An approach to significantly enhance spontaneous Raman sensitivity through the formation of a thin film via thermophoresis along with evaporation at the facet of a hollow-core photonic crystal fiber is reported for the first time. Sensitivity of detection is increased by more than 6 orders of magnitude for both organic and inorganic nanoparticles, facilitating the search for trace analytes in solution. Detection of two nanoparticles, alumina and polystyrene, is demonstrated down to 392 nM without the use of surface-enhanced Raman spectroscopy or other chemical-based procedures. This new thin-film deposition approach simplifies the simultaneous detection and analysis of small trace compounds, a previously arduous task using conventional spontaneous Raman.

1. Introduction

Nanoparticles constitute a pivotal building block in existing and emerging structured material systems. Their utility spans the entire spectrum of applications from health to industrial and agriculture domains. Monitoring nanoparticles, be it during synthesis, utilization, or as a contaminant, has emerged as a pressing necessity given their wide-spread deployment. This need and ability to carry out in situ monitoring is in contrast to techniques which can characterize a stand alone sample of nanoparticles. Numerous spectroscopy and microscopy techniques can be utilized for such tasks.

A plethora of techniques have been established to analyze sample nanoparticles, but limitations prevent facile comprehensive characterization. One of the most prevalent techniques is X-ray diffraction, which provides information on nanoparticle size, composition, and crystalline structure. Particles smaller than 3 nm or larger than 50 nm are incompatible with X-ray diffraction. Moreover, it is not suited to trace nanoparticle detection or concentration determination. Other characterization methods require similar compromise; several techniques are necessary when a certain combination of parameters is needed and are therefore not suitable for in situ monitoring.

Optical techniques are useful for nanoparticle monitoring tasks. For example, photon correlation Fourier spectroscopy has been proven as a useful tool to extract single nanoparticle emission linewidths. In addition, polarized photoluminescence has also been useful in studying the order and orientation of nanoparticles. Another approach utilizes spontaneous Raman in still and circulating fluid, liquid core waveguides and has enabled studies of nanomaterials with great sensitivity compared to conventional Raman.

Raman spectroscopy is a versatile characterization technique, non-destructively providing information on the molecular structure of materials with exceptional specificity. Raman (inelastic) scattering, however, occurs at least 10 orders of magnitude less frequently than Rayleigh (elastic) scattering. The consequence is a faint scattering signal, which is particularly exacerbated in fluidic samples due to lower molecular density. As such, Raman is primarily associated with solid samples. Raman’s potential in liquid and gaseous samples has yet to be fully realized: signal enhancement techniques such as Surface-Enhanced Raman Spectroscopy (SERS) require extensive substrate or sample preparation and lack repeatability, hindering reliable characterization. We propose here that the pairing of spontaneous Raman with optofluidics provides the necessary enhancement, offering a means to repeatably and quantitatively identify trace unknown compounds which may pose a substantial threat.

In this work we demonstrate an approach utilizing thermophoresis along with evaporation and capillary effects to extend the sensitivity of spontaneous Raman in fluidic samples to the nanomolar (nM) range for nanoparticle sensing. The technique promotes assembly of a thin-film of nanoparticles, by means of the laser source which is used to induce scattering. The coffee-ring effect acts to aggregate the solute atop a Hollow-Core Photonic Crystal Fiber (HC-PCF), and is depicted in Figure 1. The method is shown to be effective for a wide variety of samples both organic and inorganic.
The phenomenon which governs thin-film formation is known as the coffee-stain effect. This effect, which leaves a residual stain around the perimeter of a dried liquid droplet, may be exploited for novel fabrication techniques such as creating dips and rims in colloidal films, or for passive analyte pre-concentration of biological fluids. It is this thermophoresis effect in conjunction with evaporation and capillary effects at the fibre core walls combined that lead to the formation of the films. All spectra in Figure 2 have had baselines removed and are normalized to the height of the most intense peak in the spectrum.

Full details of measurement conditions and mode assignment are provided in Methods. At and below the μM regime, spectra appear identical to DIW. As the photoluminescent modes do not scale with concentration in a similar manner to Raman, they cannot be used as an indicator for LOD and thus we must conclude that LOD > 392 mM. Figure 2B demonstrates the LOD for PS. The characteristic peaks at 1001 cm$^{-1}$ and 1030 cm$^{-1}$ in the most concentrated samples but are absent below 3.92 mM; these are not Raman scattering signals, but instead correspond to the luminescence of the crystalline ruby structure at 6927 Å and 6942 Å when excited by the 632.8 nm source. At and below the μM regime, spectra appear identical to DIW. As the photoluminescent modes do not scale with concentration in a similar manner to Raman, they cannot be used as an indicator for LOD and thus we must conclude that LOD > 392 mM. Figure 2B demonstrates the LOD for PS. The characteristic peaks at 1001 cm$^{-1}$ and 1030 cm$^{-1}$ are only visible down to 24 mM. Therefore we conclude the limit of detection for PS nanospheres using spontaneous Raman in HC-PCF lies in the interval 2.4 mM < LOD < 24 mM.

These measurements demonstrate that the sensitivity of the spontaneous Raman signal obtained via optofluidic HC-PCF-enhancement does not extend to the micromolar (μM) regime for these samples.
the coffee-stain effect. It must be highlighted that coffee stain affects on a surface such as Si, for example, of the same sample type and similar concentration would not allow one to probe the precipitated film to obtain Raman spectra such as those obtained in the fiber core.

In the context of this experiment, the HC-PCF facet is efficiently heated by the Raman excitation laser, which promotes thermophoresis of the sample. In the absence of a pinned edge, the outer perimeter would evaporate uniformly and that would only induce evaporation induced effects which require days to achieve similar films for samples with similar concentrations. With a pinned edge, however, fluid which evaporates from the perimeter must be replenished, and a resulting flux transports fluid outwards from the air-liquid boundary at the center of the fiber core. This is in contrast to other experiments we carried out to induce spontaneous evaporation in the lab, which took days for the film to form and required orders of magnitude more liquid volume to obtain similar Raman spectra. The time and volume required in the case of the samples discussed here emphasise the dominant role that is played by the process of thermophoresis.

As laser-induced thermophoresis progresses, nanoparticles are transported towards the outer edge they aggregate, assisted by capillary and evaporation effects. A white-light microscope image of the waveguide facet taken before and after film formation is shown in Figure 3 (panels A–C), where greater reflection in the core is used as visual confirmation of the film. The thin film is grown inwards from the outside edge. This behaviour is observed in Scanning Electron Microscope (SEM) images of the fiber core post-measurement, seen in Figure 3 (panels D and E), showing increased nanoparticle deposition along the core’s outer rim.

The type of film generated during nanoparticle deposition is influenced by two factors: C, speed of the deposition front, and E, evaporation rate. When C ≪ E, the meniscus in the center of a droplet may contact the substrate and a single outer ring or series of rings results. Conversely, when C ≫ E, deposition outpaces evaporation and a uniform thin film is generated. SEM images of our thin films appear to indicate that we are in between these regimes. Exact modelling is beyond the scope of this work; one may refer to Kaplan et al. for further information on thin-film modeling.

4. Results

Both alumina and PS nanoparticles demonstrate mM-level or greater LOD in Figure 2 using spontaneous HC-PCF Raman. Here we demonstrate that the proposed thermophoresis enhancement principle can characterize these same nanoparticles with an enhanced sensitivity of at least 6 orders of magnitude over optofluidic-assisted spontaneous Raman.

4.1. Alumina Nanoparticles

To demonstrate the formation of an α-Al2O3 thin film via the proposed thermophoresis technique, we present results using a 0.392 nM solution. As evidenced in Figure 2A, this concentration falls below the LOD for spontaneous Raman in HC-PCFs.
No alumina modes, whether Raman or luminescent, were discernible at this concentration when tested using standard HC-PCF optofluidic enhancement.

Results from application of the proposed thermophoresis technique are illustrated in Figure 4A. Table 1 details relevant spectroscopic modes of alumina found in literature.[15,16] At the onset of measurements (Figure 4A, black spectrum), no alumina Raman modes are present and the spectrum is dominated by a strong silica response (from the HC-PCF) in the region $< 500 \text{ cm}^{-1}$. Luminescent modes in the vicinity of $1400 \text{ cm}^{-1}$ begin to become apparent after 48 hours of thermophoresis (Figure 4A, dark red spectrum). The presence of these luminescent modes is taken as an indication that the film has successfully formed and the reservoir of fluid can be removed from below the HC-PCF, allowing the sample to drain from the fiber core. Once drained, the film remains a permanent fixture atop the fiber and a spontaneous Raman spectrum (Figure 4A, bright red spectrum) reveals the characteristic Raman modes. We can now clearly see two modes at $375 \text{ cm}^{-1}$ and $417 \text{ cm}^{-1}$, consistent with literature as $E_g$ and $A_{1g}$, respectively, as well as the two luminescent modes at $1371 \text{ cm}^{-1}$ and $1401 \text{ cm}^{-1}$.[15,16] In addition to literature, these Raman modes are consistent with the reference spectrum of $\alpha$-$\text{Al}_2\text{O}_3$ (Figure 4A, grey spectrum).

### 4.2. PS Nanospheres

We wish to demonstrate that the behaviour which governs thin-film formation is not unique to alumina nanoparticles. Thus we have selected the 2.40 $\mu$M dilution of PS, a concentration established to fall below the LOD for spontaneous Raman in HC-PCFs in Figure 2B, to demonstrate increased sensitivity and breadth of applicability of the proposed thermophoresis technique.

Spontaneous Raman spectra captured during and following the proposed film-formation technique are presented in Figure 4B. Raman mode assignment in polystyrene has historically suffered some contradiction from one publication to the next, so we present here the expected and observed positions of PS modes.[19] We assign the most prominent Raman modes observed, listed in Table 2, where the first column denotes the band assignment and symmetry, consistent with polystyrene band positions of ordinary Raman by Anema et al.[19]

At the onset of measurements (Figure 4B, black spectrum), no PS Raman modes are present and the spectrum is dominated by modes belonging to DIW. After 53 h of thermophoresis (Figure 4B, dark blue spectrum), the prominent Raman mode at $1001 \text{ cm}^{-1}$ begins to become apparent, indicating successful film formation. Once the sample is allowed to drain from the HC-PCF core, a thin film remains atop the fiber which is confirmed to be PS via its spontaneous Raman signal (Figure 4B, bright blue spectrum). The most prominent modes are documented in Table 2 and closely agree with literature for PS, primarily coinciding with in- and out-of-plane bend and stretch modes of the benzene ring.[17] In addition to literature, these Raman modes are consistent with the reference spectrum of PS (Figure 4B, grey spectrum). With multimode agreement between the sample and PS literature, we can conclude that detection of PS is successful at a micromolar concentration.[17–19]
5. Discussion and Conclusion

The major distinction between this paper’s method and that in Mak et al. lies in the deliberate introduction of laser-induced thermophoresis at the laser-facing HC-PCF facet.[13] This process is depicted in Figure 1. During prolonged thermophoresis, solute nanoparticles at the fluid surface experience an evaporative flux due to edge-pinning by the HC-PCF core. This flux transports nanoparticles to the perimeter of the core, where they aggregate into a rigid thin film.[24,27,29] Using the laser to promote the coffee-ring effect, rather than external application of heat, we enable both in situ monitoring of thin-film formation, and the precise delivery of energy to the sample where evaporation near the surface takes place.

This work demonstrates for the first time that a HC-PCF coupled with this new thin-film thermophoresis technique can be used to achieve up to $10^6$ mol/L increase in the sensitivity of trace contaminants in aqueous solution. The method is shown to be effective for both organic and inorganic samples. The coffee-ring effect has been experimentally verified for both aqueous and non-aqueous fluids, and for analyte sizes ranging from the molecular up to 10 $\mu$m.[28] We were unable to replicate these results when dispersions of larger (1 $\mu$m) particles are used in the capillary fiber. A thorough investigation of size limitations for thin-film thermophoresis, and solutions to overcome them, is beyond the scope of this work. This limitation does not appear to affect the nanoparticle regime, and we anticipate that thermophoretic thin-film formation is feasible across a range of samples much wider than those presented here.

The size dependence described above, along with the evidence provided in the results section helps form the picture of how the laser not only simply accelerates evaporation, through

Table 1. Raman mode assignments for alumina.

| Assignment | Wavenumber (cm$^{-1}$) |
|------------|-----------------------|
| $E_g$      | 375                   |
| $A_{1g}$   | 417                   |
| Luminescence | 1367.4             |
| Luminescence | 1397.4             |

Table 2. Raman mode assignments for polystyrene.

| Assignment | Wavenumber (cm$^{-1}$) |
|------------|-----------------------|
| Expected$^{[17,19]}$ Observed |
| 6b $B_2$   | 623                   | 619.7              |
| 12 $A_1$   | 1002                  | 1000.6             |
| 18a $A_1$  | 1032                  | 1030.3             |
| 15 $B_2$   | 1156                  | 1154.3             |
| 9a $A_1$   | 1183                  | 1181.1             |
| 13 $A_1$   | 1196                  | 1198.5             |
| 8b $B_2$   | 1583                  | 1581.9             |
| 8a $A_1$   | 1600                  | 1601.1             |
| 7a $A_1$   | 3056                  | 3051.1             |
heating but also enables rapid film formation with orders of magnitude more film volume per unit time due to another affect that is not evaporation related. These arguments points to the dominant role of thermophoresis over others including evaporation, capillary effects and others.

Relative to established methods of nanoparticle characterization, thin-film thermophoresis offers a great deal of flexibility. X-ray diffraction, for example, is limited to particles under 50 nm in size.[4] This poses an issue for gold nanoparticles: uptake rate into mammalian cells is highly dependent on particle size, including those up to 100 nm, making that technique incompatible.[10] Alternatively, transmission electron microscopy provides more precise determination of particle size, arrangement, and agglomeration. It generates a direct image of nanoparticles, but this does not reveal the chemical identity of the sample, and imaging parameters must be carefully determined in order to prevent sample damage and to be certain the image is not skewed with respect to its orientation, providing misleading information.[4,31] Comparatively, thin-film thermophoresis is simple to perform and provides direct confirmation of the particle identity.

This work sets the stage for exciting new directions. At the most fundamental level, it offers the ability to achieve the same order of magnitude enhancement as conventional SERS, with more repeatability and less complexity. Potential extensions of this work include a novel hybrid method to form films compatible with SERS, providing additional sensitivity beyond that demonstrated here.

6. Experimental Section

Spectrum Collection: In both the benchmark and proposed thermophoresis technique, a HC-PCF (HC-800, NKT Photonics) as the HC-PCF is used. A beaker of aqueous sample is set on the microscope stage beneath the HC-PCF, which has been uniquely prepared in such a way that impedes the flow of liquid from entering the cladding holes and only permits fluid to infiltrate the core. This fashion of preparation ensures that best accuracy is obtained when determining the LOD. This solution is transported via capillary action to the top cross section of the fiber tip, where it is illuminated by the laser, which is used for both Raman measurements and, in the instances of film formation, it is also utilized for thermophoresis. All Raman measurements are performed on an Horiba HR800 Raman Spectrometer using a 632.8 nm laser and a grating of 1800 lines/mm. Samples depicted in Figure 2 were captured using a 100x objective with 1 s exposure and averaging of 3 spectra. A short spectrum collection time and optical density filter (1.1 mW incident on sample) are necessary for these samples in order to inhibit thin-film formation via thermophoresis, capturing a spectrum which is truly representative of the sample in its native state. Spectra collected during thermophoresis were excited with full laser power (11.2 mW incident on sample), 2–3 s exposure time and averaging up to 75 spectra, in order to deposit as much energy as possible to the sample without saturating the detector.

Nanoparticle Raman Mode Assignments—Alumina: Table 1 details relevant spectroscopic modes of alumina found in literature.[15,16] The modes at 1367.4 cm\(^{-1}\) and 1397.4 cm\(^{-1}\) are not Raman scattering signals, but instead correspond to the luminescence of the crystalline ruby structure at 6927 Å and 6942 Å when excited by the 632.8 nm source.[11]

Polystyrene: Raman mode assignment in polystyrene has historically suffered some contradiction from one publication to the next, so the expected and observed positions of PS modes are presented here.[19] The most prominent Raman modes observed in the first loading vector obtained from running Principal Component Analysis on the spectra from PS at 240 mM (pre-film) and 2.40 µM (post-film) are assigned. This vector represents the most dominant common spectral features between the two samples, which are expected to be consistent with PS in literature. Raman modes and their assignments are listed in Table 2, where the first column denotes the band assignment (labelled using Wilson notation) and symmetry, consistent with polystyrene band positions of ordinary Raman by Anema et al.[19]

Determination of the Limit of Detection: In order to determine the LOD, Raman spectra with the same conditions including, power, time, objective lens among others has been collected for samples with progressively reduced concentrations. The spectra were then analyzed, where peak search using the algorithms discussed in the paper were utilized to quantify the relevant Raman modes for every sample under test. The limit of detection is determined for a given material when no modes could be identified in the spectrum below a certain concentration. It is important that a given is identified when it is able to find more than one mode of its vibrational spectrum, and not just one mode. While this technique is not absolute, as it is bound by the parameters used such as power and time, it is indicative of the mechanism discussed in this work. As the detection time or the utilized power significantly can be increased, the times used in this work, and first report, highlight the utility of Thermophoresis-based approach to form films and increase the tenable LOD of spontaneous Raman in liquids for measurements with practical time durations. More absolute limits can and will be examined in dedicated work.

Supporting Information

Supporting Information is available from the Wiley Online Library or from the author.

Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

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

Keywords

nanoparticle sensing, photonic crystal fibers, Raman spectroscopy

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