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Quantitative measurement of mixtures by terahertz time–domain spectroscopy

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Abstract. Terahertz time–domain spectroscopy (THz–TDS) was applied for quantitatively analysing a series of binary mixtures and a ternary mixture. Binary mixtures having different weight ratios of two components, *m*-aminophenol and *m*-nitroaniline, were investigated by THz–TDS in the range of 0·3 to 1·5 THz, and it was found that the absorption coefficients of the components in each mixture were linearly proportional to their concentrations in the mixture. The results from analysis were in agreement with actual values with a relative error of less than 7%. The quantitative method will help in the detection of illegal drugs, poisons and dangerous materials that are wrapped or mixed with other materials.

Keywords. THz–TDS; chemical mixture; quantitative analysis; *m*-aminophenol; *m*-nitroaniline.

1. Introduction

Quantitative analysis plays an important role in chemistry, pharmacy, medicine and many other fields. A variety of quantitative methods have been widely used; these include thermoanalytical methods (e.g. differential scanning calorimetry), X-ray powder diffractometry, high-performance liquid chromatography, infrared spectroscopy and Raman spectroscopy.[1] However, each method has its limitations and a single analytical procedure is not applicable to all systems. Therefore, a simple, synchronous and non-destructive method for quantitative analysis is needed. Our previous work demonstrated that spectroscopy in the terahertz range is suitable for the quantitative analysis of weight ratios in binary mixtures.[2]

As a new technology, terahertz spectroscopy has various applications in many fields,[3–7] e.g. biology, medical and pharmaceutical sciences, information and communication technology, homeland security, earth and space science, quality control of food and agricultural products and global environmental monitoring. In quantitative applications, terahertz technology has been widely used for studying different kinds of mixtures, such as amino acids,[8] ternary chemical mixtures,[9] pharmaceuticals,[10] racemic compounds[11] and explosive samples.[12] In addition, Watanabe *et al*[13,14] quantitatively analysed the components in mixtures through terahertz spectroscopic imaging and component pattern analysis using known spectral data for pure chemicals. However, they did not consider the transmission coefficient in their work. Fischer *et al* recognized four different chemicals by defining a recognition coefficient R proportional to the height of a spectral feature with respect to the spectral baseline.[15] However, if compounds have no distinct characteristic absorption peak in the terahertz range, it would be difficult to distinguish them in chemical mixtures directly from their absorption peaks. Therefore, it is necessary to identify components and their percentage compositions in a chemical mixture by taking the complete terahertz absorption spectra as fingerprints of pure compounds.

In this paper, several groups of binary mixtures and a ternary mixture were analytically investigated by taking integrated absorption spectra as fingerprints. At the same time, the transmission coefficient at the sample surface was taken into account to improve the analytical precision. There was no intermolecular interaction or solid state reaction between

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the two or three components in a mixture. We expect that terahertz spectroscopy will be helpful in quality control, pharmacy and safety inspection.

2. Materials and methods

2.1 *Experimental set-up*

The experimental apparatus (see figure 1) for terahertz time-domain spectroscopy (THz–TDS) has been discussed in a previous report.[16] A mode-locked Ti : sapphire laser was used as the light source to generate and detect terahertz waves. The laser can provide 100-fs pulses with a central wavelength of 800 nm, a repetition rate of 80 MHz and an average power of 600 mW. The output pulse was split into two beams: a pump beam focused on the surface of a biased GaAs photoconductive emitter for terahertz generation and a probe beam for electro-optic detection using a 2-mm-thick ZnTe crystal. The whole apparatus box was purged with nitrogen gas to reduce the effect of water–vapour absorption.

2.2 *Sample preparation*

O-Phenylenediamine (o-PD) was purchased from Alfa Aesar, and *p*-phenylenediamine (p-PD) and *m*-aminophenol (m-AP) were purchased from Tokyo Chemical Industry. Other samples were obtained from Acros Organics. All samples were powders and dried at 373 K for at least one hour to remove water. Two or three pure samples were mixed in different weight ratios, gently ground using a pestle and mortar and then pressed into disks with a hydraulic press at a compression of approximately 3·5 tons. The thickness of a single tablet was approximately 1·0–1·5 mm. The tablet surfaces were kept smooth and parallel to minimize the effects of multiple reflections.

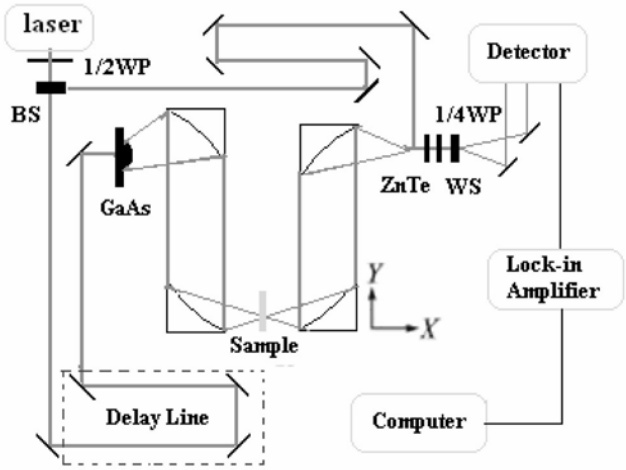

Figure 1. Experimental set-up for transmission THz–TDS.

2.3 *Analysis principle*

We suppose the mixture contains n pure compounds $S_1, S_2, \ldots, S_n$ with weights $\boldsymbol{m_1}, \boldsymbol{m_2}, \ldots, \boldsymbol{m_n}$ and absorption coefficients $a_1, a_2, \ldots, a_n$ respectively. According to the Lambert–Beer law,[17] the absorption coefficient of the mixture can be obtained from the absorption spectra of the pure compounds.

$$A = \varepsilon bc \tag{1}$$

$$\alpha(\omega) = \sum_{i=1}^{n} b_i \alpha_i(\omega) \tag{2}$$

$$b_1 : b_2 : \cdots : b_n = m_1 : m_2 : \cdots : m_n. \tag{3}$$

Relative contents in the mixtures are obtained using the complete absorption spectra of the pure compounds and their mixture and linear regression. A detailed description of the analysis principle is given in the literature.[18]

3. Results and discussion

3.1 *Mixture of m-AP and m-NA*

M-AP possesses the characteristics of both phenol and aniline. It is an important intermediate in many reactions and is widely used in the photographic, pharmaceutical and chemical dye industries. M-NA has many applications owing to its unique electro-optic and nonlinear optic effects, and it is a candidate for wideband terahertz generation.[19] Binary mixtures containing m-AP and m-NA from 10% to 90% w/w in 20% intervals were prepared. Terahertz absorption spectra of m-AP (weight ratio $\rho = 0\%$), m-NA ($\rho = 100\%$) and their mixtures from 0·3 to 1·5 THz are presented in figure 2. The values on the right axis represent the weight ratio ρ of m-NA in the sample before mixing. Pure m-AP and m-NA have a characteristic absorption peak at 1·17 THz and 0·83 THz respectively in this frequency range

and the former peak is attributed to intermolecular interactions.[20] Single crystal m-NA belongs to the orthorhombic crystal class with a space group $Pbc2_1$ containing four molecules in the unit cell. Reported unit cell parameters are $a = 6{\cdot}470$ Å, $b = 19{\cdot}26$ Å and $c = 5{\cdot}081$ Å.[21] M-NA, which has an acentric crystal structure, has two NH…O interactions (both at a distance greater than 3·2 Å), with one of the interactions occurring within the unit cell. The melting point and spectroscopic data indicate that at least one of these interactions is a hydrogen bond.[22] Therefore the absorption peak at 0·83 THz for m-NA is possibly due to the collective motion of molecules associated with hydrogen bonding.

The mixtures of m-AP and m-NA show a combination of these features, and as the proportions of m-AP and m-NA increased and decreased respectively, the spectral features changed gradually and predictably. To confirm the reproducibility of the spectra, each sample was scanned three times. The peak positions did not vary with changes in the weight ratio. Two strong peaks at 0·83 THz and 1·17 THz were selected as marker bands, and the absorption coefficients are plotted against the weight ratio of m-NA in figure 3. The plots were analysed using linear models, and the absorption coefficients at 0·83 THz increased in proportion to ρ with a correlation coefficient $r = 0{\cdot}9964$. However, the absorption coefficients at 1·17 THz decreased almost in proportion to ρ when ρ was less than 50%. This was because the absorption coefficient of m-AP at 1·17 THz is larger than that of m-NA.

Absorption spectra of pure m-AP and m-NA were set as standard spectra. Relative contents in the mixture were obtained by analysing absorption spectra of the mixtures and using linear regression. Figure 4 shows the contents of m-AP and m-NA in five different mixtures from terahertz analysis and the actual contents. The content ratios derived from analysis for two of the mixtures (30·6 : 69·4 and 51·5 : 48·5) are close to the actual ratios (30 : 70 and 50 : 50). However, the content ratios derived for the other three mixtures (10·7 : 89·3, 71·7 : 28·3 and 90·7 : 9·3) are not consistent with the actual ratios

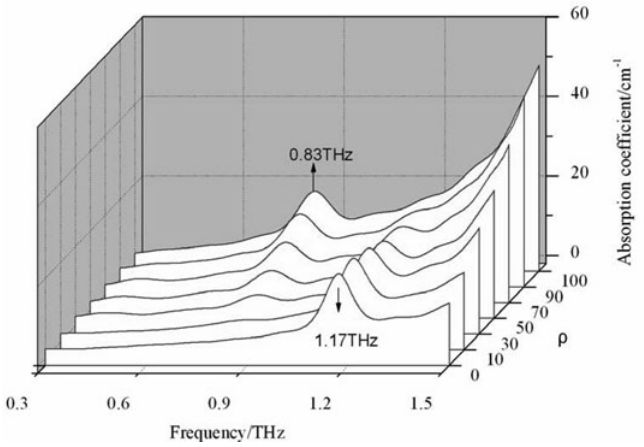

Figure 2. Terahertz absorption spectra of m-AP ($\rho = 0$), m-NA ($\rho = 100\%$) and their mixtures (20% intervals from 10 to 90%) in the frequency range of 0·3–1·5 THz. The values represent the weight ratio ρ of m-NA in the sample before mixing.

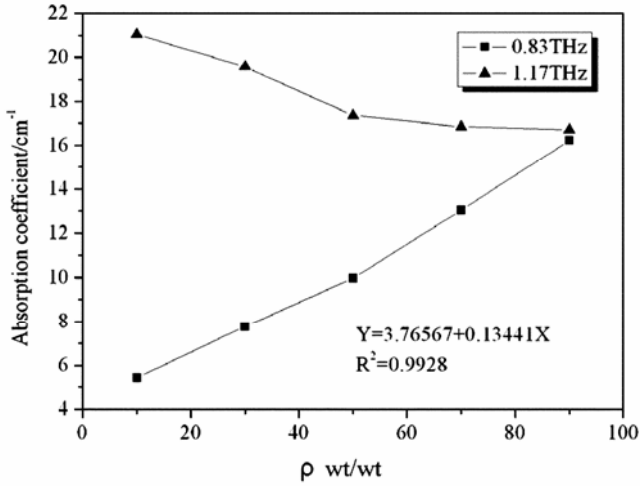

Figure 3. Dependence of the absorption coefficient of the bands at 0·83 THz (squares) and 1·17 THz (triangles) on the weight ratio of m-NA.

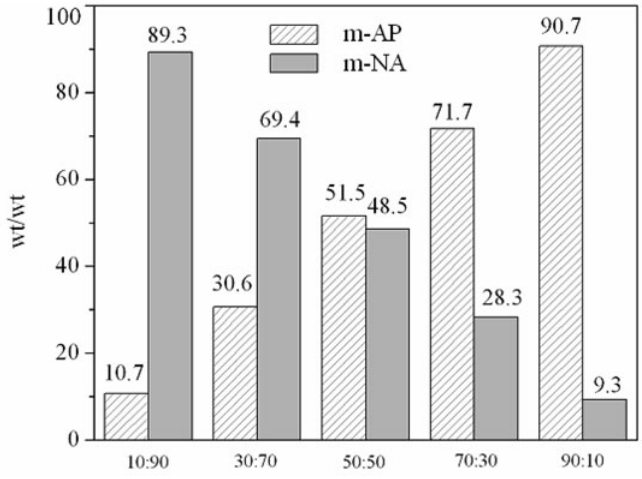

Figure 4. Comparison of contents determined by terahertz analysis for m-AP and m-NA with the actual contents.

(10 : 90, 70 : 30 and 90 : 10), considering an analytical error of less than 7%. The results demonstrate that it is possible to obtain relative contents in a mixture of m-AP and m-NA by quantitative analysis of terahertz absorption spectra.

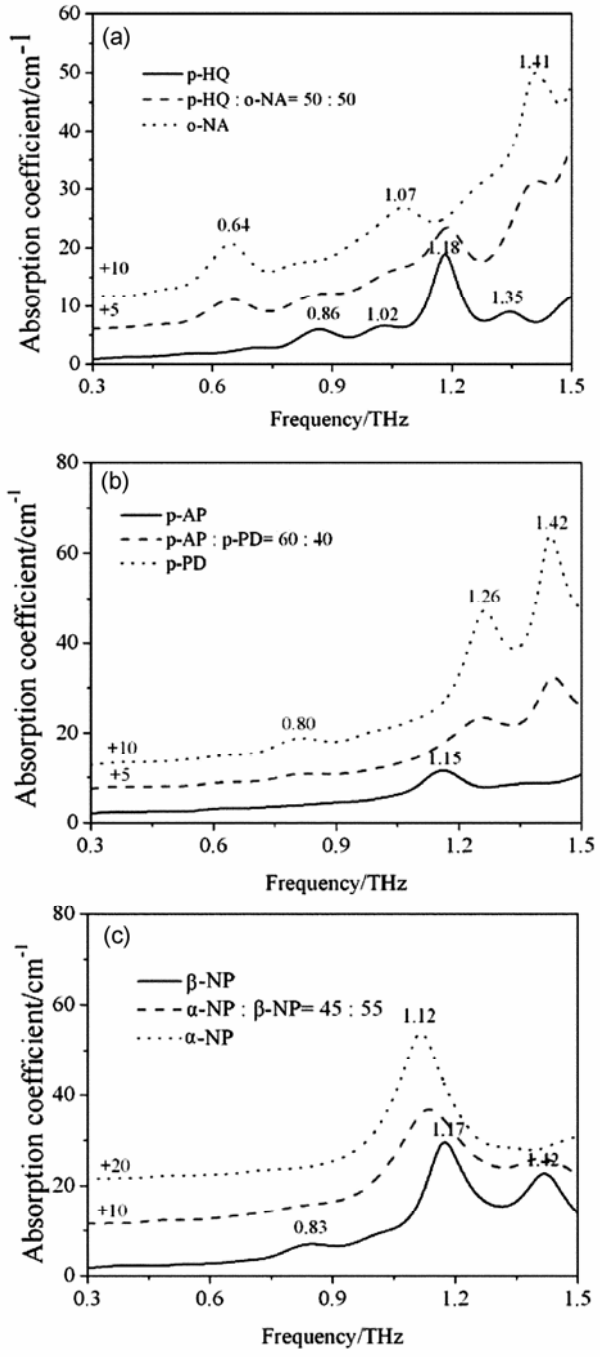

Figure 5. Terahertz absorption spectra of pure components and their mixtures: (**a**) p-HQ (straight line), o-NA (dotted line) and their mixture (dashed line), (**b**) p-AP (straight line), p-PD (dotted line) and their mixture (dashed line) and (**c**) β-NP (straight line), α-NP (dotted line) and their mixture (dashed line). Each spectrum has been shifted vertically for clarity.

The results suggest that THz–TDS is a very good technique for quantifying the mixture of m-AP and m-NA. Other binary mixtures and a ternary mixture were examined to determine the applicability of the technique to other systems.

3.2 *Other binary mixtures and a ternary mixture*

Figure 5 shows the absorption spectra between 0·3 and 1·5 THz for binary mixtures of (a) *p*-hydroquinone (p-HQ) and *o*-nitroaniline (o-NA), (b) *p*-aminophenol (p-AP) and p-PD and (c) α-naphthol (α-NP) and β-naphthol (β-NP). As seen in figure 5(a), p-HQ produced absorption peaks at 0·86 and 1·18 THz, with the 1·18 THz band having shoulders at 1·02 and 1·35 THz and being the dominant peak. o-NA had three peaks at about 0·64, 1·07 and 1·41 THz. As seen in figure 5(b), p-AP produced a wide band around 1·15 THz and p-PD had two absorption peaks centred at 1·26 and 1·42 THz.

α-NP and β-NP are isomeric compounds. α-NP is widely used as a pesticide, whereas β-NP is commonly used in the dyestuffs, pharmaceutical and cosmetics industries. Since commercially produced α-NP may contain β-NP as a by-product, the determination of α-NP and β-NP contents is of great importance in quality control and environmental chemistry. As can be seen from figure 5(c), α-NP produced a strong peak at 1·12 THz while β-NP had two absorption peaks at 1·17 and 1·42 THz. The results are in agreement with results in a previous re-

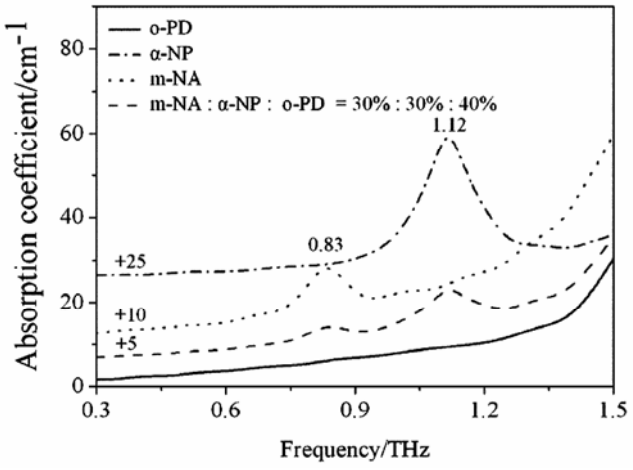

Figure 6. Terahertz absorption spectra of three pure components (m-NA (dotted line), α-NP (dashed-dotted line) and o-PD (straight line)) and their mixture (dashed line) from 0·3 to 1·5 THz.

Table 1. THz analytical contents and actual contents for binary mixtures (a) p-HQ, o-NA; (b) p-AP, p-PD; (c) α-NP, β-NP.

	p-HQ	o-NA	p-AP	p-PD	α-NP	β-NP
Analytical contents	52·5%	47·5%	58·8%	41·2%	43·5%	56·5%
Actual contents	50%	50%	60%	40%	45%	55%

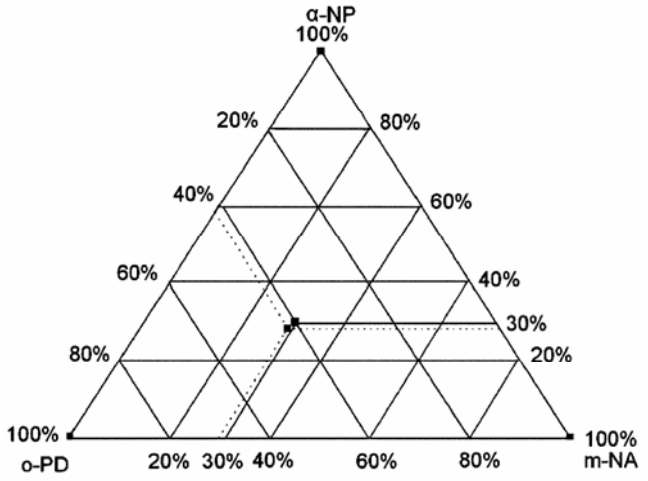

Figure 7. Ternary diagram of pure components, showing the actual location (30% m-NA, 30% α-NP and 40% o-PD) and the location determined by THz–TDS (28·9% m-NA, 28·7% α-NP and 42·4% o-PD).

port[23] and they are characteristic of the collective motion of molecules linked by hydrogen bonds. The contents of the binary mixtures determined by terahertz analysis and the actual contents are summarised in table 1. The weight ratios of p-HQ and o-NA and those of p-AP and p-PD from analysis were 52·5 : 47·5 and 58·8 : 41·2, which do not agree well with the actual ratios (50 : 50 and 60 : 40), considering an analytical error less than 5%. The content ratios determined from analysis for α-NP and β-NP (43·5 : 56·5) were consistent with the actual ratios (45 : 55). Therefore, the examples show that THz–TDS is an effective tool for the determination of relative contents in these binary mixtures.

A ternary mixture comprising 30% m-NA, 30% α-NP and 40% o-PD was prepared. Absorption spectra from 0·3 to 1·5 THz of the three pure components and their mixture are shown in figure 6. M-NA had a major absorption peak at 0·83 THz and α-NP produced a remarkable peak at 1·12 THz. In contrast to m-NA and α-NP, which produced visually distinct features in the absorption spectra, o-PD produced a featureless curved baseline. This is not unexpected because not all substances have distinct absorption features in this frequency range. Using the quantitative method described above, the relative contents of the three constituents were obtained and they are presented in figure 7. As expected, the contents determined by THz–TDS (28·9% m-NA, 28·7% α-NP and 42·4% o-PD) corresponded with the actual contents within the limit of error. This result indicates that THz-TDS can be used to quantitatively analyse the weight ratios of components in this ternary mixture, even though o-PD has featureless absorption over the entire frequency range.

4. Conclusions

Binary mixtures of m-AP and m-NA having different weight ratios were investigated by THz–TDS in the range of 0·3 to 1·5 THz. The results show the absorption coefficient of a component is proportional to its concentration in the mixture in this frequency range. Using THz–TDS and taking into account the transmission coefficient at the sample surface, the relative contents determined by analysis were close to the actual contents within a relative error of 7%. The quantitative analysis method was also found applicable to other binary mixtures and a ternary mixture even though one chemical component had featureless absorption. The study suggests that terahertz spectroscopy is an excellent analytical choice for application in quality control, pharmacy and safety inspection; thus, the investigated technique can be used for the detection of illegal drugs, poisons and dangerous materials that are wrapped or mixed with other components.

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