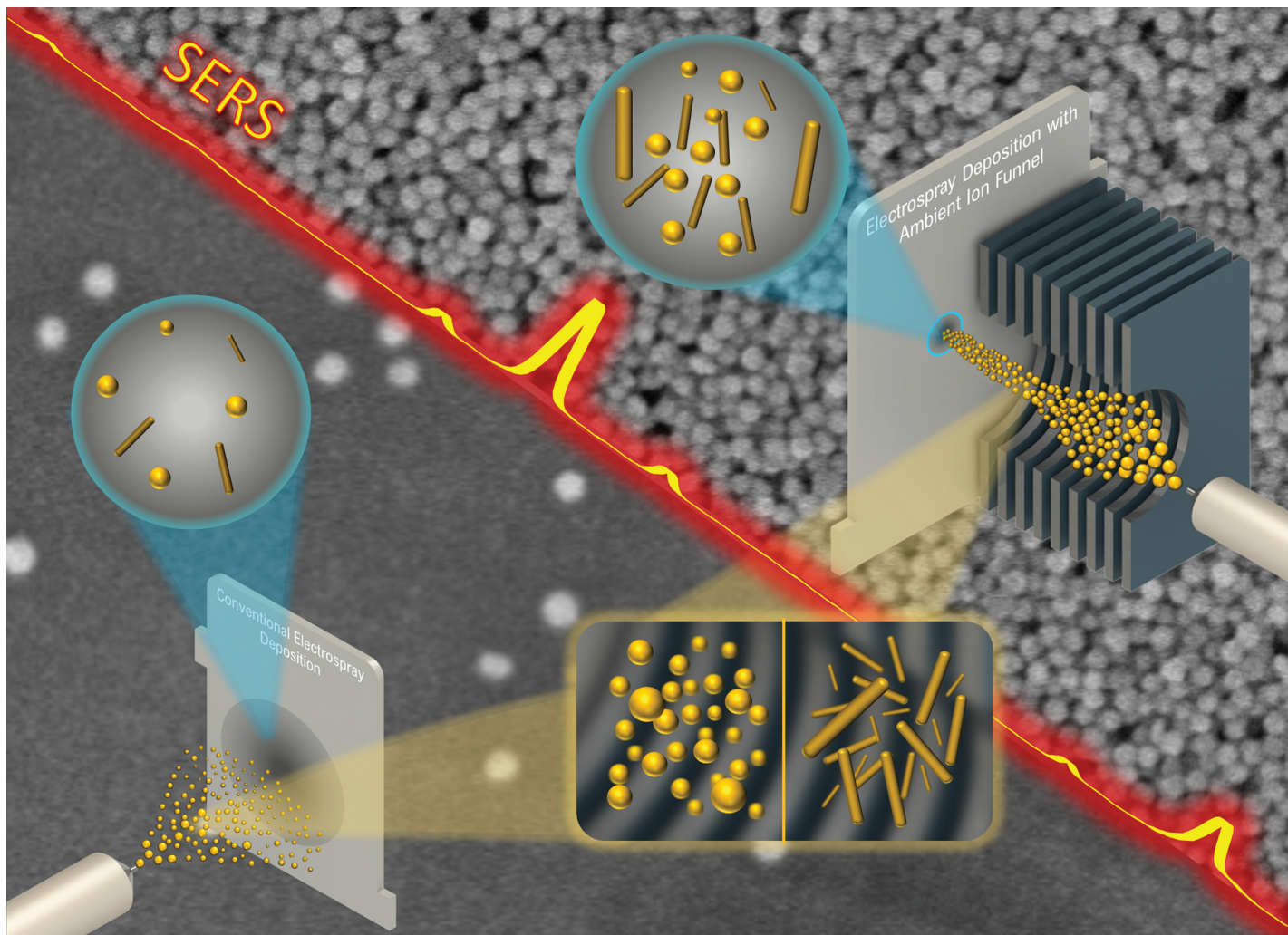


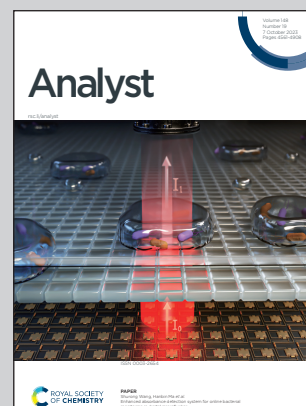


Showcasing research from Professor Simon Maher's laboratory ([www.liv.ac.uk/mass-spec](http://www.liv.ac.uk/mass-spec)), Department of Electrical Engineering and Electronics, University of Liverpool, UK.

Focusing ion funnel-assisted ambient electrospray enables high-density and uniform deposition of non-spherical gold nanoparticles for highly sensitive surface-enhanced Raman scattering

A novel ambient focusing ion funnel coupled with electrospray deposition (FIF-ESD) was designed to enable direct, intact, large-area, high-density and uniform deposition of nanoparticles (NPs), which was used to fabricate a high-performance nanoplasmonic substrate for SERS analysis. Image designed and illustrated by authors: Barry Smith, Baris Akbali and Simon Maher.

### As featured in:



See Simon Maher *et al.*, *Analyst*, 2023, **148**, 4677.


Cite this: *Analyst*, 2023, **148**, 4677

# Focusing ion funnel-assisted ambient electrospray enables high-density and uniform deposition of non-spherical gold nanoparticles for highly sensitive surface-enhanced Raman scattering†

Baris Akbali,<sup>a,b</sup> Cedric Boisdon,<sup>a</sup> Barry L. Smith,<sup>a</sup> Boonphop Chaisrihwun,<sup>c</sup> Kanet Wongravee,<sup>d</sup> Tirayut Vilaivan,<sup>d</sup> Cassio Lima,<sup>e</sup> Chen-Han Huang,<sup>f</sup> Tsan-Yao Chen,<sup>b</sup> Royston Goodacre<sup>e</sup> and Simon Maher<sup>e,\*a</sup>

Surface-enhanced Raman scattering (SERS) is a powerful technique for detecting trace amounts of analytes. However, the performance of SERS substrates depends on many variables including the enhancement factor, morphology, consistency, and interaction with target analytes. In this study, we investigated, for the first time, the use of electrospray deposition (ESD) combined with a novel ambient focusing DC ion funnel to deposit a high density of gold nanoparticles (AuNPs) to generate large-area, uniform substrates for highly sensitive SERS analysis. We found that the combination of ambient ion focusing with ESD facilitated high-density and intact deposition of non-spherical NPs. This also allowed us to take advantage of a polydisperse colloidal solution of AuNPs (consisting of nanospheres and nanorods), as confirmed by finite-difference time domain (FDTD) simulations. Our SERS substrate exhibited excellent capture capacity for model analyte molecules, namely 4-aminothiophenol (4-ATP) and Rhodamine 6G (R6G), with detection limits in the region of  $10^{-11}$  M and a relative standard deviation of <6% over a large area ( $\sim 500 \times 500 \mu\text{m}^2$ ). Additionally, we assessed the quantitative performance of our SERS substrate using the R6G probe molecule. The results demonstrated excellent linearity ( $R^2 > 0.99$ ) over a wide concentration range ( $10^{-4}$  M to  $10^{-10}$  M) with a detection limit of 80 pM.

Received 21st June 2023,  
Accepted 24th August 2023  
DOI: 10.1039/d3an01021j  
rsc.li/analyst

## Introduction

Noble metal nanoparticles (NPs) sustain a dipole-like surface plasmon resonance (SPR) through collective excitation of conduction electrons creating a significant and highly localised amplification of the incident electromagnetic field close to the metal NP.<sup>1–3</sup> Surface-enhanced Raman scattering (SERS) is a

well-known optical phenomena caused by localised SPR (LSPR).<sup>4,5</sup> Coupling of plasmonic dipoles produces highly concentrated, localised electromagnetic hot spots and is therefore considered a major source of the SERS phenomenon.<sup>6–9</sup> Plasmonic materials permit and encourage complementary spectroscopic techniques when used as sensors, enabling the detection of chemical species at very low concentrations based on their vibrational ‘fingerprint’.<sup>10–12</sup>

Typically, manufacturing SERS substrates involves mixing plasmonic NPs with analytes, spin/drop-casting analyte solutions on solid surfaces, or incubating particles with analyte solutions.<sup>13,14</sup> While drop-casting has proven to be effective in producing a satisfactory SERS substrate, it is susceptible to the undesirable coffee-ring effect whereby suspended particles are deposited mainly at the periphery of the drop following solvent evaporation. This effect can have a detrimental impact on the method’s reproducibility and sensitivity.<sup>15</sup> One way to address this issue is to treat the surface of the substrate prior to drop-casting, which can effectively mitigate the coffee-ring effect.<sup>16,17</sup> For example, a method introduced by Dabodiya *et al.*,<sup>18</sup> relies on the evaporation of self-lubricating drops of noble metal NPs and has achieved a remarkable detection

<sup>a</sup>Department of Electrical Engineering and Electronics, University of Liverpool, Brownlow Hill, Liverpool, L69 3GJ, UK. E-mail: s.maher@liverpool.ac.uk

<sup>b</sup>Department of Engineering and System Science, National Tsing Hua University, Hsinchu 30013, Taiwan

<sup>c</sup>Program in Petrochemistry and Polymer Science, Faculty of Science, Chulalongkorn University, Bangkok 10330, Thailand

<sup>d</sup>Department of Chemistry, Faculty of Science, Chulalongkorn University, Bangkok 10330, Thailand

<sup>e</sup>Centre for Metabolomics Research, Department of Biochemistry, Cell and Systems Biology, Institute of Systems, Molecular and Integrative Biology, University of Liverpool, Biosciences Building, Crown Street, Liverpool, L69 7ZB, UK

<sup>f</sup>Department of Biomedical Engineering, National Central University, Zhongli 10608, Taiwan

† Electronic supplementary information (ESI) available. See DOI: <https://doi.org/10.1039/d3an01021j>



limit of  $10^{-16}$  M with R6G dye-molecule. However, such approaches require additional, and sometimes complex or time consuming, preparative steps. Nevertheless, reproducibility of SERS experiments still needs to be carefully considered,<sup>10,12</sup> especially when the aim is to achieve highly accurate quantitative results.<sup>19,20</sup>

In order to enhance the uniformity of the SERS signal, various substrates composed of long-range ordered noble metal nanostructure arrays have also been developed utilising template-assisted techniques,<sup>21,22</sup> electron beam lithography,<sup>23</sup> droplet-based biphasic reactions in microfluidic devices,<sup>24,25</sup> and nanoimprint lithography.<sup>26,27</sup> Recently Kanike *et al.* developed a droplet-based microfluidic approach to fabricate ordered silver nanostructures over a surface area  $>60\text{ cm}^2$ .<sup>28</sup> They achieved a limit of detection with R6G of  $10^{-12}$  M. Whilst these approaches have shown promise, they are often associated with high cost and complexity. Furthermore, they may not be suitable for mass production, particularly when achieving a consistent SERS signal across a large area is necessary.

Ambient electrospray deposition is a viable alternate method for making SERS substrates.<sup>29–32</sup> By applying a high DC voltage (of a few kV) to liquids contained in a micro-capillary, ambient electrospray can ensue leading to the generation of charged micro and nano-droplets capable of direct deposition of polyatomic ions onto a targeted area with very small kinetic energies (close to zero).<sup>30</sup> Several interesting studies have reported on the deposition of NPs on conductive surfaces by combining ambient electrospray and ion soft landing.<sup>31,33–36</sup> This approach also offers tremendous potential to deposit bespoke NP geometries (*i.e.*, non-spherical) with peculiar properties, whilst preserving their distinctive shapes – which to the best of our knowledge remains unexplored. In any case, despite successes in utilising electrospray to deposit NPs, the process has inherent drawbacks. In particular, the applied electric field and subsequent coulombic expansion that occurs during Taylor cone formation leads to a spray plume that is many times larger than the capillary diameter. Furthermore, the distribution of charge within the plume is non-uniform leading to a non-homogenous distribution of NPs. In a bid to overcome these disadvantages some strategies have been employed. For instance, Li *et al.*<sup>31</sup> implemented an electrically floating metallic mask to elicit charge-induced focusing of an ESI spray plume containing AgNPs. The mask was manufactured with a series of holes creating a pattern of circular, highly active areas on the SERS substrate located behind the mask. In another study, Ahuja and co-workers electrosprayed silver nanoparticles on to a dropcast film of analyte for detection of *Escherichia coli* bacteria achieving a SERS signal enhancement factor of  $10^8$  and a detection limit of  $10^2$  CFU  $\text{mL}^{-1}$ .<sup>27</sup>

The main bottleneck for homogeneous deposition of AuNPs on SERS substrates is the capacity to focus high intensity plumes of NPs at atmospheric pressure. In moderate vacuum ( $<30$  Torr) this would generally be accomplished by using radio frequency (RF) voltages with either an ion funnel electrode arrangement<sup>37</sup> or multipole guide structure.<sup>38</sup> At

atmospheric pressure the RF voltage required to focus ions is impractically large and available approaches are limited.<sup>39</sup> Recently, Hollerbach *et al.*<sup>40</sup> reported a novel method for focusing ions at atmospheric pressure using non-linear DC voltage gradients applied across a conventional stacked ring ion guide. They employed quadratic and exponential voltage gradients to define a field curvature within the ion guide that forces ions radially inward as they traverse its length. Independently and prior to the interesting publication of Hollerbach *et al.*,<sup>40</sup> we designed and built an ambient ion focusing array that operates on a similar principle, using a non-linear (exponential) DC potential gradient. We hypothesised that ambient ion focusing in this way can augment high density deposition of NPs, including non-spherical NP geometries, enabling fabrication of high-performance SERS substrates.

In this study we have designed, built, and optimised a novel ambient focusing ion funnel, using a non-linear DC-only field, which can focus ions onto a spot size of  $\leq 6\text{ mm}^2$ . Two model compounds were chosen for testing, 4-aminothiophenol (4-ATP) and Rhodamine 6G (R6G), as well-studied molecules to assess the performance of the SERS substrate, specifically: the enhancement factor, signal uniformity across the substrate, and standard analytical figures of merit. Moreover, the performance of the focusing ion funnel electrospray setup was carried out with both spherical and non-spherical (*i.e.*, rod shaped) AuNPs to demonstrate that a diversity of SERS substrates can be generated by this general approach.

## Experimental

### Materials and sample preparation

Gold(III) chloride solution (99.9% –  $\text{HAuCl}_4$ ), sodium borohydride (99% –  $\text{NaBH}_4$ ), hexadecyltrimethylammonium bromide (CTAB), silver nitrate (99.9% –  $\text{AgNO}_3$ ), 4-aminothiophenol (97% – 4-ATP), Rhodamine 6G (95% – R6G) and  $\text{CuCl}_2$  were purchased from Sigma Aldrich. Other reagents were of analytical grade and used without any further purification or treatment. Deionised water (DI) ( $\sim 18.2\text{ M}\Omega$ ) was purified using a Milli-Q Advantage A10 water purification system (Millipore, MA, USA) before use in this study. Stainless steel sheets with a thickness of  $100\text{ }\mu\text{m}$  were purchased from RS Components Ltd (Northants, UK).

### Preparation of gold nanorods (AuNRs)

The synthesis of AuNRs was performed based on a modified seed-mediation growth technique.<sup>41–43</sup> Briefly, 10 mL of 0.2 M CTAB (stabiliser template) was combined with 10 mL of 0.5 mM  $\text{HAuCl}_4$  (gold precursor). Subsequently, 1.2 mL of 0.01 M  $\text{NaBH}_4$  as a strong reducing agent was injected which results in a transformation from yellow to brown colour. The obtained colloidal mixture was sonicated and successively utilised as the seed solution for AuNR synthesis. Then, the growth stock solution was prepared by mixing 50 mL of 0.2 M CTAB, 50 mL of 1 mM  $\text{HAuCl}_4$ , and 0.25 mL of 4 mM  $\text{AgNO}_3$ . To generate the AuNRs, 0.7 mL of 0.0788 M ascorbic acid was



Analyst, 2023, **148**, 4677–4687 | **4679**

| Gradient | $C$  | $m$    |
|----------|------|--------|
| 10       | 10   | 0.6907 |
| 50       | 50   | 0.5128 |
| 100      | 100  | 0.4369 |
| 500      | 500  | 0.2892 |
| 1000     | 1000 | 0.1991 |

A visual representation of applied voltages across a 9-electrode ion funnel are shown in Fig. S1.† The gradients are mirrored about the  $x$ -axis to operate the focusing ion funnel with the target substrate held at  $-5$  kV. Note, the electrospray is operated at approximately 5 kV above the first electrode voltage to maintain a consistently decreasing potential from emitter tip to SERS substrate. Also shown in Fig. S1† is a conventional linear gradient funnel, whereby the same value resistor is used between each electrode (this also acts as a control for comparison).

The associated resistor values to facilitate generation of each exponential gradient are found in Table S1† and calculated to ensure the available power supply current ( $I_{sc} = 2$  mA) is not exceeded. The nearest available standard resistor value was purchased or generated by series/parallel combinations if the standard value deviated by more than 2% from the values calculated in Table S1.† Note, the large voltage drops (>1 kV) across the last few resistors in the steepest exponential gradients (Fig. S1†) necessitated procurement of resistors with high standoff voltage ratings.

The stacked ring ion guide was constructed from printed circuit boards (PCBs) similar to the literature<sup>50</sup> and shown in Fig. S2† (cut-away view). Briefly, as depicted in Fig. S2† with numerical labels, nine ring electrodes (9), with an inner diameter of 16 mm, were constructed using conventional PCBs and slotted into an interface PCB (3) containing evenly spaced slots to set the linear distance to 1 mm between ring electrodes. A PCB accommodating the resistor chains (2) set out in Table S1† is attached to the interface PCB by standoffs (1). Spring loaded pins (4) transfer voltages to each ring electrode *via* connections on the interface board. Swappable resistor PCBs enable rapid switching and testing of different exponential resistor chains. High voltage connections to the resistor PCB are made through high voltage banana plugs (5). AuNPs in solution are pumped into an ESI emitter (6) *via* a syringe driver (not shown in Fig. S2†) and sprayed towards a conductive stainless-steel sheet (8). A small circular region (7) illustrates the deposition of AuNPs on the substrate surface.

### Simulation of focusing ion funnel

Particle trajectory modelling was performed in Simion 8.1 using a statistical diffusion simulation (SDS) model. The conductive geometry (Fig. S2†) was coded in a *.gem* file containing: ESI emitter (5 mm  $\times$  0.2 mm) held at 5 kV, nine ring electrodes (ID = 16 mm, OD = 20 mm, thickness = 1.6 mm, spacing = 1 mm) with corresponding voltages as shown in Fig. S1,† and

SERS target held at  $-5$  kV. 2000 ions of mass 200 000 and charge +10 were arbitrarily chosen to represent the AuNPs. The simulation is devised to provide a qualitative indication of the focusing effect from the ambient DC-only ion funnel and not as a quantitative design tool since several important processes are not modelled, *e.g.*, momentum of electro-sprayed droplets emanating from ESI emitter, nebulising nitrogen gas flow due to unknown velocity and spatial charging, *etc.*

Fig. 2 shows the qualitative simulation results for each exponential gradient examined, and also a linear gradient for comparison. The linear gradient, which is akin to a conventional drift tube-ion mobility spectrometer (DT-IMS)<sup>51</sup> type ion guide, provides a baseline comparison. As expected, an immediate expansion of the ion cloud is evident due to high E-field created by the ESI emitter at 5 kV. Upon entering the ion guide, the ions traverse with generally constant velocity and limited radial focusing. The non-uniformity of velocity and slight focusing effect observed is due to field penetration from the ESI emitter and the conductive SERS substrate. Usually in a DT-IMS the entrance would have a gridded electrode across it to prevent field ingress.

In stark contrast, the steepest exponential gradient,  $C = 10$ , exhibited a much broader ion cloud expansion due to essentially a field free region around the first few electrodes where the applied voltage is close to 0 V. The ESI emitter field can therefore penetrate much further into the ion guide resulting in a more widely dispersed ion cloud. In fact, for this particular case, which is the steepest exponential gradient tested, the ion cloud diameter actually exceeds that of the inner diameter of the electrodes, which reduces the overall ion transmission.

Physical processes not modelled here would presumably be useful, in practice, to assist ions through this field free region. For instance, the nitrogen gas will, through collisions, impart an assisting velocity in the positive  $x$  direction. As ions traverse the ion guide the field curvature created by the exponential gradient effectively ‘funnels’ ions radially inwards. Field maps for each gradient can be seen in Fig. S3,<sup>†</sup> clearly demonstrating that for steeper exponential gradients a higher degree of inward field curvature is generated.

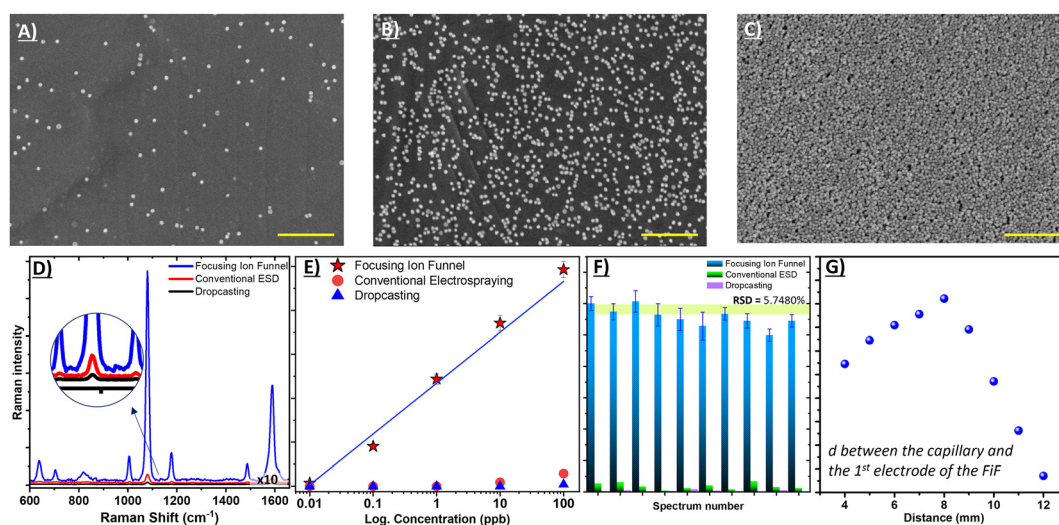
**Fig. 2** Particle trajectory maps colour-coded to ion velocity for various voltage gradients as labelled.

Fig. S4A† (left panel) shows a series of hit maps for  $y$  and  $z$  coordinates of simulated ions where they strike the substrate at the end of the ion guide, for each gradient. The radius of the observed landing pattern decreases with an increase in the exponential gradient corroborating the field map data. Transmission of ions is 100% for the first four gradients simulated, after which the ion plume starts to expand beyond the inner dimensions of the funnel and discharge on the first and second electrodes ( $C = 10$ ). Therefore, the density (ions per  $\text{mm}^2$ ) is highest for the field gradient denoted by  $C = 50$  (Fig. S4A,† right panel). The simulated ion densities broadly follow the experimental data for the linear ion guide which exhibited a higher intensity Raman spectrum than  $C = 1000$  and  $C = 400$  (shown later in Results and Discussion section, Fig. 5C). It is important to note that the simulation study is only designed to give a qualitative indication of the electrodynamic effects one can expect from the ion funnel. It does not consider other physical phenomenon at play, for instance the influence of the nebuliser gas on the particle dynamics which can also influence the distribution of NPs deposited on the substrate. To examine the surface coverage, we also obtained SERS line scan data, for linear and  $C = 50$ , with corresponding photographs of the deposited areas also shown in Fig. S4B† insert. These results demonstrate consistent SERS signal intensity across each AuNP-coated region, indicating good uniformity (RSDs of 6.5% and 5.7% for linear and  $C = 50$ , respectively). Further consideration of this is given in the Results section (Fig. 3).

### Ambient electro spray deposition (ESD) of AuNPs by focusing ion funnel

To reduce the surface tension and speed up solvent evaporation, the solution was diluted with an equivalent volume of DI water. Using the syringe pump, the diluted suspension was

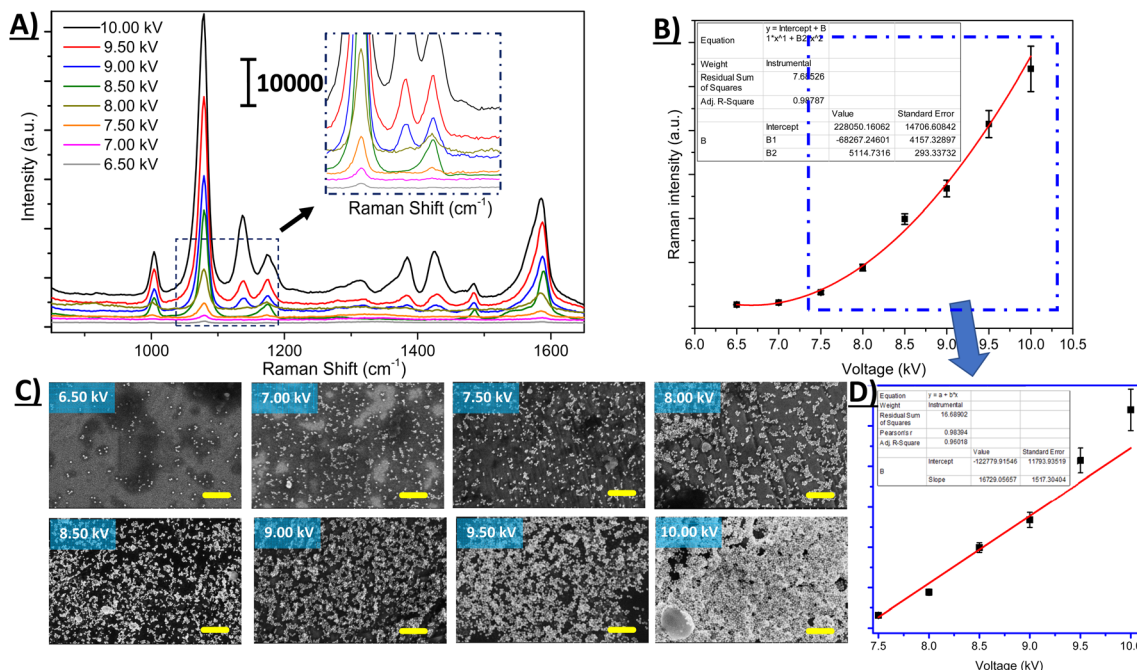
infused into the ESI probe at the desired liquid flow rate. The spray nozzle exit was directly coupled to the entrance of the focusing ion funnel, to focus the ionised beam of AuNPs on to the substrate, which was charged at 3.5–5.0 kV with a high-voltage power supply. The ESI probe also incorporates a nebuliser gas (nitrogen) which was supplied from a Nitrogen generator (Genius XE35, Peak Scientific USA), with a flow rate of 1  $\text{L min}^{-1}$  to enhance desolvation of the electrosprayed solution. Also, an IR lamp (HE015, Vet-Tech, UK) was placed directly above the ESD setup for the same purpose, to aid solvent evaporation. The average temperature in the vicinity with the IR lamp on was  $\sim 55^\circ\text{C}$ . The substrate was attached to the last electrode of the focusing ion funnel and negatively charged at  $-3.5$ – $5.0$  kV by using the same high-voltage power supply. AuNPs were electrosprayed for one hour at ambient pressure (1 atm) onto the substrate with a flow rate of 3  $\mu\text{L min}^{-1}$ . Heating the nebuliser gas is an effective means to improve desolvation, as is routinely the case for regular electrospray ionisation mass spectrometry. Since we did not have this feature available, we utilised an IR lamp instead. A simple experiment was conducted to demonstrate its influence within the experimental setup, whereby a series of SERS measurements were carried out with and without the IR lamp. As expected (Fig. S5†), in the absence of IR heating, an increased variability of the SERS signal intensity is observed. Fig. S5B and C† further show corresponding scanning electron microscopy (SEM) images of AuNP surface coverage with and without the IR lamp, respectively. Without the additional heat from the IR lamp, there is evidence of AuNP aggregation on the surface (Fig. S5B†). Under ambient conditions, this can be ascribed to insufficient evaporation of the electrospray droplets. At room temperature there is an increased likelihood of droplets landing on the substrate, resulting in localised wetting and on-surface evaporation. Hence, the increased temperature afforded by the IR



**Fig. 3** SEM images after depositing gold nanoparticles by (A) dropcasting, (B) conventional ESD, (C) ESD with ambient focusing ion funnel, (D) SERS spectra comparison of the 3 substrate samples, (E) SERS intensity variation with different concentrations of 4-ATP, (F) SERS signal uniformity analysis from 10 random locations for each sample, (G) SERS intensity variation *versus* distance between the ESD capillary and the 1<sup>st</sup> electrode of the focusing ion funnel. For the focusing ion funnel experiments,  $C_{\text{gradient}} = 50$  (at 10 kV) was used. All scale bars are 500 nm.







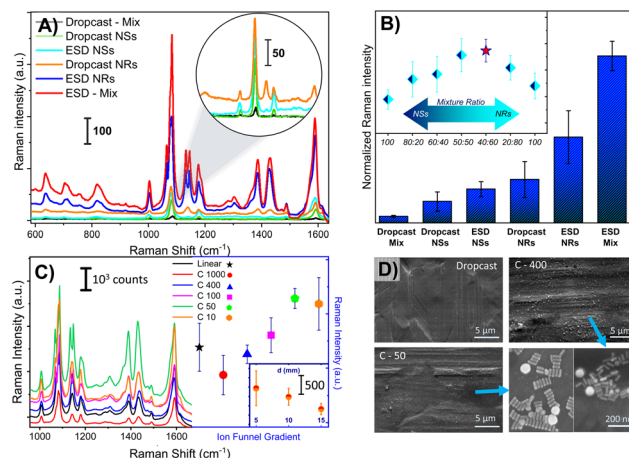
**Fig. 4** (A) SERS intensity variation for different applied voltages, (B) corresponding calibration curve and (C) SEM images for different ESI voltages as labelled. All scale bars are 500 nm. In (B) and (D) means are shown with standard deviation error bars from 10 replicates.

(AuNPs per unit area) increases with ESI voltage increase. The highest AuNP coverage was obtained with 10.0 kV ESI voltage (the maximum voltage output of the power supply available).

### Focusing ion funnel-ESD of a mixture containing different AuNP geometries

The focused ESD technique reported herein has been optimised to develop substrates with high density AuNPs and high uniformity, making them ideal for quantitative SERS analysis. Additionally, we further investigated our focusing ESD setup to determine whether it can facilitate effective deposition including mixing within charged droplets comprising diverse AuNP geometries (including non-spherical shapes), which can potentially be advantageous for a SERS substrate. Although the production of spherical AuNPs has been researched extensively, rod-shaped gold NPs have also gained a lot of interest due to their optical anisotropic nature.<sup>59,60</sup> Specifically, gold nanorods have two plasmonic bands, which can be tuned based on the aspect ratio of the nanoparticle, making them particularly versatile and useful.<sup>60–62</sup>

Even though combining different shapes of nanoparticles can be advantageous in terms of SERS efficiency, it requires either complicated chemical synthesis or lengthy sample preparation steps.<sup>63–65</sup> In Fig. 5, we presented SERS results of electrospray deposited gold nanorods (NRs) and gold nanospheres (NSs) separately, and furthermore a mixture of the two geometries (AuNRs/AuNSs), in comparison with dropcasting. SERS results are shown in Fig. 5A, clearly showing the superior performance of ESD by focusing ion funnel compared to drop casting for all samples. The ESD process allows for better



**Fig. 5** (A) SERS spectra comparison and (B) SERS intensity comparison of AuNSs and AuNRs by FIF-ESD and dropcasting techniques, where bars represent mean values and the error bars are standard deviations from 10 replicates (inset: SERS intensity vs. mixture ratio) (C) SERS spectra obtained from ESD by focusing ion funnel with different gradients (inset: mean SERS intensity variation by changing the inter-electrode distances for C-1000; error bars relate to standard deviations from 10 replicates), (D) SEM images from dropcasting, and ESD by FIF using C-400 and C-50 gradients.

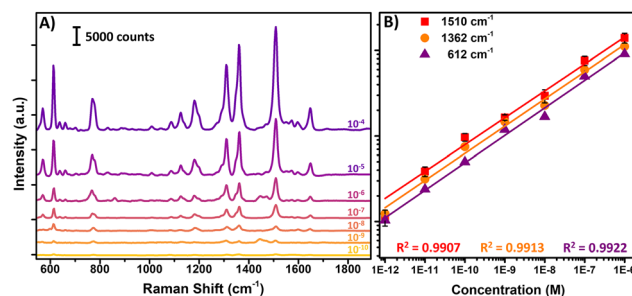
control of NP density on the substrate surface, which can be quite challenging for dropcasting methods. Additionally, our FDTD calculations (Fig. S7†) support the observation that coatings of AuNRs yield better enhancement than AuNSs, regardless of the coating technique used. As demonstrated in Fig. S7A,† the local electric field intensity enhancement of

### Enhancement factor of the substrate

The effectiveness of the focused-ESD-SERS substrate developed herein can be evaluated by considering the enhancement factor ( $E_F$ ), which measures the contribution to the enhanced Raman spectra of R6G molecules. To calculate the enhancement factor of the substrate, the most dominant Raman peak located at  $1585\text{ cm}^{-1}$  was chosen. The enhancement factor is calculated by using the following formula (eqn (2)),<sup>68,69</sup>

$$E_F = \frac{\frac{I_{\text{SERS}}}{N_{\text{SERS}}}}{\frac{I_{\text{NR}}}{N_{\text{NR}}}} \quad (2)$$

where  $I_{\text{NR}}$  and  $I_{\text{SERS}}$  are the Raman signal intensities for normal Raman and SERS measurements, respectively.  $N_{\text{SERS}}$  and  $N_{\text{NR}}$  are the average number of molecules within laser irradiation for normal Raman measurements.<sup>70</sup> The value of  $I_{\text{SERS}}$  and  $I_{\text{NR}}$  were measured as  $7.204 \times 10^4$  and  $2.871 \times 10^2$ , respectively. For  $N_{\text{NR}}$  and  $N_{\text{SERS}}$  calculations, assuming that R6G constitutes a single layer on the surface of the SERS substrate,  $N_{\text{SERS}}$  can be determined by dividing the laser illumination area (approximately 2  $\mu\text{m}$  in diameter) by the area of a single R6G molecule ( $\sim 1.5 \text{ nm}^2$ ), resulting in a value of



**Fig. 6** SERS spectra of (A) R6G on ESD by focusing ion funnel substrate from  $10^{-4}$  M to  $10^{-10}$  M and (B) the Raman signal intensity of R6G at 612, 1362, and 1510  $\text{cm}^{-1}$  peaks as a function of molecular concentration (log scale).

$\sim 2.09 \times 10^6$  molecules. Similarly,  $N_{\text{NR}}$  can be estimated as  $\sim 2.8 \times 10^{12}$  molecules. Therefore, the  $E_{\text{F}}$  is estimated to be  $\sim 3.4 \times 10^8$ .

## Conclusions

We have successfully developed an ambient (DC-only) focusing ion funnel coupled with electrospray deposition (ESD) that enables uniform, high-density, large-area and intact coating of noble metal nanoparticles, including non-spherical geometries, for high performance SERS substrate fabrication. Compared to dropcasting and conventional electrospray, our ESD-focusing ion funnel arrangement demonstrated significantly more intense SERS signals with  $\sim 70$ -fold and  $\sim 20$ -fold increase, respectively. Additionally, our uniformity analysis showed that the ESD-focusing ion funnel provides an excellent coating of AuNPs with a relative standard deviation  $< 5.75\%$ . We also optimised some operating parameters of the focused-ESD technique, such as the distance between the ESI capillary and the focusing ion funnel, spacing between the electrodes, exponential focusing ion funnel gradient, and applied voltage, which affect the coating quality of AuNPs in terms of uniformity and density. Moreover, we demonstrated that the focused-ESD approach can be used to successfully coat mixtures of AuNSs and AuNRs, whereby the electrosprayed mixture provides a better signal enhancement than electrospraying either the AuNSs or AuNRs separately. FDTD calculations indicate that the near-field enhancement between adjacent AuNRs and AuNSs is higher than the enhancement between AuNSs or AuNRs. Using R6G as a model analyte, we assessed the enhancement factor of the SERS substrate, finding it to be  $\sim 3.4 \times 10^8$ . Furthermore, the substrates developed by focused-ESD were further examined in terms of their analytical figures of merit. A calibration curve was generated for R6G which exhibited excellent linearity ( $R^2 > 0.99$ ) over a wide concentration range with a detection limit of 80 pM.

The fabrication method in this work provides a sound basis that other researchers can readily implement. Possible improvements to this work might include using a heated nebuliser gas, with optimised gas temperature and flow rate. Furthermore, the electrospray flow rate and capillary diameter can be further optimised depending upon the colloidal solution to be deposited. Indeed, this approach can also be readily coupled to nano electrospray. However, particular attention should be given to the internal diameter of the capillary and any associated tubing when using NPs to avoid blockages. The same focusing-ESD apparatus can also be used to apply analyte solution to the same SERS substrate, which may yield even better SERS signal uniformity. Moreover, as demonstrated herein, this approach allows non-spherical NP geometries to be soft landed, thus there is an exciting opportunity to deposit a range of bespoke NPs with peculiar geometries. It is also worth noting that this surface preparation method is not limited to SERS substrate fabrication with AuNPs. Indeed, elec-

tro spray ionisation can be carried out with a wide range of materials including non-metallic plasmonic NPs. The high uniformity and precise control over the amount of material deposited using the focused-ESD setup could prove useful for a range of other applications. In conclusion, ESD by focusing ion funnel offers a versatile and effective method to augment uniform and high-density coating of both spherical and non-spherical, homo- and hetero-dispersed metal colloidal nanoparticle solutions for high performance SERS analysis.

## Author contributions

The manuscript was written through contributions of all authors.

## Conflicts of interest

There are no conflicts to declare.

## Acknowledgements

S. M., T.-Y. C. and B. A. acknowledge funding from the University of Liverpool (UK) and National Tsing Hua University (Taiwan) dual-award PhD degree partnership. S. M. and R. G. gratefully acknowledge support from the EPSRC (EP/V001019/1). Authors R. G. and C. L. would like to thank LIV-SRF for financial support for Raman. Furthermore, R. G. and C. L. would also like to thank EPSRC-SFI (EP/V042882/1) for support. Authors T. V., S. M., K. W. and B. C. acknowledge the National Science, Research and Innovation Fund (NSRF) via the Program Management Unit for Human Resources & Institutional Development, Research and Innovation (B16F640101) for supporting this research.

## References

- U. Kreibig and M. Vollmer, in *Optical Properties of Metal Clusters*, ed. U. Kreibig and M. Vollmer, Springer Berlin Heidelberg, Berlin, Heidelberg, 1995, pp. 203–274, DOI: [10.1007/978-3-662-09109-8\\_3](https://doi.org/10.1007/978-3-662-09109-8_3).
- C. F. Bohren and D. R. Huffman, *Absorption and scattering of light by small particles*, John Wiley & Sons, 2008, pp. 12–56.
- U. Kreibig, M. Vollmer, U. Kreibig and M. Vollmer, *Optical Properties of Metal Clusters*, 1995, pp. 203–274.
- M. Moskovits, *J. Chem. Phys.*, 1978, **69**, 4159–4161.
- M. Moskovits, *Rev. Mod. Phys.*, 1985, **57**, 783.
- T. R. Jensen, M. D. Malinsky, C. L. Haynes and R. P. Van Duyne, *J. Phys. Chem. B*, 2000, **104**, 10549–10556.
- S.-Y. Ding, J. Yi, J.-F. Li, B. Ren, D.-Y. Wu, R. Panneerselvam and Z.-Q. Tian, *Nat. Rev. Mater.*, 2016, **1**, 1–16.
- L.-L. Tay and J. Hulse, *J. Mod. Opt.*, 2013, **60**, 1107–1114.



- 9 L.-L. Tay, J. Hulse, D. Kennedy and J. P. Pezacki, *J. Phys. Chem. C*, 2010, **114**, 7356–7363.
- 10 J. Langer, D. J. de Aberasturi, J. Aizpurua, R. A. Alvarez-Puebla, B. Auguie, 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*, 2020, **14**, 28–117.
- 11 T. S. Alomar, N. AlMasoud, Y. Xu, C. Lima, B. Akbali, S. Maher and R. Goodacre, *Sensors*, 2022, **22**, 7832.
- 12 H. Fisk, C. Westley, N. J. Turner and R. Goodacre, *J. Raman Spectrosc.*, 2016, **47**, 59–66.
- 13 P. Z. El-Khoury, G. E. Johnson, I. V. Novikova, Y. Gong, A. G. Joly, J. E. Evans, M. Zamkov, J. Laskin and W. P. Hess, *Faraday Discuss.*, 2015, **184**, 339–357.
- 14 D. Wang, F. Liang, P. Ma, Q. Yang, D. Gao, D. Song and X. Wang, *Food Anal. Methods*, 2016, **9**, 934–941.
- 15 D. Mampallil and H. B. Eral, *Adv. Colloid Interface Sci.*, 2018, **252**, 38–54.
- 16 H. Tan, S. Wooh, H.-J. Butt, X. Zhang and D. Lohse, *Nat. Commun.*, 2019, **10**, 478.
- 17 B. R. D. Deegan, T. F. Dupont, G. Huber, S. R. Nagel and T. A. Witten, *Nature*, 1997, **389**, 827–829.
- 18 T. S. Dabodiya, S. G. Sontti, Z. Wei, Q. Lu, R. Billet, A. V. Murugan and X. Zhang, *Adv. Mater. Interfaces*, 2022, **9**, 2201998.
- 19 S. E. J. Bell, G. Charron, E. Cortés, J. Kneipp, M. L. de la Chapelle, J. Langer, M. Procházka, V. Tran and S. Schlücker, *Angew. Chem., Int. Ed.*, 2020, **59**, 5454–5462.
- 20 R. Goodacre, D. Graham and K. Faulds, *TrAC, Trends Anal. Chem.*, 2018, **102**, 359–368.
- 21 B. Chen, G. Meng, Q. Huang, Z. Huang, Q. Xu, C. Zhu, Y. Qian and Y. Ding, *ACS Appl. Mater. Interfaces*, 2014, **6**, 15667–15675.
- 22 H. Zhang, M. Liu, F. Zhou, D. Liu, G. Liu, G. Duan, W. Cai and Y. Li, *Small*, 2015, **11**, 844–853.
- 23 Q. Yu, P. Guan, D. Qin, G. Golden and P. M. Wallace, *Nano Lett.*, 2008, **8**, 1923–1928.
- 24 Q. Wu, R. Liu, F. Miao, G. Zhang, W. Li and Y. Song, *Chem. Eng. J.*, 2023, **452**, 139355.
- 25 R. Liu, Q. Wu, X. Huang, X. Zhao, X. Chen, Y. Chen, D. A. Weitz and Y. Song, *RSC Adv.*, 2021, **11**, 37814–37823.
- 26 S. Kumar, S. Cherukulappurath, T. W. Johnson and S.-H. Oh, *Chem. Mater.*, 2014, **26**, 6523–6530.
- 27 T. Ahuja, A. Ghosh, S. Mondal, P. Basuri, S. K. Jenifer, P. Srikrishnarka, J. S. Mohanty, S. Bose and T. Pradeep, *Analyst*, 2019, **144**, 7412–7420.
- 28 C. Kanike, H. Wu, A. W. Zaibudeen, Y. Li, Z. Wei, L. D. Unsworth, A. Atta and X. Zhang, *Chem. Eng. J.*, 2023, **470**, 144019.
- 29 A. Jaworek, *J. Mater. Sci.*, 2007, **42**, 266–297.
- 30 A. K. Badu-Tawiah, C. Wu and R. G. Cooks, *Anal. Chem.*, 2011, **83**, 2648–2654.
- 31 A. Li, Z. Baird, S. Bag, D. Sarkar, A. Prabhath, T. Pradeep and R. G. Cooks, *Angew. Chem., Int. Ed.*, 2014, **53**, 12528–12531.
- 32 A. Ghosh, T. Ahuja, K. Chaudhari and T. Pradeep, *J. Phys. Chem. C*, 2020, **124**, 16644–16651.
- 33 A. Li, Q. Luo, S.-J. Park and R. G. Cooks, *Angew. Chem., Int. Ed.*, 2014, **53**, 3147–3150.
- 34 S. J. Clark, R. Argelaguet, C.-A. Kapourani, T. M. Stubbs, H. J. Lee, C. Alda-Catalinas, F. Krueger, G. Sanguinetti, G. Kelsey and J. C. Marion, *Nat. Commun.*, 2018, **9**, 781.
- 35 J. Wang, L. Yang, B. Liu, H. Jiang, R. Liu, J. Yang, G. Han, Q. Mei and Z. Zhang, *Anal. Chem.*, 2014, **86**, 3338–3345.
- 36 A. Li, Q. Luo, S. J. Park and R. G. Cooks, *Angew. Chem., Int. Ed.*, 2014, **53**, 3147–3150.
- 37 R. T. Kelly, A. V. Tolmachev, J. S. Page, K. Tang and R. D. Smith, *Mass Spectrom. Rev.*, 2010, **29**, 294–312.
- 38 A. V. Tolmachev, H. R. Udseth and R. D. Smith, *Int. J. Mass Spectrom.*, 2003, **222**, 155–174.
- 39 B. L. Smith, C. Boisdon, D. Romero-Perez, T.-T. Sham, B. Bastani, Y. Zhou, S. McWilliam, A. K. Badu-Tawiah and S. Maher, *Int. J. Mass Spectrom.*, 2022, **471**, 116737.
- 40 A. L. Hollerbach, Y. M. Ibrahim, R. V. Norheim, T. O. Metz and R. G. Ewing, *Int. J. Mass Spectrom.*, 2022, **482**, 116948.
- 41 N. Wiriyaichai, P. Srisurat, J. Cherngsuwanwong, N. Sangsing, J. Choniratt, S. Attavitaya and S. Bamrungsap, *New J. Chem.*, 2019, **43**, 8502–8507.
- 42 B. Nikoobakht and M. A. El-Sayed, *Chem. Mater.*, 2003, **15**, 1957–1962.
- 43 S. Bamrungsap, A. Treetong, C. Apiwat, T. Wuttikhun and T. Dharakul, *Microchim. Acta*, 2016, **183**, 249–256.
- 44 A. Parnsubsakul, C. Sapcharoenkun, C. Warin, S. Ekgasit and P. Pienpinijtham, *Colloids Surf., B*, 2022, **217**, 112702.
- 45 M. Sánchez-Purrà, M. Carré-Camps, H. de Puig, I. Bosch, L. Gehrke and K. Hamad-Schifferli, *ACS Infect. Dis.*, 2017, **3**, 767–776.
- 46 J. Sun, Z. Zhang, C. Liu, X. Dai, W. Zhou, K. Jiang, T. Zhang, J. Yin, J. Gao and H. Yin, *Anal. Bioanal. Chem.*, 2021, **413**, 5469–5482.
- 47 R. K. Saini, A. K. Sharma, A. Agarwal and R. Prajesh, *Mater. Chem. Phys.*, 2022, **287**, 126288.
- 48 A. Lewis, R. Gaifulina, M. Isabelle, M. L. Woods, G. R. Lloyd, K. Lau, M. Rodriguez-Justo, C. Kendall, N. Stone and G. M. Thomas, *J. Raman Spectrosc.*, 2017, **48**, 119–125.
- 49 H. Kotrange, A. Najda, A. Bains, R. Gruszecki, P. Chawla and M. M. Tosif, *Int. J. Mol. Sci.*, 2021, **22**, 9596.
- 50 T. Reinecke and B. H. Clowers, *HardwareX*, 2018, **4**, e00030.
- 51 B. L. Smith, C. Boisdon, I. S. Young, T. Praneenarat, T. Vilaivan and S. Maher, *Anal. Chem.*, 2020, **92**, 9104–9112.
- 52 H. Ko, S. Singamaneni and V. V. Tsukruk, *Small*, 2008, **4**, 1576–1599.



- 53 V. Merk, J. Kneipp and K. Leosson, *Adv. Opt. Mater.*, 2013, **1**, 313–318.
- 54 M. Osawa, N. Matsuda, K. Yoshii and I. Uchida, *J. Phys. Chem.*, 1994, **98**, 12702–12707.
- 55 J. S. Page, R. T. Kelly, K. Tang and R. D. Smith, *J. Am. Soc. Mass Spectrom.*, 2007, **18**, 1582–1590.
- 56 N. M. Sari, D. Romero-Perez, B. Bastani, M. Raulytanapanit, C. Boisdon, T. Praneenararat, H. A. Tajuddin, Z. Abdullah, A. K. Badu-Tawiah and S. Maher, *Sci. Rep.*, 2020, **10**, 21504.
- 57 J. F. De La Mora and I. G. Loscertales, *J. Fluid Mech.*, 1994, **260**, 155–184.
- 58 V. Gundabala, N. Vilanova and A. Fernández-Nieves, *Phys. Rev. Lett.*, 2010, **105**, 154503.
- 59 M. Grzelczak, J. Pérez-Juste, P. Mulvaney and L. M. Liz-Marzán, *Chem. Soc. Rev.*, 2008, **37**, 1783–1791.
- 60 S. Nam, N. Oh, Y. Zhai and M. Shim, *ACS Nano*, 2015, **9**, 878–885.
- 61 Q. Jiang, Y. Shi, Q. Zhang, N. Li, P. Zhan, L. Song, L. Dai, J. Tian, Y. Du and Z. Cheng, *Small*, 2015, **11**, 5134–5141.
- 62 X. Qian, D. Peng and Q. Ansari, *Nat. Biotechnol.*, 2008, **26**, 83–90.
- 63 M. P. Davies, C. S. McKinney, J. M. Serrano, T. J. Mullen and S. P. Stagon, *Appl. Phys. Lett.*, 2017, **110**, 053109.
- 64 N. Yang, T.-T. You, X. Liang, C.-M. Zhang, L. Jiang and P.-G. Yin, *RSC Adv.*, 2017, **7**, 9321–9327.
- 65 D. Lee and S. Yoon, *J. Phys. Chem. C*, 2016, **120**, 20642–20650.
- 66 R. Que, M. Shao, S. Zhuo, C. Wen, S. Wang and S. T. Lee, *Adv. Funct. Mater.*, 2011, **21**, 3337–3343.
- 67 X. Li, G. Chen, L. Yang, Z. Jin and J. Liu, *Adv. Funct. Mater.*, 2010, **20**, 2815–2824.
- 68 B. Akbali, M. Yagmurcukardes, F. Peeters, H.-Y. Lin, T.-Y. Lin, W.-H. Chen, S. Maher, T.-Y. Chen and C.-H. Huang, *J. Phys. Chem. C*, 2021, **125**, 16289–16295.
- 69 X. Yan, M. Wang, X. Sun, Y. Wang, G. Shi, W. Ma and P. Hou, *Appl. Surf. Sci.*, 2019, **479**, 879–886.
- 70 E. C. Le Ru, M. Meyer, E. Blackie and P. G. Etchegoin, *J. Raman Spectrosc.*, 2008, **39**, 1127–1134.

