystr. 20, 5081 Anif, Austria

²Profactor GmbH, Im Stadtgut D1, 4407 Steyr-Gleink, Austria

³LEONHARD KURZ Stiftung & Co. KG, Schwabacher Str. 482, 90763 Fürth, Deutschland

⁴Mycropartners, Ernst-Grein-Straße 33, 5026 Salzburg-Aigen, Austria

⁵Fachbereich Chemie und Physik der Materialien, Universität Salzburg, Jakob-Haringer-Strasse 2a, 5020 Salzburg, Austria

^{a)}Author to whom correspondence should be addressed: i.prinz@stratec.com

ABSTRACT

We present a perspective of the industrial realization of plasmonic devices especially for life science and *in vitro* diagnostic applications. The \approx we present a perspective of the industrial realization of plasmonic devices especially for the science and *m vitro* diagnostic applications. The main focus is on the manufacturing technologies Nanoimprint Lithography and injection molding as scalable processes for high volume manufacturing. Both technologies have their individual strengths and technical restrictions, which are discussed along different examples for plasmonic applications especially for biosensor applications. *Published under license by AIP Publishing.* https://doi.org/10.1063/5.0039152

I. INTRODUCTION

Plasmonics-the science and technology of understanding and using plasmons-is an exciting field of R&D offering fundamental insights into light-matter interaction as well as interesting business opportunities.

Substantial research over the last few decades has contributed to the understanding and manipulation of light-matter interactions on the nanoscale. The focus of research was and still is on metallic nanostructures that allow the excitation of surface plasmons. Localized Surface Plasmons (LSPs) on isolated metal nanostructures (i.e., metallic nanoparticles) and Surface Plasmon Polaritons (SPPs) propagating at metal-dielectric interfaces are the basis of many biosensor applications. In particular, corrugated and periodically structured metal surfaces are of great interest due to the easy excitation of SPP. Also, non-metallic materials can be used for plasmonics [e.g., aluminum-zinc-oxide (AZO), TiN, ZnO,¹ or in general transition metal nitrides, transition metal carbides, and metal oxides (e.g. Ref. 2) or conductive polymers],³ but in the context of industrial applications and this paper we will restrict the discussion to metallic nanostructures, although especially polymers for plasmonics could be interesting in the context of injection molding and nanoimprinting. This will, however, not be discussed here.

With the significant advances in the field of nanotechnology over the last few decades, plasmonic devices have attracted much attention and a large number of plasmonic sensor applications have been developed.⁴ In recent years, biosensor applications in life science and in vitro diagnostic (IVD) applications exploiting several plasmonic effects emerged.⁵ For example, the quantification of serum biomarkers plays an important role in medical science. Biomarkers are used for risk stratification, detection of disease, and therapy monitoring in patient cohorts in all clinical areas. Very often, their concentrations in human blood are very low, which creates a permanent need for raising the sensitivity of the used assay methods. Details on the basic physics and functioning of different applications will not be given here, since we will mainly focus on the fabrication aspects. More details on plasmonic sensors for life science applications can be found in recent reviews.⁴,

Specifically in the case of sensors that use periodically nanostructured metal surfaces,⁴ the necessity of a cost-effective production of these components is often decisive for their later use. When it comes to cost-effective nanostructure manufacturing, injection molding and Nanoimprint Lithography are among the most important manufacturing processes, each with its own strengths.

Within this publication, we want to focus on three different exemplary applications, realized by injection molding or Nanoimprint Lithography (NIL). The first application is utilizing plasmonic nanoparticles and the observation of their rotational dynamics,⁹⁻¹¹ the second is using the effect of metal enhanced fluorescence (MEF),¹² and the third is exploiting Surface Enhanced Raman Spectroscopy (SERS).¹³

Each application aims to detect biomarkers in lower subpicomolar concentration by enhancing the optical signal^{14–16} that were exclusively enabled by the fact that cost-effective manufacturing techniques in the nanometer scale got more and more established for biosensor applications,^{12,13} serving the needed reproducibility and pattern fidelity.

II. NANOIMPRINT AS MANUFACTURING METHOD

Nanoimprint Lithography (NIL)¹⁷⁻¹⁹ is a technology for the replication of micro- and nanostructures offering a large flexibility as far as substrates, structures, structured areas, and structured materials are concerned. In course of a typical NIL process, a nanostructured stamp containing the negative of the desired nanostructures is pressed into a liquid layer of material, e.g., a resist, which is coated in a thin layer on a substrate. This is schematically shown in Fig. 1(a). After solidification of the material, which is done by ultra violet (UV)-curing in the case of UV-NIL [Fig. 1(b)], or by cooling below the glass transition temperature for hot embossing, the stamp is removed and the micro- or nanostructure was replicated [Fig. 1(c)]. In many cases, the structured material will form an integral part of the final device and no further pattern transfer (using, e.g., reactive ion etching) is necessary. However, NIL also offers the possibility for pattern transfer via etching²⁰⁻²² and lift-off processes.^{23,24} Advantages of nanoimprinting are the possibility to span a wide range of feature sizes, from sub-10 nm²⁵ to several $100 \,\mu$ m,^{26–28} the possibility to create complex structures in a single fabrication step^{29,30} and a large flexibility concerning the choice of materials.³¹⁻³⁴ In contrast to conventional optical lithography, nanoimprinting can also be performed on non-flat substrates.³

Traditional nanoimprint uses wafers or wafer-sized substrates in various forms and target applications. Usually, this type of nanoimprint equipment works in a plate-to-plate process; however, roller-based processes are also possible. This ensures that large



FIG. 1. Schematic nanoimprint process. (a) Micro/nanostructured stamp (green), substrate (gray), and resist (red), (b) stamp is imprinted into the resist. For UV imprinting, the resist is cured using UV light; for Hot Embossing, the resist is heated and imprinted (c) after separation of stamp a copy is created on the substrate.

areas can be processed using NIL. For a plate-to-plate process, full wafer imprints have been shown up to 300 mm diameter substrates³⁸ as well as step and repeat nanoimprint processes with a throughput of up to 90 wafers/h.³⁹ For display or photovoltaics applications, sheet-to-plate imprints on substrates of Gen 3 $(550 \times 650 \text{ mm}^2)^{40,41}$ and roll-to-plate imprints even in the m² area^{42,43} have been demonstrated.

A critical component in cost of ownership considerations is the lifetime of the stamps that are used, i.e., how many imprints can be done before the stamp has to be changed. In this context, it has to be mentioned that in a large number of cases the actual stamp that is used for nanoimprinting is itself a copy of a nanostructured master. The stamp lifetime critically depends on the type of structures and the materials used.^{44,45} It has been reported that stamps can be used several hundred or thousands of times,^{45–48} which is already in the range of what is suitable for industrial applications (e.g. Ref. 39).

Nowadays, NIL is used in the production of diffractive optical elements (e.g., structured light applications like face ID in Apple iPhones),⁴⁹ microlenses,^{50,51} gratings for lasers,⁵² as well as in life science applications.^{53–55} Nanoimprinting is also used in display production,⁵⁶ photonics crystals,^{57,58} negative index materials,²³ sensors,⁵⁹ and many more applications. It is also widely established in research.

III. INJECTION MOLDING AS MANUFACTURING METHOD

For the mentioned applications, an injection molding process based on former Blu-ray Disc and DVD manufacturing with a throughput around a few thousand units per hour was adapted to get serve also typical life science or *in vitro* diagnostic formats. Using this technique, i.e., an injection compression process as shown in Fig. 2 nanostructures as well as microstructures can be created using materials such as PMMA, polycarbonate (PC), or cyclic clafin polymers (CCD). olefin polymer (COP). For biosensing application, usually COP is preferred, having a high transparency and a low level of background fluorescence in the visible region. For a high quality replication of micro- or nanostructures, a nickel insert needs to be created. For most applications, photo lithography, laser lithography, or e-beam lithography is used to generate the needed features and copied into Nickel by electroplating, which finally serves as an insert for the mold (see Fig. 2). In addition, a vario-thermal process supports the reproduction of high fidelity pattern, especially in the nanometer regime as usually needed for the plasmonic effect. Vario-thermal means that the mold can be heated and cooled during the injection molding cycle, which allows the part to be cooled before the mold is separated, thus maintaining the patterns with a high fidelity. The compression that is applied during the heating cycle enables the exact filling of the micro- or nanometersized structures. High aspect ratio features can hardly be injection molded using standard molding techniques.

IV. REALIZATION OF PLASMONIC DEVICES

In order to realize products that allow plasmon excitation, typically nanostructured metal layers are needed. Therefore, a thin layer of metal can be deposited on a pre-structured surface either fabricated by NIL or injection molding.



FIG. 2. Schematic drawing of injection compression molding. (a) The micro or nanostructured insert (green) is mounted inside the mold, the mold is heated and closed to embossing nip, afterward the polymer (black) is injected. (b) Compression after volumetric filling is used in order to achieve evenly distributed melt pressure for reduced frozen stress and precise replication of micro- or nanostructures. (c) While mold is closed, the part is cooled down. (d) After cooling down, the mold is opened and the part is removed by automated handling.

In the case of injection molding, the nanostructures as well as the part itself are made of the same polymer due to the injection process. For UV-Nanoimprint, typically an additional thin resin layer on top of a substrate, mostly glass, silicon, or polymer films is applied and structured. For nanoimprinting, several ways can be chosen to generate metal structures, like lift-off processes generating isolated metal structures or full area coatings. In this respect, nanoimprint is very flexible and standard semiconductor processes are applicable as shown in Fig. 3. The nanoimprint process allows for additional process steps and enables lift-off processes, which can be used to realize a greater variety of nanostructures.

For injection molding, the metal layer is usually deposited homogeneously across the entire surface by, e.g., sputter coating processes. An example of such an industrial sputter coating equipment is shown in Fig. 4. Due to the nature of the injection molded part, a lift-off process is simply not possible as it is made of the entirely same material. Therefore, the plasmonic response has to be created with a large-area coating over nanostructures. This restricts the design freedom of the plasmonic device but, on the other hand, leads to fewer production steps and is therefore cost effective.

Not only the nanostructures and metallic coatings are important



FIG. 3. Schematic drawing of the lift-off process. (a) Micro/Nanostructured stamp (green), substrate (gray), imprint (red), and lift-off resist (yellow). (b) Nanoimprint step. (c) Substrate with lift-off layer and imprinted resist. (d) Etching through imprint residual layer and lift-off layer. (e) Deposition of metal layer. (f) Lift-off layer, resulting in a substrate with metallized gratings.



FIG. 4. Picture of the sputter coating process established at Stratec Consumables for high volume throughput. (a) Two black carbon PP substrates are automatically loaded into the sputter coating machine and (b) unloaded after the sputter coating process of the metal film. The metal coating is done homogeneously across the whole substrate surface.

means that the nanostructured part [Fig. 5(a)] needs to be connected with a cover containing microfluidic structures, flow cells [Fig. 5(b)], or with a microtiter plate in order to enable liquids to be guided across the sensing surface. In the case of injection molding, the micro or nanostructured part can easily be assembled to another injection molded cover, usually by bonding or welding [Figs. 5(c) and 5(d)]. The nanoimprint substrates usually contain different materials like glass or silicon as such a more complex assembly step is needed, but certainly can also be integrated or connected to injection molded covers or glass/silicon parts, depending on the application.

V. EXAMPLE OF PLASMONIC DEVICES MADE BY NIL OR INJECTION MOLDING

The first application we present within this perspective is the realization of highly monodisperse magnetic-plasmonic nanoparticles by using UV-NIL at PROFACTOR GmbH. The principal fabrication process is depicted in Fig. 3, by using NIL as patterning technology together with thin-film deposition and a lift-off process. The fabrication process has been developed for the use in novel point of care testing for the detection of biomarkers in *in vitro* homogeneous biosensors.^{11,60} This detection method relies on the binding of analyte molecules to magnetic-plasmonic nanoparticles, so-called nanoprobes, which results in a measurable change in the hydrodynamic volume of the particles. This change in hydrodynamic volume can be detected by the change in rotation behavior of the magnetic nanoprobes in a rotating external magnetic field.^{11,61–63} The scattering cross section of nanoparticles supporting plasmonic resonances is by a factor of 100 higher than that of nonplasmonic particles, which leads to a lower particle concentration in the analyte sample and to a significant increase in sensitivity.¹¹ To achieve high sensitivity, monodisperse magnetic-plasmonic nanoparticles are of advantage.

The fabrication process is as follows: first, a suitable substrate (e.g., a silicon wafer) is coated with a layer of LOR1A⁶⁴ resist followed by a layer of the actual nanoimprint resin mr-NIL212.4 This double layer approach is used to allow a reliable lift-off N process later on. After the imprint process and the separation of of the stamp from the substrate, an anisotropic oxygen plasma etch is used to remove the residual layer of the imprint and etch through the LOR1A resist. This is followed by a developing step in diluted MICROPOSIT MF-24A to selectively etch the LOR1A and thus create an undercut. Once the imprinting is completed, the layer \vec{s} sequence for the particles gets sputter deposited. Depending on the functionality of the final particles, various plasmonic, magnetic, passivation, and sacrificial layers are necessary. With the help of the undercut in the LOR1A layer, the mask can be lifted off the substrate by immersion in MF-24A. The nanoparticles, which remain on the substrate after this first lift-off process, can be brought into solution through a second immersion in a developer, which selectively etches the bottom sacrificial layer. In a final step, the nanoparticles are transferred into ultra-pure water by magnetic separation using conventional permanent magnets. More details on these processes can be found in Refs. 23, 46, and 66.

The NIL-based fabrication process is ideally suited to produce flat monodisperse nanoparticles of various shapes that consist of a multimaterial stack, which cannot be fabricated by other chemical synthesis methods.^{9,11} Depending on the shape, given by the nanoimprint stamp, and the material combination of the individual layers, plasmonic and magnetic properties can be specifically tailored and controlled. The shape of the particles can be changed simply by using a stamp with a different geometry (i.e., elliptical, rectangular, circular, and nanopockets). The plasmonic and magnetic properties can be achieved and controlled by the alternating deposition of metal, ferromagnetic, and dielectric layers. In Fig. 6, scanning electron microscopic (SEM) images of different steps

oplied Physics		jap
	(b	
(C)	1	4)

FIG. 5. (a) Injection molded part with eight nanostructured fields in microscope slide format. (b) Injection molded part with 8 flow cells and 16 through holes to be used as inlet and outlet for the liquids. (c) Schematic drawing of an assembled microfluidic device. Lower part shows the nano/microstructured part typically including the plasmonic structures [like shown in a)], middle part includes through holes and flow cells [like shown in (b)] and inlets are often connected with tubings. (d) Microfluidic device filled with red ink. Typically, microfluidic devices have several functionalities and contain several inlets and outlets, depending on the application and assay needs.

during an elliptical nanoparticle fabrication process are presented. The size distribution of the monodisperse nanoparticles, before the final separation from the substrate [Fig. 6(c)], shows a Gaussian distribution of ±3% of the particle area.⁹ Preliminary results on the detection using particles fabricated by NIL have been published here.¹¹ The functionalization of the nanoparticles, which results in the final so-called nanoprobes, and detailed results on detection will be published elsewhere.⁶

(d)

scitation.org/iournal/ian

PERSPECTI



FIG. 6. SEM images representing steps in the production of nanoparticles. (a) SEM image showing the imprinted mask after the etching steps. (b) Mask after thin-film deposition. (c) Sample after performed mask lift-off process showing the remaining highly uniform particles on the substrate. (d) Accumulation of final nanoparticles after separation of the substrate. Scale bar is 500 nm in all images. Adapted from T. Mitteramskogler, M. J. Haslinger, A. Shoshi, S. Schrittwieser, J. Schotter, H. Brueckl, and M. Muehlberger, Proc. SPIE 10775, 107750Y (2018). Copyright 2018, SPIE.

Journal of



FIG. 7. 10 × 10 cm² glass substrate with 8×8 Imprints performed in an S&R tool. Each imprint contains 100×10^6 holes and after processing the same amount of nanoparticles (left). Typical SEM image of nanopatterns showing the high uniformity of the imprint (right). Scale bar is $5 \mu m$.

The ability of NIL to make multiple copies of nanostructures allows the production costs to be greatly reduced. Specifically by using a step and repeat NIL process (S&R), a large amount of imprints in reasonable time is possible. In Fig. 7, it is shown that multiple imprints can be performed on one glass substrate by using an S&R NIL process at PROFACTOR GmbH with high pattern fidelity. Such imprinted substrates are ideally suited for the production of a large amount of nanoparticles. As an outlook, we consider using roll-to-plate (R2P) Nanoimprint Lithography to make way for a scale up of the fabrication speed of such particles. Considering slow imprint speeds on lab and wafer scale, we expect that a reasonably developed (but not fully for high speed production optimized) roll-to-plate nanoimprint process will be able to achieve 30 large-area substrates $(30 \times 60 \text{ cm}^2)$ per hour (instead of four wafers in a simple manual plate-to-plate process) resulting in a factor of 95 improvement in throughput: (substrates per hour)_{R2P}/(substrates per hour)_{wafer scale NIL} × (imprinted area R2P/imprinted area wafer) = $(30/4)^*(20 \times 50 \text{ cm}^2/5^2\pi \text{ cm}^2) \cong 95$

(assuming the imprint area for R2P is still significantly smaller than the substrate itself). One single $30 \times 60 \text{ cm}^2$ substrate has the capability to contain several 10 s of mg of nanoparticles. Sputtering on such large substrates is commercially available; also, commercial R2R sputter coaters might potentially be adapted for the R2P process. To obtain a large-area imprinting plate for roll-to-plate step-and-repeat nanoimprinting can be used to multiply a small area master (see Fig. 7, left).⁴⁶

By using an inverse imprint structure (negative) and the same process as discussed above, tailored particles with the shape of nano-pockets, i.e., particles having nano-cavities, can be created (Fig. 8). These particles then can be transferred to solution resulting in a nanoparticle dispersion. Again the physical properties of such nano-pockets can be specifically tailored and manipulated during the fabrication process.⁶⁷ The whole NIL-based fabrication process is very well suited to produce nanoparticles with tailored magnetic and plasmonic properties for a variety of sensing applications.

Nanoimprinting has been used for a broad range of plasmonic applications in the literature. Li *et al.*⁶⁸ used wafer-scale hot



FIG. 8. (a) Schematics of a nanopocket composed of different layers of different materials. A 3D presentation of a nanopocket is shown on the left, together with a cross-sectional view on the right. (b) SEM image of randomly orientated multifunctional nanopockets. (c) Detailed SEM image of the top, bottom, and side view of a nanopocket. Adapted from S. Schrittwieser, J. Schotter, T. Maier, R. Bruck, P. Muellner, N. Kataeva, K. Soulantika, F. Ludwig, A. Huetten, and H. Brueckl, S. Schrittwieser, M. J. Haslinger, T. Mitteramskogler, M. Mühlberger, A. Shoshi, H. Brückl, M. Bauch, T. Dimopoulos, B. Schmid, and J. Schotter, anomaterials 9(12), 1790 (2019). Copyright 2019 Author(s), licensed under a Creative Commons Attribution 4.0 License.⁶²

embossing on 4-in. wafers and reactive ion etching to prepare SiO₂ pillars on Si wafers that were coated with gold to achieve uniform SERS substrates. Also, roll-to-roll nanoimprinting has been used to fabricate localized surface plasmon resonance substrates.⁶⁹ Many groups employed nanoimprinting to prepare a wide range of metallic nanoislands on different substrates for life science applications, e.g., gold on glass^{70,71} or on polymers like polyurethane acrylate (PUA)⁶ or polycarbonate (PC)⁷² or silver on polymers.⁷³ Interesting variants of nanoimprinting to fabricate nano-sized metal islands are also nano-transferprinting⁷⁴ or nano-contact printing.⁷⁵ A similar nanoimprint approach without pattern transfer was used by Shahidan et al.⁷⁶ to create plasmonic colors. Interestingly, they control the imprinting depth in their process and can tune the resulting color this way while using the same stamp. Glangchai et al.77 describe a process to fabricate polymeric nanoparticles using UV-based nanoimprinting for controlled release of biomolecules. In many cases in the literature, however, plasmonic nanoparticles are metallic nanoislands, which are fixed on a substrate, which is in contrast to what was discussed in our work above, where the nanoislands are removed from the substrate and brought into solution.

In the second part of this Perspective, we want to focus on two realized applications by STRATEC Consumables, which we have chosen to show the capabilities of injection molding for two applications: MEF and SERS. It is well established that MEF results from localized surface plasmons generated by the interaction of the excitation light with nanometer-sized metal structures.

The principles of MEF (metal enhanced fluorescence) are well understood and described in the literature.^{14,15,78} MEF structures dramatically increase the quantum yield of fluorescent molecules, thus leading to highly sensitive detection systems, e.g., for fluorescent immunoassays.

A prerequisite is the proper design of those nanostructures, i.e., shape, size, and distance to each other.¹⁶ Since the plasmonic behavior supports only the readout of the molecules which actually



FIG. 9. Principle of metal enhanced fluorescence: only the fluorescence of molecules (yellow stars) close to the nanostructures is enhanced. Those further away (>50 nm distance) do not increase in emission. This discrimination between bound/unbound molecules (e.g., fluorescent labeled antibodies) allows detection in the presence of the bulk solution, thus eliminating the need for washing steps [taken from G. Hawa, L. Sonnleitner, A. Missbichler, A. Prinz, G. Bauer, and C. Mauracher, Anal. Biochem. 549, 39 (2018). Copyright 2018, Elsevier Inc.].1

bound to the surface (for explanation, see Fig. 9), the typical workflow can be simplified and no washing steps during the assay steps need to be performed.

Design and manufacturing reproducibility of the required metal structures is a key requisite for optimizing the enhancement effect and reliability of the assay system. This is why commercial application of this technology has failed so far. Lift-off processes need multiple steps for manufacturing and are therefore expensive. STRATEC Consumables GmbH and FIANOSTICS successfully solved these problems by using highly reproducible nanostructuring technologies, originally developed for Blu-Ray and DVD manufacturing, for designing and manufacturing novel plasmonic structures for MEF. The needed microstructures with diameters below 500 nm, an aspect ratio of about two, and $1\,\mu m$ pitch are manufactured using laser writing and copied into nickel by electroplating. This nickel insert is used for injection molding and can be replicated several hundred thousand shots. In order to enable a plasmonic effect on the surface, the injection molded parts are coated with a silver alloy leading to the MEF effect. Finally, the parts are laser welded to a microtiter plate frame in order to perform assays on the metal structures and to make the technology available for standard fluorescent readouts. Figure 10 shows the subsequent manufacturing steps and an example of the achieved enhancement using a standard assay performed within the "plasmonic" microtiter plate proofing 150-300-fold enhancement (dependent on fluorophore applied), as such giving better results in comparison to standard high binding microtiter plates. This application shows very well how plasmonic effects can support N high sensitivity detection even using a cost-effective standard fluo-Oct rescence reader.

The second application we like to discuss within this Perspective is based on Raman spectroscopy. Raman spectroscopy is a key method for biosensing since it is an optical non-invasive method for molecular sensing and has been proven to work for the \vec{s} characterization and identification of biological samples such as cells, tissues, and bacteria.

The target of Surface Enhanced Raman Spectroscopy (SERS) is maximizing by a locally enhanced radiation field, the Raman scattering signal of an analyte species on the surface of a structured substrate. This method has been investigated in the past by several institutes.

Here plasmonics comes into play, which has the potential to enhance signal at the surface by introducing metal particles or layers in order to create surface plasmon polaritons as so-called SERS hot spots.

The metal coating has two advantages, the molecule of interest can be easily bound to metals and it significantly enhances the Raman scattering signal of the molecules adsorbed onto it, due to both electromagnetic field enhancement and chemical enhancement at these hot spots.

As stated by Balčytis et al.,96 the "adoption of SERS is limited, in large part due to the difficulties associated with fabricating effective, consistent and affordable nanostructured plasmonic platforms."

Similar processes based on injection molding, as already discussed for the MEF process, were used to generate periodic microstructured polymer substrates coated with a thin Ag film.¹³ In addition, a chemical etching step is used to produce a high-density



FIG. 10. (a) Process steps for MEF microtiter plates manufacturing by injection molding. (b) Signal enhancement of absorbed Cy5 labeled goat anti-rabbit antibody with MEF substrates compared to standard high binding microtiter plate. (c) Dependency of enhancement of fluorophore used. A 150–300 fold enhancement of the fluorescence signal was achieved. Reproduced with permission from G. Hawa, L. Sonnleitner, A. Missbichler, A. Prinz, G. Bauer, and C. Mauracher, Anal. Biochem. 549, 39 (2018). Copyright 2018, Elsevier Inc.

Ag nanoparticle film at the polymer surface [Fig. 11(b)], the polymeric microstructure supporting the formation of Ag nanoparticles and influencing their size and density especially around the polymer wells, and causing the strong Raman signal enhancement as described in more detail in Ref. 13. Due to the nanoparticle formation step, very homogeneous and large SERS enhancement factors have been achieved, leading to an increase in Raman signal intensity of up to 6×10^6 with $\pm 7\%$ variation over the entire microstructured, SERS active circular surface, each field having an area of ~38.5 mm². SERS performance comparison with commercially

27 October 2023 09:01:36



FIG. 11. (a) Raman spectra of 1,4-benzenedithiol (1,4-BDT) on a commercial SERS substrate (SERStrate by Silmeco ApS), obtained with 532 nm laser excitation (light green) and 780 nm laser excitation (light red), and on our best performing SERS substrate M4 (dark green and dark red. respectively). The spectra were collected using a microscope objective with 10× magnification, 1 mW laser power on the sample, and three accumulations each with 15 s acquisition time. (b)Typical SEM pictures of the microstructured substrates after chemical etching showing a high-density Ag nanoparticle film. Reproduced with permission from A. Reyer, A. Prinz, S. Giancristofaro, J. Schneider, D. Bertoldo Menezes, G. Zickler, G. R. Bourret, and M. E. Musso, ACS Appl. Mater. Interfaces 9, 25445 (2017), Copyright 2017 American Chemical Society.

27 October 2023 09:01:36

available SERS substrates (SERStrate from Silmeco ApS) demonstrates the validity of this method to prepare inexpensive, reliable, and sensitive SERS substrates for biosensing applications [Fig. 11(a)].

VI. DISCUSSION ON NANOIMPRINT TECHNOLOGY VS INJECTION MOLDING

Advantages of nanoimprinting are-among other things-the possibility to span a wide range of feature sized, from sub-10 nm²⁵ to several $100 \,\mu m$,^{26,27,97} the possibility to create complex structures in a single fabrication step^{29,30} and a large flexibility as far as the choice of materials is concerned $^{31-34}$. Due to the fact that complex features can be replicated in a single process step^{30,98} and that ultra-high resolution can be achieved in a single step,⁹⁹ for many applications the number of process steps can be significantly reduced. A broad number of different features can be replicated using NIL, even undercut features can be replicated.¹⁰⁰⁻¹⁰² Only real 3D features, which are, e.g., hollow, cannot be replicated. Furthermore, since the stamp is in full contact with the substrate, no complex illumination optics is required [like for optical lithography (deep UV and extreme UV (DUV and EUV)], resulting in much simpler equipment and easier processing.¹⁰³ Furthermore, simple UV light sources can be utilized like UV-LEDs, which results in a low energy consumption of the process (especially as compared to EUV).¹⁰⁴ In addition, roller-based NIL technologies, i.e., R2P or R2R give the possibility to achieve very high throughput fabrication.¹⁰

Another great advantage of NIL for optical application is the realization of a high flatness very close to the substrate (e.g., wafer) flatness across the whole device surface, which is often a requirement for optical applications being close to the substrates quality, i.e., wafer flatness.

For injection molding, the flatness is a challenge and even though values of $<1 \mu$ m/mm can be achieved, still some application cannot be realized requiring tighter specifications especially for optical applications.

For injection molding, the combination of macro-, micro-, and nanofeatures is restricted. There are some applications where it has been shown to work, e.g., combining macrofeatures and microchannels (see product microtiter plate of company MyCartis), however, with a high investment effort for dedicated tools and engineering, since the injection molding process needs to be adjusted to structure dimension. Specifically in the case of combining all three dimensional challenges, i.e., macro (cm, mm), micro (several 100 μ m), and nano (<1 μ m) features, injection molded parts often need to be realized in separated layers, means, e.g., one injection molded parts contains the nanofeatures and one layer contains the micro- and macrofeatures. However, due to the fact that the part is fully made of the same polymer, it is easy to do further processing like laser welding or bonding, i.e., merging the parts to the final product. As such full integration is very easy including inlets and outlets for fluids which is of paramount importance for microfluidic applications like needed for biosensing applications. This is one drawback of NIL. Even when imprinting on film, there is no way to realize through holes easily without the need of processes generating dust particles.

Therefore, depending on the needs and requirements of the application, either injection molding or nanoimprint can be chosen to realize high volume applications as shown and discussed within this Perspective. Table I provides an overview and might act as a guideline.

In the last few years, more and more applications in the Life Science and Diagnostic market are appearing, which would benefit from an industrial manufacturing combining NIL and injection molding, i.e., micro- and nanostructured thin films in combination with injection molded parts.

Not only the film structuring (also called replication) can be so done on large roll to roll machines, but also the vacuum coating of metals needed for the plasmonic effect. In order to combine the batch process of injection molding with thin-film technology, the film is converted to labels. This gives the opportunity to install highly automated bonding of the injection molded part with the thin-film label. These processes are already established and used to, e.g., laminate films onto injection molded microfluidic substrates nowadays and therefore as such proven to be scalable. The cycle times of such manufacturing lines typically depend on the alignment tolerances needed and the materials involved; however,

TABLE I. Ove	erview comparison	table between i	injection molding and NIL	

	Injection molding	Nanoimprinting	
Materials (Polymers)	Thermoplastic	Thermoplastic, UV-curing, thermally curing	
Semiconductor process compatibility	No lift-off processes	Yes	
Throughput	High: cycle times between few seconds	Comparably low (up to 90 wafers $/h$) ³⁹ for wafer scale	
	and 1 min depending on the complexity and size of the part	processes, higher for roller-based processes, e.g., 2.5 m ² per minute published by Joanneum ¹⁰⁵ and very high in industrial realization with 30 m ² per minute (KURZ Group)	
Substrate necessary	No (can be used in some cases, e.g., back injection molding)	Yes (UV-NIL), typically also for hot embossing (exceptions are possible)	
Feature sizes achievable	20 nm ^{106,107} and less up to μ m and macro features	Sub-10 nm (e.g., Refs. 25 and 108) up to several 100 μm (e.g., Refs. 27, 28, and 97)	
Through holes	Possible	Challenging	

TABLE II. Overview of STRATEC injection molding (left column) and KURZ thin-film technology (right column) capabilities. The middle column shows the potential and advantage in combining both technologies.

	STRATEC injection molding	KURZ thin-film technology meets STRATEC injection molding	KURZ thin-film technology
Minimum film or substrate thickness	300 µm	Integration of thin film is advantageous for IMAGING and THERMOCYCLING typically done for PCR applications in life science and IVD products	$12\mu m$ or even down to $6\mu m$ for some applications
Flexibility of final product	Relatively stiff	Combines advantages of both for HIGH THROUGHPUT application via winding/unwinding of thin-film integrated in the product itself	Very flexible
Materials	COP/COC/PP/PS/PC, etc.	Easy integration of FUNCTIONAL SURFACES necessary for several life science and IVD application, e.g., for biosensor applications in order to bind molecules to the surface	High variety of surface functionalizations possible
Surface area	From several cm ² up to MTP format	Easy and cost-effective realization of microstructures on LARGE AREA for thin-film technology. These large area structures can be easily integrated in a cost-efficient way to injection molded format	High variety of widths possible up between 1.30 m and 5 mm on endless roll
Interfaces	Macro features can be realized	Combination of both enables easy INTERFACING to instruments, e.g., thin films can be laminated to an injection molded cover with inlets and outlets	No macrofeatures possible
Design	Nano, micro, and macro difficult to realize in one injection molded part	Creates DESIGN FREEDOM for combining macro, micro, and nanofeatures. The design can be chosen very smart in separating the different dimensions to injection molded and/or thin films	Micro and nanostructures feasible

ranges are typically between one minute down to few seconds, resulting in cost-effective microfluidic devices for life science and IVD applications.

Table II shows the benefit of combining thin-film technology and injection molding. We want to emphasize that the parameter shown in Table II is valid for the capabilities at STRATEC and KURZ which might not be applicable to other manufacturers. However, the overall conclusion is valid for the technologies mentioned.

In order to enable application that need such benefits, i.e., imaging, thermocycling, high throughput, functional surfaces, large-area substrates, easy interfacing, and device design freedom, first steps have been done to combine roll to roll thin films with injection molding by Mycropartners collaborating with STRATEC Consumables and KURZ Group.

VII. CONCLUSIONS AND OUTLOOK

In this article, we have discussed the realization of plasmonic devices by nanoimprint or injection molding. Both techniques have their advantages in powerfully serving industrial products in the Life Science and In vitro Diagnostic market. Specifically important is the fact that these technologies provide a possibility to manufacture plasmonic substrates in a cost-efficient way giving us solutions for biosensors for unique detection methods.

The presented NIL-based fabrication process of highly monodisperse nanoparticles is very well suited to produce tailored nanoparticles with magnetic and plasmonic properties for rota-tional dynamics measurements. With the small achieved size distribution, the nanoparticles are not only suitable for measuring changes in the rotational dynamics but could also be interesting for $\vec{\omega}$ a variety of other methods.

For highly demanding applications, a first outlook has been given to combine roll-to-roll as well as injection molding. These efforts are done by Mycropartners collaborating with STRATEC Consumables and KURZ Group with the aim to manufacturing micro and nanostructured products for the Life Science and Diagnostics market.

ACKNOWLEDGMENTS

The contribution by PROFACTOR GmbH was financially supported by the Austrian Research and Promotion Agency (Project LAMPION, No. 861414).

DATA AVAILABILITY

The data that support the findings of this study are available from the corresponding author upon reasonable request.

REFERENCES

¹W. Liu, Y. Chen, X. Hu, L. Wen, L. Jin, Q. Su, and Q. Chen, Appl. Opt. 56, 4861 (2017).

²S. Ishii, S. L. Shinde, and T. Nagao, Adv. Opt. Mater. 7, 1800603 (2019).

27

³S. Chen, E. S. H. Kang, M. Shiran Chaharsoughi, V. Stanishev, P. Kühne, H. Sun, C. Wang, M. Fahlman, S. Fabiano, V. Darakchieva, and M. P. Jonsson, Nat. Nanotechnol. **15**, 35 (2020).

⁴M. E. Stewart, C. R. Anderton, L. B. Thompson, J. Maria, S. K. Gray, J. A. Rogers, and R. G. Nuzzo, Chem. Rev. 108, 494 (2008).

⁵X. Han, K. Liu, and C. Sun, Materials 12, 1411 (2019).

⁶B. Spackova, P. Wrobel, M. Bockova, and J. Homola, Proc. IEEE 104, 2380 (2016).

⁷R. T. Hill, Wiley Interdiscip. Rev. Nanomed. Nanobiotechnol. 7, 152 (2015).

⁸M. Soler, C. S. Huertas, and L. M. Lechuga, Expert Rev. Mol. Diagn. 19, 71 (2019).

⁹M. Haslinger, T. Mitteramskogler, A. Shoshi, J. Schotter, S. Schrittwieser, M. Mühlberger, and H. Brückl, in Proc. SPIE **107222**, 1072220 (2018).

 ¹⁰T. Mitteramskogler, M. J. Haslinger, A. Shoshi, S. Schrittwieser, J. Schotter, H. Brueckl, and M. Muehlberger, Proc. SPIE 10775, 107750Y (2018).

¹¹A. Shoshi, P. Schneeweiss, M. J. Haslinger, T. Glatzl, G. Kovács, J. Schinerl, M. Muehlberger, and H. Brueckl, Proceedings 1, 541 (2017).

¹²G. Hawa, L. Sonnleitner, A. Missbichler, A. Prinz, G. Bauer, and C. Mauracher, Anal. Biochem. **549**, 39 (2018).

¹³A. Reyer, A. Prinz, S. Giancristofaro, J. Schneider, D. Bertoldo Menezes, G. Zickler, G. R. Bourret, and M. E. Musso, ACS Appl. Mater. Interfaces 9, 25445 (2017).

¹⁴D. Darvill, A. Centeno, and F. Xie, Phys. Chem. Chem. Phys. 15, 15709 (2013).

¹⁵W. Deng, F. Xie, H. T. M. C. M. Baltar, and E. M. Goldys, Phys. Chem. Chem. Phys. 15, 15695 (2013).

¹⁶B. Yang, N. Lu, D. Qi, R. Ma, Q. Wu, J. Hao, X. Liu, Y. Mu, V. Reboud, N. Kehagias, C. M. S. Torres, F. Y. C. Boey, X. Chen, and L. Chi, Small 6, 1038 (2010).

¹⁷H. Schift, J. Vac. Sci. Technol. B 26, 458 (2008).

¹⁸S. Y. Chou, P. R. Krauss, and P. J. Renstrom, J. Vac. Sci. Technol. B 14, 4129 (1996).

¹⁹J. Haisma, M. Verheijen, K. van den Heuvel, and J. van den Berg, J. Vac. Sci. Technol. B 14, 4124 (1996).

²⁰I. Bergmair, W. Hackl, M. Losurdo, C. Helgert, G. Isic, M. Rohn, M. M. Jakovljevic, T. Mueller, M. Giangregorio, E.-B. Kley, T. Fromherz, R. Gajic, T. Pertsch, G. Bruno, and M. Muehlberger, Nanotechnology 23, 335301 (2012).

²¹E. Lausecker, M. Brehm, M. Grydlik, F. Hackl, I. Bergmair, M. Mühlberger, T. Fromherz, F. Schäffler, and G. Bauer, Appl. Phys. Lett. **98**, 143101 (2011).

22 E. Lausecker, M. Grydlik, M. Brehm, I. Bergmair, M. Mühlberger, T. Fromherz, and G. Bauer, Nanotechnology 23, 165302 (2012).

²³I. Bergmair, B. Dastmalchi, M. Bergmair, A. Saeed, W. Hilber, G. Hesser, C. Helgert, E. Pshenay-Severin, T. Pertsch, E. B. Kley, U. Hübner, N. H. Shen, R. Penciu, M. Kafesaki, C. M. Soukoulis, K. Hingerl, M. Muehlberger, and R. Schoeftner, Nanotechnology **22**, 325301 (2011).

²⁴B. S. Kwon, W. Zhang, Z. Li, and K. M. Krishnan, Adv. Mater. Interfaces 2, 1400511 (2015).

²⁵F. Hua, Y. Sun, A. Gaur, M. A. Meitl, L. Bilhaut, L. Rotkina, J. Wang, P. Geil, M. Shim, J. A. Rogers, and A. Shim, Nano Lett. 4, 2467 (2004).

²⁶L. Yde, J. F. Stensborg, T. Voglhuber, W. Hackl, H. Außerhuber, S. Wögerer, L. R. Lindvold, T. Fischinger, and M. Mühlberger, paper presented at International conference on Nanoimprint and Nanoprint Technology (NNT), Braga, Portugal, 2016, see http://www.nntconf.org/submissions/rollerNIL% 20NNT%20R2P%20v1.pdf (last accessed February 10, 2021).

27S. Dal Zilio, G. D. Giustina, G. Brusatin, and M. Tormen, Microelectron. Eng. 87, 1143 (2010).

²⁸J. Dunkel, F. Wippermann, A. Reimann, A. Brückner, and A. Bräuer, Opt. Express 23, 31915 (2015).

29S. Waid, H. D. Wanzenboeck, M. Gavagnin, R. Langegger, M. Muehlberger, and E. Bertagnolli, J. Vac. Sci. Technol. B 31, 041602 (2013).

³⁰A. R. Moharana, H. M. Außerhuber, T. Mitteramskogler, M. J. Haslinger, and M. M. Mühlberger, Coatings 10, 301 (2020). ³¹L. J. Guo, Adv. Mater. 19, 495 (2007).

³²V. Reboud, I. Obieta, L. Bilbao, V. Saez-Martinez, M. Brun, F. Laulagnet, and S. Landis, <u>Microelectron. Eng.</u> **111**, 189 (2013).

³³S. Lochmann, J. Grothe, K. Eckhardt, D. Leistenschneider, L. Borchardt, and S. Kaskel, Nanoscale 10, 10109 (2018).

³⁴H. Schmitt, L. Frey, H. Ryssel, M. Rommel, and C. Lehrer, J. Vac. Sci. Technol. B 25, 785 (2007).

³⁵T. Köpplmayr, L. Häusler, I. Bergmair, and M. Mühlberger, Surf. Topogr.: Metrol. Prop. 3, 024003 (2015).

³⁶M. J. Haslinger, M. Mühlberger, K. Julia, M. Ikeda, A. Fuchsbauer, T. Faury, T. Köpplmayr, H. Ausserhuber, J. Kastner, C. Wögerer, and D. Fechtig, Proc. SPIE 10446, 1044601 (2017).

Fechtig~NNT2019_Abstract_amohar_final.pdf (last accessed February 10, 2021).
³⁸S. Landis, V. Reboud, T. Enot, and C. Vizioz, Microelectron. Eng. 110, 198 (2013).

³⁹Y. Takabayashi, T. Iwanaga, M. Hiura, H. Morohoshi, T. Hayashi, T. Komaki, O. Morimoto, K. Sakai, W. Zhang, A. Cherala, S.-H. Im, M. Meissl, and J. Choi, in 2020 4th IEEE Electron Devices Technology and Manufacturing Conference (EDTM), Penang, Malaysia (IEEE, 2020), pp. 1–4.

⁴⁰See http://electroiq.com/blog/2016/03/ev-group-scales-up-nanoimprint-lithography-for-display-manufacturing/ for Solid State Technology, EV Group scales up nanoimprint lithography for display manufacturing (last accessed November 30, 2020).
 ⁴¹See https://www.evgroup.com/products/nanoimprint-lithography/uv-nil-smartnil/

'See https://www.evgroup.com/products/nanoimprint-lithography/uv-nil-smartnil/ evg-7200-la/ for EV Group, Large-Area SmartNIL UV Nanoimprint Lithography System (last accessed November 30, 2020).

⁴²See https://www.morphotonics.com/roll-to-plate-nanoimprint/ for "Morphotonics, Roll-to-Plate Nanoimprint Lithography" (last accessed November 26, 2020).

⁴³S. Kommeren, "Roll-to-plate nanoimprint lithography for large-area applications: Of equipment, materials and processes," in *International conference on Nanoimprint feednology (NNT), Boston, USA, 2019, see https://nnt2019.org/ go documents/uploads/Sander_Kommeren~NNT2019_Abstract_Morphotonics.* pdf (last accessed February 10, 2021).
 ⁴⁴M. Mühlberger, I. Bergmair, A. Klukowska, A. Kolander, H. Leichtfried, and Managemanne and Manag

 ⁴⁴M. Mühlberger, I. Bergmair, A. Klukowska, A. Kolander, H. Leichtfried, E. Platzgummer, H. Loeschner, C. Ebm, G. Grützner, and R. Schöftner, Microelectron. Eng. 86, 691 (2009).

⁴⁵M. J. Haslinger, M. A. Verschuuren, R. van Brakel, J. Danzberger, I. Bergmair, and M. Mühlberger, Microelectron. Eng. **153**, 66 (2016).

and M. Mühlberger, Microelectron. Eng. 153, 66 (2016).
⁴⁶M. J. Haslinger, T. Mitteramskogler, S. Kopp, H. Leichtfried, M. Messerschmidt, M. W. Thesen, and M. Mühlberger, Nanotechnology 31, 345301 (2020).

M. W. Thesen, and M. Mühlberger, Nanotechnology **31**, 345301 (2020). **47**T. Eriksson, S. Yamada, P. V. Krishnan, S. Ramasamy, and B. Heidari, Microelectron. Eng. **88**, 293 (2011).

48T. Marumo, S. Hiwasa, and J. Taniguchi, Nanomaterials 10, 1956 (2020).

⁴⁹A. Bietsch, O. Ripoll, L. Bogaert, L. Yu, E. Iseni, S. Bellini, T. Bischof, S. Grossmann, O. Rossi, and M. Rossi, paper presented at Beams & More 2018, Stuttgart, 2018.

50G. Kreindl, T. Glinsner, R. Miller, D. Treiblmayr, and R. Födisch, J. Vac. Sci. Technol. B 28, C6M57 (2010).

⁵¹A. Brückner, A. Oberdörster, J. Dunkel, A. Reimann, M. Müller, and F. Wippermann, Proc. SPIE **9193**, 91930W (2014).

⁵²M. A. Verschuuren, P. Gerlach, H. A. van Sprang, and A. Polman, Nanotechnology 22, 505201 (2011).

⁵³R. N. Jiawook, J. Appl. Biotechnol. Bioeng. 3, 321 (2017).

⁵⁴M. Smolka, A. Haase, and U. Palfinger, in *ECI Digital Archives, Proceedings Single-Use Technologies II: Bridging Polymer Science to Biotechnology Applications, see https://dc.engconfintl.org/cgi/viewcontent.cgi?article=1012&context=biopoly_ii (last accessed February 11, 2021).*

⁵⁵M. Smolka, S. Ruttloff, D. Nees, C. Prietl, V. Satzinger, B. Lamprecht, P. Hütter, J. Hesse, G. Kokkinis, G. Kriechhammer, D. Scheidl, and B. Wilfing, Proceedings 2, 1054 (2018).

27

⁵⁶See https://www.morphotonics.com/applications/#display for "Morphotonics" (last accessed November 30, 2020).

⁵⁷T. Glinsner, P. Lindner, M. Mühlberger, I. Bergmair, R. Schöftner, K. Hingerl, H. Schmid, and E.-B. Kley, J. Vac. Sci. Technol. B. 25, 2337 (2007).

58 M. Mühlberger, I. Bergmair, W. Schwinger, M. Gmainer, R. Schöftner, T. Glinsner, C. Hasenfuß, K. Hingerl, M. Vogler, H. Schmidt, and E. B. Kley, icroelectron. Eng. 84, 925 (2007).

⁵⁹M. J. Haslinger, D. Sivun, H. Pöhl, B. Munkhbat, M. Mühlberger, T. A. Klar, M. C. Scharber, and C. Hrelescu, Nanomaterials 10, 1866 (2020).

60S. Schrittwieser, B. Pelaz, W. Parak, S. Lentijo-Mozo, K. Soulantica, J. Dieckhoff, F. Ludwig, A. Guenther, A. Tschöpe, and J. Schotter, Sensors 16, 828 (2016).

⁶¹S. Schrittwieser, F. Ludwig, J. Dieckhoff, K. Soulantica, G. Viau, L.-M. Lacroix, S. M. Lentijo, R. Boubekri, J. Maynadié, A. Huetten, H. Brueckl, and J. Schotter, ACS Nano 6, 791 (2012).

62S. Schrittwieser, J. Schotter, T. Maier, R. Bruck, P. Muellner, N. Kataeva, K. Soulantika, F. Ludwig, A. Huetten, and H. Brueckl, Procedia Eng. 5, 1107 (2010).

⁶³J. Dieckhoff, M. Schilling, and F. Ludwig, Appl. Phys. Lett. 99, 112501 (2011). 64 See https://kayakuam.com/wp-content/uploads/2019/09/KAM-LOR-PMGI-Data-

Sheet-11719.pdf for information regarding the LOR series materials (last accessed March 26, 2021).

⁶⁵M. Messerschmidt, A. Greer, F. Schlachter, J. Barnett, M. W. Thesen, N. Gadegaard, G. Grutzner, and A. Schleunitz, J. Photopolym. Sci. Technol. 30, 605 (2017).

66H. Brueckl, A. Shoshi, S. Schrittwieser, B. Schmid, P. Schneeweiss, T. Mitteramskogler, M. Haslinger, M. Muehlberger, and J. Schotter, Sci. Rep. 11, 6039 (2021).

67S. Schrittwieser, M. J. Haslinger, T. Mitteramskogler, M. Mühlberger, A. Shoshi, H. Brückl, M. Bauch, T. Dimopoulos, B. Schmid, and J. Schotter, Nanomaterials 9, 1790 (2019).

68W.-D. Li, F. Ding, J. Hu, and S. Y. Chou, Opt. Express 19, 3925 (2011).

69S. H. Baek, H. W. Song, S. Lee, J.-E. Kim, Y. H. Kim, J.-S. Wi, J. G. Ok, J. S. Park, S. Hong, M. K. Kwak, H. J. Lee, and S.-W. Nam, Front. Chem. 8, 285 (2020).

⁷⁰G. Barbillon, F. Hamouda, S. Held, P. Gogol, and B. Bartenlian, Microelectron. Eng. 87, 1001 (2010).

71G. Barbillon, Micromachines **3**, 21 (2012).

72V. Suresh, L. Ding, A. B. Chew, and F. L. Yap, ACS Appl. Nano Mater. 1, 886 (2018).

73J. Kim, N. Abbas, S. Lee, J. Yeom, M. A. Asgar, M. A. Badshah, X. Lu, Y. K. Kim, and S.-M. Kim, Polymers 13, 48 (2021).

74R. D. Nagel, S. Filser, T. Zhang, A. Manzi, K. Schönleber, J. Lindsly, J. Zimmermann, T. L. Maier, G. Scarpa, K. Krischer, and P. Lugli, J. Appl. Phys. 121, 084305 (2017).

75 E. Lausecker, W. Schwinger, I. Bergmair, M. Mühlberger, and R. Schöftner, J. Phys. Conf. Ser. 100, 052024 (2008).

⁷⁶M. F. S. Shahidan, J. Song, T. D. James, and A. Roberts, Nanoscale Adv. 2, 2177 (2020).

77 L. C. Glangchai, M. Caldorera-Moore, L. Shi, and K. Roy, J. Controlled Release 125, 263 (2008).

78C. D. Geddes, Phys. Chem. Chem. Phys. 15, 19537 (2013).

79D. Yang, H. Zhou, C. Haisch, R. Niessner, and Y. Ying, Talanta 146, 457 (2016).

80J. W. Kang, P. T. C. So, R. R. Dasari, and D.-K. Lim, Nano Lett. 15, 1766 (2015).

⁸¹Y. Chen, X. Bai, L. Su, Z. Du, A. Shen, A. Materny, and J. Hu, Sci. Rep. 6, 19173 (2016).

82 R. H. Lahr and P. J. Vikesland, ACS Sustainable Chem. Eng. 2, 1599 (2014).

⁸³K. Kong, C. Kendall, N. Stone, and I. Notingher, Adv. Drug Deliv. Rev. 89, 121 (2015).

84J. Langer, D. Jimenez de Aberasturi, J. Aizpurua, R. A. Alvarez-Puebla, B. Auguié, J. J. Baumberg, G. C. Bazan, S. E. J. Bell, A. Boisen, A. G. Brolo, J. Choo, D. Cialla-May, V. Deckert, L. Fabris, K. Faulds, F. J. García de Abajo, R. Goodacre, D. Graham, A. J. Haes, C. L. Haynes, C. Huck, T. Itoh, M. Käll,

J. Kneipp, N. A. Kotov, H. Kuang, E. C. Le Ru, H. K. Lee, J.-F. Li, X. Y. Ling,

- S. A. Maier, T. Mayerhöfer, M. Moskovits, K. Murakoshi, J.-M. Nam, S. Nie,
- Y. Ozaki, I. Pastoriza-Santos, J. Perez-Juste, J. Popp, A. Pucci, S. Reich, B. Ren,
- G. C. Schatz, T. Shegai, S. Schlücker, L.-L. Tay, K. G. Thomas, Z.-Q. Tian,
- R. P. Van Duyne, T. Vo-Dinh, Y. Wang, K. A. Willets, C. Xu, H. Xu, Y. Xu,
- Y. S. Yamamoto, B. Zhao, and L. M. Liz-Marzán, ACS Nano 14, 28 (2020).
- ⁸⁵R. S. Das and Y. K. Agrawal, Vib. Spectrosc. 57, 163 (2011).

86K. Kneipp, H. Kneipp, I. Itzkan, R. R. Dasari, and M. S. Feld, Curr. Sci. 77, 915 (1999).

87X.-M. Qian and S. M. Nie, Chem. Soc. Rev. 37, 912 (2008).

88S. Schlücker, ChemPhysChem 10, 1344 (2009).

⁸⁹C. Krafft and J. Popp, Anal. Bioanal. Chem. 407, 699 (2015).

90J. Feng, L. Xu, G. Cui, X. Wu, W. Ma, H. Kuang, and C. Xu, Biosens. Bioelectron. 81, 138 (2016).

⁹¹C. Muehlethaler, M. Leona, and J. R. Lombardi, Anal. Chem. 88, 152 (2016).

92Z.-Q. Tian, J.-F. Li, C. L. Haynes, M. Moskovits, and G. C. Schatz, J. Raman ectrosc. 52, 263 (2021).

⁹³D. L. Jeanmaire and R. P. Van Duyne, J. Electroanal. Chem. Interfacial Electrochem. 84, 1 (1977).

94 M. Moskovits, J. Chem. Phys. 69, 4159 (1978).

95Z. A. Nima, A. Biswas, I. S. Bayer, F. D. Hardcastle, D. Perry, A. Ghosh, E. Dervishi, and A. S. Biris, Drug Metab. Rev. 46, 155 (2014).

96 A. Balčytis, Y. Nishijima, S. Krishnamoorthy, A. Kuchmizhak, P. R. Stoddart, R. Petruškevičius, and S. Juodkazis, Adv. Opt. Mater. 6, 1800292 (2018).

97L. Yde, L. Lindvold, J. Stensborg, T. Voglhuber, H. Außerhuber, S. Wögerer, 😋 ¹¹ L. Yde, L. Lindvold, J. Stensoorg, I. Voginuber, H. Ausernuber, S. Wogerer, S. T. Fischinger, M. Mühlberger, and W. Hackl, paper presented at *International Conference on Nanoimprint and Nanoprint Technology (NNT)* (Braga, Portugal, 2016); see http://www.nntconf.org/727submissions/rollerNIL%20NNT%20R2P%
 ¹⁹ M. Li, L. Chen, and S. Y. Chou, Appl. Phys. Lett. **78**, 3322 (2001).
 ⁹⁹ W. Trybula, R. L. Wright, K. M. Adusumili, and R. K. Goodall, in *Proceedings of Winter Simulation Conference* 2005 (IEEE, Orlando, FL, 2005), pp. 2218–2222.

Winter Simulation Conference 2005 (IEEE, Orlando, FL, 2005), pp. 2218-2222.

100S. Möllenbeck, N. Bogdanski, M. Wissen, H.-C. Scheer, J. Zajadacz, and K. Zimmer, Microelectron. Eng. 84, 1007 (2007).

101S. Möllenbeck, N. Bogdanski, H.-C. Scheer, J. Zajadacz, and K. Zimmer, ficroelectron. Eng. 86, 608 (2009).

102 M. Mühlberger, S. Ruttloff, A. Prinz, P. Taus, J.-P. Perrin, D. Nees, M. Schinnerl, C. Neuhauser, M. Behrens, H. Außerhuber, A. Moharana, G. Hesser, L. Häusler, C. Wögerer, M. Panholzer, and H. D. Wanzenboeck, paper presented at International Conference on Nanoimprint and Nanoprint Technology (NNT), Braga, Portugal, 2016, see http://www.nntconf.org/ submissions/rollerNIL%20NNT%20T-structures%20v2.pdf (last accessed February 11, 2021).

¹⁰³D. J. Resnick and J. Iwasa, Proc. SPIE **10810**, 108100E (2018).

104 T. Asano, K. Sakai, K. Yamamoto, H. Hiura, T. Nakayama, T. Hayashi, Y. Takabayashi, T. Iwanaga, and D. J. Resnick, Proc. SPIE 11178, 111780I (2019).

105 M. Leitgeb, D. Nees, S. Ruttloff, U. Palfinger, J. Götz, R. Liska, M. R. Belegratis, and B. Stadlober, ACS Nano 10, 4926 (2016).

¹⁰⁶Y. Kim, Y. Choi, and S. Kang, Microsyst. Technol. 11, 464 (2005).

¹⁰⁷W. Michaeli and F. Klaiber, J. Vac. Sci. Technol. B 27, 1323 (2009).

108 M. D. Austin, H. Ge, W. Wu, M. Li, Z. Yu, D. Wasserman, S. A. Lyon, and

S. Y. Chou, Appl. Phys. Lett. 84, 5299 (2004).