Observation of spurious spectral features in mixed-powder compressed pellets measured by terahertz time-domain spectroscopy.

Keir N Murphy, Daniel Markl, Alison Nordon and Mira Naftaly

Abstract— **Spurious loss features were observed in mixed-powder compressed pellets measured in transmission using terahertz time-domain spectroscopy. Loss features were identified in two types of pellets: PTFE-glass microspheres and PTFE-lactose. The features were found to be dependent on grain size and concentration. An explanation is proposed, based on varying optical thickness of the sample material.**

***Index Terms*— Spectroscopy, Terahertz Radiation, Terahertz Materials.**

I. INTRODUCTION

One of the most significant applications of terahertz time-domain spectroscopy (THz TDS) is in studying and identifying biochemical and pharmaceutical materials [1]–[3]. Such materials are typically produced in the form of powders and must be compressed into pellets to enable quantitative spectroscopic measurements. They often have multiple strong polymorphic form-specific absorption features, such that pellets of practical thickness exceed the dynamic range of THz TDS instruments at frequencies above 2 THz [4]. Consequently, in order to study the vibrational spectra of these materials over extended frequency bands, they are often mixed with a THz-transparent dilutant powder such as polyethylene or polytetrafluoroethylene (PTFE) [1]. Studying spectra of organic materials in mixed-powder compressed pellets using THz TDS is a widely employed and well-established technique. In using this method, it is assumed that the measured THz spectra of target materials are not altered by the sample preparation process, which includes factors such as material concentrations, mixing, and compaction.

In this Letter we bring to light a possible issue that may arise when employing this approach. We report observations of spurious loss features in two types of mixed-powder pellets: PTFE-glass microspheres and PTFE-lactose. The intensity and frequency of these features are seen to be dependent on grain size and concentration.

II. Results

THz TDS transmission measurements were carried out using a Teraflash Pro (Toptica) spectrometer, with the beam path purged with dry air. The THz beam path used 4 parabolic mirrors arranged in a Z-configuration. All mirrors were F/2, with 25 mm mirror diameter and 50 mm effective focal length. Sample diameter was 9 mm; samples were placed in the focal plane between mirrors 2 & 3. Fig. 1 shows the source amplitude spectrum and its noise floor.

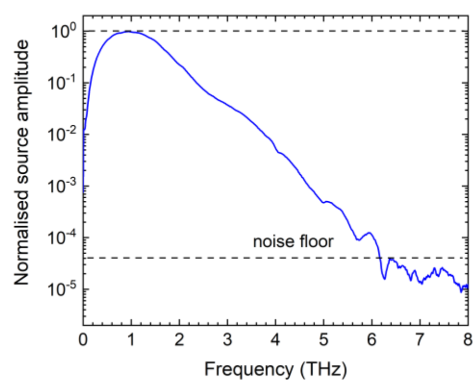

Fig 1. Normalised source amplitude and its noise floor.

The frequency dependent loss coefficient ($\alpha_{\text{loss}}(\nu)$) and refractive index ($n(\nu)$) were calculated using the standard formulas:

$$\alpha_{\text{loss}}(\nu) = -\frac{2}{L}\ln\left[\frac{(n+1)^2}{4n}\frac{E_s(\nu)}{E_r(\nu)}\right] \qquad (1)$$

The work at NPL was supported by the UK government's Department for Science, Innovation and Technology (DSIT).

Keir N Murphy, Strathclyde Institute of Pharmacy & Biomedical Sciences, Centre for Continuous Manufacturing and Advanced Crystallisation (CMAC), University of Strathclyde, Glasgow, UK. keir.murphy@strath.ac.uk
Mira Naftaly, National Physical Laboratory, London, UK. mira.naftaly@npl.co.uk
Alison Nordon, WestCHEM, Department of Pure and Applied Chemistry University of Strathclyde, Centre for Continuous Manufacturing and Advanced Crystallisation (CMAC), Glasgow, UK. alison.nordon@strath.ac.uk.
Daniel Markl, Strathclyde Institute of Pharmacy & Biomedical Sciences, Centre for Continuous Manufacturing and Advanced Crystallisation (CMAC), University of Strathclyde, Glasgow, UK. daniel.markl@strath.ac.uk.

Color versions of one or more of the figures in this article are available online at http://ieeexplore.ieee.org

This is a peer reviewed, accepted author manuscript of the following research article: Murphy, K. N., Markl, D., Nordon, A., & Naftaly, M. (2023). Observation of spurious spectral features in mixed-powder compressed pellets measured by terahertz time-domain spectroscopy. I*EEE Transactions on Terahertz Science & Technology*. https://doi.org/10.1109/tthz.2023.3290118

$$n_{(\upsilon)} = \frac{(\varphi_{s(\upsilon)} - \varphi_{r(\upsilon)})c}{2\pi f L} \quad (2)$$

where $E_r(\nu)$ and $E_s(\nu)$ are the frequency dependent field amplitude of the reference and sample signals, respectively. Details of sample preparation are reported in [5]. Sample thickness (L) was measured using a micrometer (± 0.005 mm); all samples were between 0.5-1.0 mm thick.

In a previous study, we have reported measurements of THz scattering in compacts consisting of PTFE powder and borosilicate glass microspheres [5] with a range of microsphere sizes and concentrations. Loss spectra and refractive indices of these compacts were measured at frequencies in the range 0.2 - 1.2 THz and the scattering effects were analyzed as a function of grain size and concentration [6-7].

Subsequently, we extended the frequency range of the study to 4.0 THz. Unexpected loss features were seen in the spectra of the samples; some examples are shown in Figs 2a&b. In the frequency range examined, the absorption spectra of both PTFE and borosilicate glass are monotonically rising functions [5]. Therefore, the loss spectra are expected to appear as a featureless rising edge. The observed features must therefore be considered spurious, arising from beam propagation through the sample material, rather than due to absorption. These features were dependent on the grain size and concentration, as seen in Fig 2a&b.

Fig 2c shows the refractive indices of these samples. As expected, the refractive indices of two samples containing 20% glass are similar below 2 THz and are higher than that of the sample containing 10% glass. At the frequencies where sharp loss features occur, there is a corresponding pronounced rise in the refractive index. Note that phase unwrapping may be ambiguous where there is a steep change in the refractive index, as occurs at 2.3 THz for the sample containing 20% v/v beads of 90-106 μm (red line). Such cases may be clarified by examining multiple samples with similar properties. This is particularly relevant for mixed-powder samples, such as these, because they often exhibit strong narrow loss peaks accompanied by steep dispersion of the refractive index.

A possible explanation of these spurious spectral features may be arrived at by considering the effects of variable optical thickness of the material experienced by different parts of the traversing THz beam due to the inhomogeneous nature of the mixed-powder compacts. Variations in the optical thickness of the sample give rise to spurious loss features in the transmission spectrum because a time-domain trace containing multiple pulse peaks can be regarded as a convolution of a single pulse with a number of delta functions. In the frequency domain, this is translated to the product of the Fourier transform (FT) of a single pulse with the FT of a set of delta functions, as shown in Fig 3. The dependence of the observed spurious spectral features on the grain size and concentration may then be explained by the geometrical effects of these parameters on the beam path length variability through the sample material.

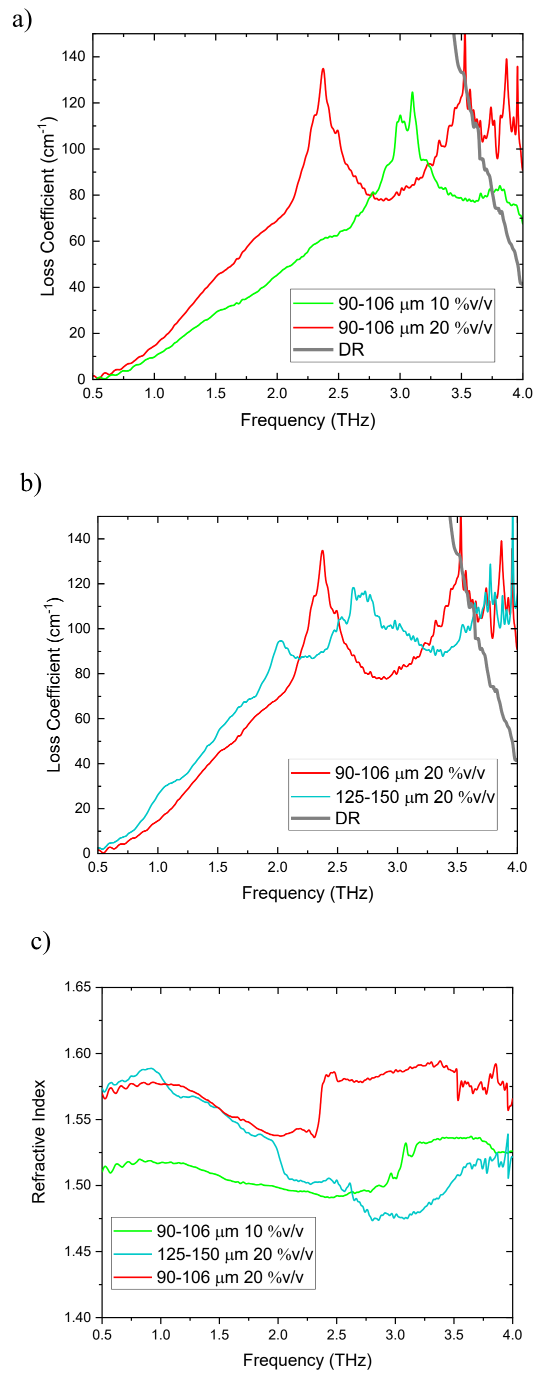

Fig 2. Loss coefficient measured by THz-TDS in compressed pellets of PTFE and glass microspheres. Spectra of samples with a) varying glass microspheres volume/volume (v/v) concentration (10 and 20 %v/v) and b) varying grain size ranges, i.e., 90-106 μm and 125-150 μm, are shown. The dynamic range limit (DR) was calculated according to Ref. [4].

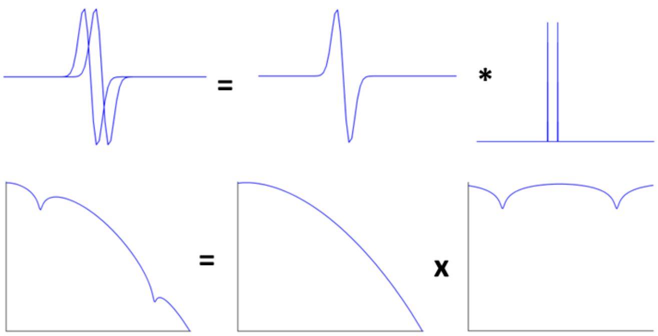

Fig. 3 Model data explaining the appearance of spurious loss features due to path length difference in the sample material. The convolution of the two functions is denoted with the symbol *.

To verify the presence of this effect in a material that is more relevant to spectroscopic studies, we examined pellets consisting of PTFE (Sigma Aldrich, free flowing, mean grain size 1 µm, 2.2 g cm^{-3}) and varying concentrations of α-lactose monohydrate (Sigma Aldrich, D_{50} = 50 µm [8]). Fig 4a presents the loss coefficients as measured, and Fig 4b shows them normalised to the peak at 1.4 THz for ease of comparison. In Fig 4b, the spectrum of the pure lactose pellet shows reduced scattering loss at frequencies above ~2 THz due to higher homogeneity of this material. Two spurious features are clearly observed in pellets containing 20% and 30% lactose; the profile of the feature at 3.3 THz differs between the two concentrations, whereas the feature at 2.9 THz remains constant. It may be supposed that the frequency of spurious features in lactose-PTFE pellets is determined by the grain size, as it appears to be in the glass-PTFE pellets in Fig. 2, and that therefore their overlap with the absorption bands is coincidental. Fig 4c shows the refractive indices of the pellets. As expected, the refractive index increases with lactose concentration and exhibits anomalous dispersion corresponding to the lactose absorption peaks. In addition, at frequencies corresponding to spurious loss features, the refractive index shows a pronounced dip.

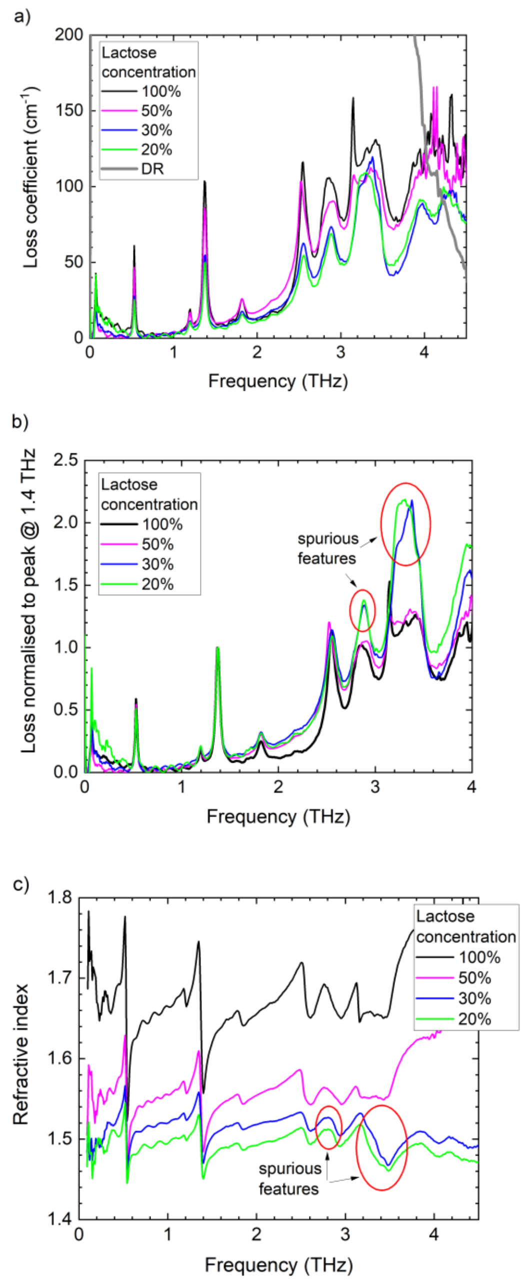

Fig. 4 a) Loss coefficient measured in mixed PTFE and lactose pellets with different concentrations of lactose; DR limit was calculated from [4] is also shown. b) Loss spectra of pellets shown in (a) normalized to the peak at 1.4 THz for ease of comparison. Spurious features are highlighted. c) refractive indices of pellets shown in (a).

V. Conclusion

THz TDS in transmission is widely used for spectroscopic measurements on powders of biochemical and pharmaceutical materials. A common method for preparing such materials for measurements is to dilute them with THz-transparent powder and to compress the mixture into pellets. In this Letter we report observations of spurious loss features in such pellets.

Loss features that do not arise from absorption in the constituent materials were observed in two types of mixed-powder pellets: PTFE-glass microspheres and PTFE-lactose. The features were seen to be dependent on grain size and concentration.

We propose an explanation of the effect as due to the variability of the optical path length through the inhomogeneous pellet material.

When employing THz TDS for transmission studies of mixed-powder pellets, it is advisable to examine a range of samples with different concentrations of constituent powders, and if possible, with different grain sizes.

Similar considerations may apply to FTIR measurements, which are also based on detecting the optical path length through the sample, and employ a FT to obtain spectral information.

Work is currently underway aimed at clarifying the dependence of loss peak frequency and intensity on the grain size, concentration, and material. It is expected that the frequency and profile of the spurious features may be used to estimate the size and concentration of scatterers in granular materials.

References

[1] J. A. Zeitler, "Terahertz Spectroscopy and Imaging," in *Terahertz Spectroscopy and Imaging*, K.-E. Peiponen, Ed., 1st ed.Berlin: Springer, 2016, pp. 171–222. doi: 10.1007/978-1-4939-4029-5_5.

[2] T. Mancini, R. Mosetti, A. Marcelli, M. Petrarca, S. Lupi, and A. D'Arco, "Terahertz Spectroscopic Analysis in Protein Dynamics: Current Status," *Radiation*, vol. 2, no. 1, pp. 100–123, Feb. 2022, doi: 10.3390/radiation2010008.

[3] D. F. Plusquellic, K. Siegrist, E. J. Heilweil, and O. Esenturk, "Applications of terahertz spectroscopy in biosystems," *ChemPhysChem*, vol. 8, no. 17. Wiley-VCH Verlag, pp. 2412–2431, Dec. 03, 2007. doi: 10.1002/cphc.200700332.

[4] P. U. Jepsen and B. M. Fischer, "Dynamic range in terahertz time-domain transmission and reflection spectroscopy," 2005.

[5] K. N. Murphy, M. Naftaly, A. Nordon, and D. Markl, "The Effect of Particle Size and Concentration on Low-Frequency Terahertz Scattering in Granular Compacts," 2023. doi: https://doi.org/10.48550/arXiv.2304.10974.

[6] K. N. Murphy, M. Naftaly, A. Nordon, and D. Markl, "Effect of Microsphere Concentration and Size in Compacts on Terahertz Scattering," *2021 51st Eur. Microw. Conf. EuMC 2021*, no. April, pp. 994–997, 2021, doi: 10.23919/EuMC50147.2022.9784372.

[7] K. N. Murphy, M. Naftaly, A. Nordon, and D. Markl, "Analysis of THz Scattering of Compacted Granular Materials using THz-TDS.," in *International Conference on Infrared, Millimeter, and Terahertz Waves, IRMMW-THz*, 2022, vol. 2022-August, doi: 10.1109/IRMMW-THz50927.2022.9895792.

[8] M. Naftaly, I. Tikhomirov, P. Hou, and D. Markl, "Measuring open porosity of porous materials using thz-tds and an index-matching medium," *Sensors (Switzerland)*, vol. 20, no. 11, 2020, doi: 10.3390/s20113120.

Keir N Murphy is a final year icase PhD student at the University of Strathclyde working closely with the National Physical Laboratory, UK.

Daniel Markl is a Reader at the University of Strathclyde, UK.

Alison Nordon is a Professor in the Department of Pure and Applied Chemistry at the University of Strathclyde.

Mira Naftaly is at the National Physical Laboratory, UK.