Analysis of THz Scattering of Compacted Granular Materials using THz-TDS.

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***Abstract*— Scattering of terahertz radiation in compacts is of great interest due to its potential to non-destructively assess various structural elements such as particle size and defects in compacts. In this study, we isolate the scattering contributions to the loss coefficient of borosilicate glass microspheres suspended in a polytetrafluoroethylene (PTFE) compact measured by terahertz time-domain spectroscopy. The particle size and concentration of microspheres in the compacts were varied to resolve their effect on terahertz scattering.**

I. INTRODUCTION

Terahertz time-domain spectroscopy (THz-TDS) is a non-destructive and non-ionising technique currently being employed in various industries for process monitoring [1]. Current applications in the pharmaceutical industry are tablet coating analysis, identification of polymorphic forms and determination of porosity in solid oral dosage forms [1], [2], [3]. One promising and underdeveloped application of THz-TDS is the estimation of the size of structural components, e.g., particle size changes in pharmaceutical tablets due to agglomeration or fragmentation that impacts product performance.

Transmission THz-TDS enables the measurement of both the effective refractive index (RI) and the loss coefficient of a sample and more specifically a compact composed of various materials [1]. The loss coefficient as a function of frequency (α(f)) is the sum of the absorption contribution (α_{abs}) of the two materials (PTFE and glass) and the scattering contribution (α_{scatt}) determined by particle size and shape

$$\alpha(f) = \alpha_{Abs} + \alpha_{Scatt} \tag{1}$$

It has been shown that the Christiansen model [4] can be applied to estimate the scattering contributions in compacts given material knowledge such as the particle size, concentration, and refractive index of the various components. Along with these material properties, this model also requires knowledge of the area of the wavefront covered by scattering objects which is commonly fitted from experimental data [4].

In this study we extract the scattering contributions of borosilicate microspheres suspended in a PTFE matrix. Both the concentration and particle size of the microspheres was varied in the compacts to determine their effect on scattering. The creation of this well controlled data set facilitates the modelling of scattering contributions and lays the foundation for the development of particle size models for more complex formulations, i.e., prediction of particle size changes in complex pharmaceutical formulations from THz-TDS measurements.

II. METHODS

A. Sample Preparation

Compacts were fabricated from different concentrations and particle sizes of borosilicate microspheres (Cospheric, Borosilicate Solid Glass Microspheres) within a PTFE matrix (PTFE powder, particle size 6 - 9 µm, free flowing). Four microsphere sizes were used, with particle size (diameter) distributions of 38 - 45 µm, 90 - 106 µm, 125 - 150 µm and 150-180 µm. Six concentration levels were employed: 2.5, 5, 10, 15, 20 and 30% w/w. The compacts were fabricated using a compaction simulator (HB50, Huxley-Bertram Engineering) and a compaction pressure of 392 MPa to create plane-parallel cylindrical samples with a diameter of 9 mm and thickness of 1 mm [5]. Ten compacts were made from each of the 24 blends.

B. THz-TDS Analysis and Data Processing

THz-TDS measurements were carried out on a commercial system (TeraPulse Lx, Teraview), with a frequency resolution of 20 GHz. Measurements were performed under a nitrogen atmosphere. The frequency-domain field amplitude ($E(f)$) and phase ($\phi(f)$) were obtained from the time-domain data by applying a fast Fourier transform. Then the frequency-dependent refractive index ($n(f)$) and loss coefficient ($\alpha(f)$) were calculated using the following equations [6]:

$$n(f) = \frac{\left(\phi_s(\mathrm{f}) - \phi_r(\mathrm{f})\right)\mathrm{c}}{2\pi f L} \tag{2}$$

$$\alpha(f) = -\frac{2}{L} ln\left[\frac{(n+1)^2}{4n}\frac{E_s(f)}{E_r(f)}\right] \tag{3}$$

where c is the speed of light, L is the sample thickness, and the subscripts "s" and "r" refer to the sample and reference data, respectively.

C. Extraction of Scattering Contributions

THz-TDS measurements were conducted on borosilicate microspheres (38 – 45 µm) in a cuvette, both saturated and unsaturated with paraffin oil [7]. The analysis with paraffin oil allows for the determination of voids between microspheres in the cuvette. Accounting for these voids facilitates the

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approximation of the absorption contribution from the microspheres (Abs$_{\mathrm{glass}}$) [2]. Combined with the absorption from PTFE (Abs$_{\mathrm{PTFE}}$), the absorption contributions for the compacts at a given concentration level can be obtained by

$$\alpha_{Abs} = Abs_{glass} + Abs_{PTFE} \tag{4}$$

Subtracting the absorption contributions from the extracted loss coefficient yields the scattering contributions of the microspheres:

$$\alpha_{Scatt} = \alpha(f) - \alpha_{Abs} \tag{5}$$

III. RESULTS

The scattering contributions for the compacts extracted at 1 THz (Figure 1) clearly show an increase with particle size as expected. It is also observed that the scattering contributions maximise at difference concentration levels depending on particle size.

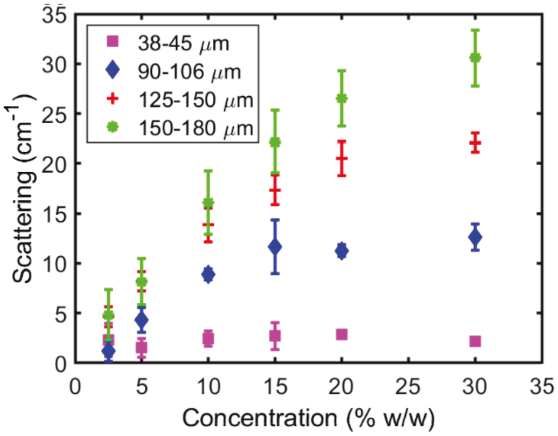

Figure 1 *Extracted scattering contributions for four particle sizes (38 - 45, 90 - 106, 125 - 150 and 150 - 180 μm) at varying concentration levels. Values plotted are the mean and the error bars denote ± one standard deviation (n=10).*

The scattering contributions for compacts with a particle size of 90 - 106 μm (Figure 2b), 125 - 150 μm (Figure 2c) and 150 - 180 μm (Figure 2d) vary with the fourth power of frequency in line with the theory of Rayleigh scattering. This trend is, however, not seen for the compacts containing glass microspheres with the smallest particle size (38 – 45 μm) where maximum scattering is observed at concentrations of 15% w/w (Figure 2a). The scattering contribution for compacts fabricated with 90 - 106 μm glass microspheres reaches a maximum at 20% w/w while for microspheres with a diameter of 125 - 150 and 150 - 180 μm maximum scattering is observed no earlier than 30% w/w.

IV. CONCLUSION

In conclusion, we have extracted the scattering contributions of borosilicate microspheres embedded in a PTFE matrix. The accurate extraction and analysis of scattering contributions could aid the determination of particle size. The ability to determine particle size using a nondestructive technique would have a wide-ranging impact from pharmaceuticals to paint and ceramic industries. Further work consists of modelling the scattering contributions utilising this data set and existing theories such as the Christiansen effect.

V. REFERENCES

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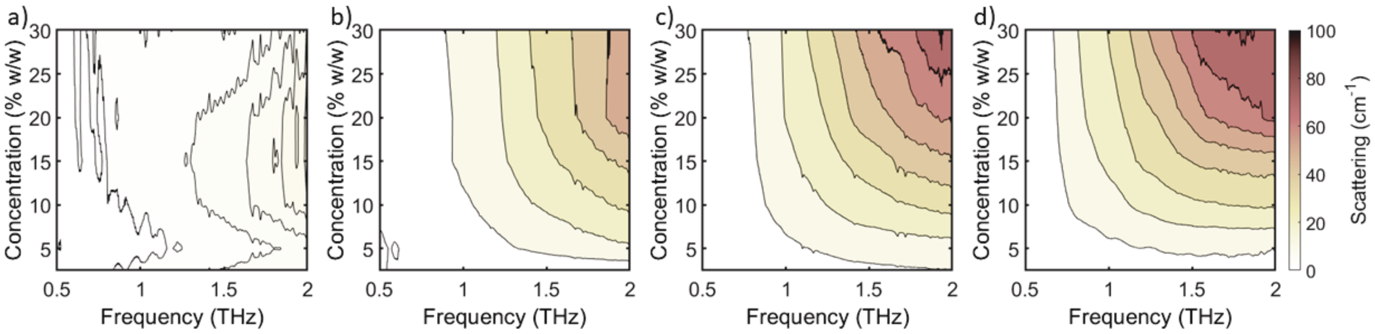

Figure 2 *Extracted scattering contribution for four particle sizes (a) 38-45, (b) 90-106, (c) 125-150 and d)150-80 μm as a function of both concentration and frequency. Values plotted are the mean (n=10).*