I-design terahertz microfluidic chip for attomole-level sensing

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Abstract

We developed a nonlinear optical crystal-based compact terahertz (THz)-microfluidic chip with several I-design meta-atoms for attomole (amol)-level sensing of trace amounts of solution samples. The I-design meta-atom consists of a metallic strip with a micrometer-sized gap sandwiched by other metallic strips. It is periodically arrayed in a row of $1 \times 5$ units. A point THz source locally generated by optical rectification at the irradiation spot of a femtosecond-pulse laser beam induces a tightly confined electric-field mode at the gap regions and modifies the resonance frequency when a microchannel fabricated along the space between the metallic strips is filled with solutions. Using this chip, we could detect minute changes in the concentration of trace amounts of ethanol- and glucose-water solutions and mineral water by measuring the shift in the resonance frequencies. We succeeded in detecting 472 amols of solutes in solutions less than 100 picoliters using an effective sensing area of $0.10 \lambda_{\text{THz}} \times 0.57 \lambda_{\text{THz}}$, which indicates an improvement of approximately one order of magnitude compared to the performance of existing chips. This technique compactifies THz-microfluidic chips with high sensitivity and would accelerate the development of microfluidics integrated with THz technology, such as lab-on-a-chip devices and THz micro total analysis systems.

1. Introduction

Microfluidics is a prospective technology for biochemical analyses and medical diagnoses. Microfluidic devices offer novel approaches for the development of highly sensitive biochip systems that integrate chemical processes, such as sample mixing, reaction, separation, and analysis, into one compact system. They can perform measurements with a sample volume of the picoliter (pl) level [1–3]. The technology has been applied to various biometrics, such as the enzyme-linked immunosorbent assay method, microcapillary electrophoresis, and surface plasmon sensors, and breakthroughs have been achieved in nucleic acid, cellular, and exosome studies [4–8].

Biosensing with terahertz (THz) waves (0.1–10 THz) has also received remarkable attention owing to its potential in the noninvasive and label-free detection of the functional expression of biomolecules [9–13]. THz time-domain spectroscopy (THz-TDS) plays a major role in clarifying unique biomolecular collective motions, such as intermolecular vibration, rotation, and hydrogen bonding [14–21]. Integrating THz and microfluidic technologies can establish new sensing fields, and the development of practical THz sensor chips is a critical challenge to future biosensing devices. However, the strong absorption of THz waves into polar solvents [22] and their low spatial resolution (1 THz $\approx 300 \mu m$) are major obstacles to developing highly sensitive and compact THz sensor chips.

The use of metamaterials offers highly sensitive biosensing with THz waves [23–25], including the detection of viruses [26, 27], bacteria [28], microorganisms [29], DNA [30–32], protein [33], and cells [34], and even detectable sensitivities up to several 10 ng ml$^{-1}$ have been achieved by combining with two-dimensional (2D) materials [35]. However, these studies used dried samples and overlooked the detailed...
properties of the samples because of far-field THz-wave irradiation, which requires a sensing area larger than the diffraction limit of THz waves. To overcome the resolution, near-field probes or high-power optical sources have been incorporated into THz biosensing [36–38]. However, there are still difficulties in real applications, including precise alignment, compactification, and ease of usage. For probe-less techniques, sample measurements on the sub-wavelength scale have been achieved using a laser THz emission microscope (LTEM) [39, 40]. In LTEM, femtosecond (fs) pulse laser beams are focused onto samples, and the generated THz waves at the irradiation spots are measured. Therefore, the resolution is limited by the wavelength of the optical laser source. With similar features as LTEM, we have developed a near-field THz emission system named scanning-point THz source (SPoTS) microscope [41, 42]. Here, a nonlinear optical crystal (NLOC) is employed as a 2D-THz emitter, and a point THz source is created in the process of optical rectification at the irradiation spots of fs pulse laser beams [43]. By setting samples in the vicinity of the THz source, THz-TDS and THz imaging have been realized on samples of sub-THz wavelength scale [44–48].

Based on this, we proposed an NLOC-based THz-microfluidic chip with a few arrays of meta-atoms, a unit cell of metamaterials, and applied it to the measurements of femtomole (fmol) levels of solute in sub-nanoliter (nl) amounts of solution samples [49, 50]. The microfluidic chip induces resonance phenomena by near-field THz excitation of a single meta-atom, and the arrangement of the surrounding meta-atoms greatly affects the resonance response [51]. A solution sample flowing into a microchannel fabricated near the meta-atom modifies the resonance frequency in the transmission spectra. Using this chip, we succeeded in detecting 1.4 fmol of solutes in a 128 pl solution using an effective sensing area of 0.75 \( \lambda_{THz} \times 0.75 \lambda_{THz} \), where \( \lambda_{THz} \) is a center wavelength of 0.4 THz in the broadband spectra of the generated THz waves [50]. Gupta et al reported that 'I'-design-based planar meta-atom arrays containing small cavities show tight electric-field confinement by irradiating them with far-field THz wave. The ‘I’-design was named because it resembled the letter ‘I’ when viewed from above. They also show improved sensitivity compared to the compatible meta-surface with split-ring resonators (SRRs) in spite of the lower Q value [52]. Since such electric-field confinement occurs prominently at small cavity gap regions following the Purcell effect [53], this new meta-atom design can more effectively interact with solution samples in the THz-microfluidic chip and contribute to a more compact chip design, maintaining its higher sensitivity.

In this study, to further compactify the chip design and enhance the sensitivity, we developed a THz-microfluidic chip with I-design meta-atoms and evaluated the sensitivity by comparing it with existing chips using a picoliter-order volume of solutions. We examined the resonance characteristics under near-field THz excitation. As a result, we could obtain a sufficient resonance response with only five units of meta-atoms, indicating a 20% improvement in the number of meta-atoms and an order of magnitude in the effective sensing area compared to SRR-based chips [50]. Despite such a small effective sensing area, 472 attomole (amol) of solutes in an 85 pl solution could be sensitively detected. This indicates an improvement of approximately one order of magnitude compared to the performance of existing chips [49, 50].

2. THz-microfluidic chip with I-design meta-atoms

Figure 1(a) shows a schematic of a THz-microfluidic chip. The chip consists of a single microchannel and a single array of meta-atoms fabricated on a 500 \( \mu \text{m} \) thick (110)-oriented gallium arsenide (GaAs) wafer (undoped and semi-insulating GaAs with resistivity of 0.8–4.8 \( \times 10^4 \) \( \Omega \text{ cm} \), MTI Corporation). The meta-atom is shown in figure 1(b). A photoresist (S1818G, Rohm and Haas Electronic Materials KK) was spin-coated on the surface of a GaAs. A strip design with a 2 \( \mu \text{m} \) linewidth, containing a 3 \( \mu \text{m} \times 2 \mu \text{m} \) split gap at the center was fabricated at the center, and 16.5 \( \mu \text{m} \times 85 \mu \text{m} \) strip designs were fabricated at either side of the central strip design with 25 \( \mu \text{m} \) spaces by a conventional photolithographic process (MJBS SUSS Microtech mask aligner). These designs formed a single meta-atom and were periodically arrayed in a row of 1 \( \times 5 \) units with a period of 85 \( \mu \text{m} \). Then, after sputtering a 1 nm thick titanium adhesion layer, a 180 nm thick gold layer was deposited and lift-off in acetone to obtain the meta-atom array structures. Finally, a single microchannel with a depth of 10 \( \mu \text{m} \), a width of 25 \( \mu \text{m} \), and a length of 2 mm was fabricated along one of the spaces by wet etching in a \( \text{H}_2\text{SO}_4:\text{H}_2\text{O}_2:\text{H}_2\text{O} \) etchant with composition 3:1:1 at 50 °C. In the measurements, the SPoTS microscope with a fs-laser source at a center wavelength of 1560 nm is used. The SPoTS microscope is one of the near-field THz spectroscopic systems developed by our group [41, 42]. The basic operating principle is the same as a conventional THz-TDS, but the THz emitter has been replaced by the developed chip. Detailed setup and operating principle are described in section S1 of supplementary material. The obtained THz pulses have a frequency range up to 4 THz, a signal-to-noise ratio of \( \sim 1000 \), and a spectral resolution of \( \sim 10 \text{ GHz} \) (see the characteristic of typical THz time-domain waveform of the GaAs wafer and the corresponding frequency spectrum shown in figures S1(c) and S1(d) (available online at stacks.iop.org/JPhoton/4/034005/mmedia), respectively, in supplementary material). When the pump laser
beam is focused on the bottom surface of a microchannel with a beam waist of 20 µm, THz waves are generated via optical rectification at the irradiation spot. This is considered a point-like THz source in which the beam diameter is almost equal to the laser beam diameter. Then, the point THz source efficiently interacts with solution samples flowing via the microchannel and meta-atoms, and the THz electric field is coupled to adjacent meta-atoms on a picosecond time scale, resulting in a resonance peak in the spectrum. Therefore, the chip can determine the solution concentration by measuring the shift in the resonance frequency. To obtain the spectrum, the THz beams transmitted via the solution sample and meta-atom are focused onto a bow-tie-shaped photoconductive antenna, and their amplitudes are measured using a typical THz-TDS technique. Figure 1(c) shows the measured and simulated transmitted THz spectra of the fabricated chip when the central meta-atom is excited with a 20 µm THz source with polarization parallel to the gap direction. Here, we calculated the THz transmittance spectra \( T(\omega) = \frac{E_I(\omega)}{E_r(\omega)} \), where \( E_I(\omega) \) and \( E_r(\omega) \) are the frequency-dependent THz amplitudes calculated by fast Fourier transform of their time-domain THz amplitudes measured at the microchannel with and without I-design meta-atoms, respectively. A resonance peak is observed at approximately 0.53 THz, which is in good agreement with the simulation results (ANSYS Lumerical Software ULC: ANSYS, Inc.). Details on the simulation are described in section S2-1 of supplementary material. The inset shows the simulated THz electric-field distribution at the resonance frequency. The THz electric field was firmly confined around the gap region, which is also in good agreement with previous reports [52].
3. Results and discussion

To design this chip, it is important to understand the effects on the number and periods of meta-atoms around the excited meta-atom. In our previous studies, at least $5 \times 5$ arrays of SRRs (corresponding to $0.75 \lambda_{\text{THz}} \times 0.75 \lambda_{\text{THz}}$ as an effective sensing area) were required to obtain sufficient LC or Fano resonance responses [49–51]. This is because THz electric-field coupling occurs via the floating capacitance between SRRs. Therefore, surrounding meta-atoms can serve as amplifiers for the resonance. However, the properties of the resonance on I-design meta-atoms excited with a localized THz source have not yet been investigated.

To understand this point, we simulated the THz electric-field distribution of multiple arrays of I-design meta-atoms. Figure 2(a) shows the simulated THz electric-field distribution of $9 \times 9$ arrays of I-design meta-atoms and the THz electric-field distribution at a resonance frequency of 0.5 THz. The polarization direction of THz waves was set parallel to the gap direction, which is the same condition as reported in [52]. Detailed polarization dependence is shown in section S2-2 of supplementary material. A resonance peak was observed at 0.54 THz in the spectrum, and THz electric-field coupling occurred symmetrically in the direction parallel to the central metallic strips, indicating strong confinement of the THz electric field at the gap regions. The resonance response was mainly caused by horizontal-oriented meta-atoms rather than vertical-oriented ones. Further, we prepared compatible Fano resonance meta-atoms (size 60 $\mu$m, linewidth 6 $\mu$m, gap 3 $\mu$m, and $d$ 15 $\mu$m, corresponding to 12.8% of structural asymmetricity [52]) periodically arrayed with a period of 85 $\mu$m and $9 \times 9$ units. The Fano meta-atom refers to an asymmetric SRR structure having two gaps where only one gap is shifted from the center of the structure as shown in the schematic in figure 2(b). Such a structure can be regarded as a coupling between meta-atoms having different Q values, and Fano resonance similar to the electromagnetically induced transparency can be obtained by excitation with THz waves. It is known as a resonance mode with a higher Q value than the LC resonance [54]. In this case, a resonance peak derived from the Fano resonance was observed at approximately 0.4 THz in the spectrum as shown in the lower-left figure in figure 2(b). The lower-right figure in figure 2(b) shows the THz electric-field distribution at the resonance frequency of 0.4 THz when the center of the central meta-atom is excited with a localized THz source. Unlike the case of I-design meta-atoms, THz electric-field coupling spreads in all directions around the excited meta-atom.

To determine the effective number in a single array of I-design meta-atoms, we prepared 1 unit, $1 \times 3$, $1 \times 5$, and $1 \times 9$ units of I-design meta-atoms and measured their THz transmittance spectra, as shown in figure 3(a). No resonance peak was observed for the 1-unit meta-atom, whereas a weak resonance peak was observed at 0.58 THz for the $1 \times 3$ units. As the number was increased to $1 \times 5$, the resonance peak was more pronounced at 0.54 THz and was saturated in the case of $1 \times 9$ units with a slight shift to a lower resonance frequency. The increase in the resonance intensities is attributed to the increase in the electric-field confinement points, and the shift in the resonance frequencies to lower values with an increase in the number of meta-atoms is due to the increase in capacitance between the center and either side of the metallic
strips [51]. Note that the slight widening of full width at half maximum (FWHM) with the increase in the number of meta-atoms may be due to the influence of the scattering that occurs when the densely coupled meta-atoms are excited with far-/near-field THz waves [45, 51, 55]. Therefore, electric-field coupling of up to $1 \times 5$ arrays meta-atoms, which significantly decreased the chip, dominated to induce the resonance responses. For comparison, we prepared compatible Fano resonance meta-arrays and measured their THz transmittance spectra (figure 3(b)). Unlike the case of I-design meta-atoms, no significant resonance peak was observed in their spectra, even when the number of meta-atoms was increased to $1 \times 5$ and $1 \times 9$. This is because of the absence of vertically-arranged meta-atoms, which are necessary for the amplification of the resonance [51], and thus, the resonance responses were insufficient (figure 2(b)).

To determine the linewidth of the microchannel, we investigated the effects on the space between two outer metallic strips. Figure 4(a) shows the measured THz transmittance spectra of $1 \times 5$ arrays of I-design meta-atoms with spaces of 15.5, 20, and 25 µm. With the 25 µm space, a resonance peak was observed at 0.54 THz with a Q factor of 4.12. Notably, the Q factors decreased with an increase in space: the resonance was enhanced with a decrease in space, accompanied by a slight shift in resonant frequency (see also S4 in supplementary material). This trend agrees well with the simulation results (figure 4(b)). This is because the meta-surface becomes closer to a periodic structure for typical filtering effects [56] when the space is increased, resulting in a frequency dip at approximately 0.6 THz. We also calculated the amplitudes of the THz electric field around the gap regions at their resonance frequencies as a function of the spaces, as shown in figure 4(c). The amplitudes at the gap were maximum when the space was 25 µm. Considering the strong signal attenuation in the solution measurements with THz waves, a higher resonance intensity with a Q factor of at least 3 is desired [49, 50]. Therefore, we employed chip parameters with $1 \times 5$ arrays of I-design meta-atoms having a 25 µm space for the microchannel (figure 1(a)).

We calculated the sensitivity of the I-design meta-atom chip in comparison with that of the compatible $5 \times 5$ arrays of the Fano meta-atom chip using a 10 µm thick analyte that filled in the microchannel, and the refractive index of the analyte was varied (figure 5). Herein, we define sensitivity as a change in the resonance frequency shift per refractive index unit (RIU), expressed as $\Delta f / \Delta n$, where $\Delta f$ and $\Delta n$ are the changes in the resonance frequency shift ($\Delta f_i$) and refractive index, respectively [57]. Herein, $\Delta f_i \equiv |f_n - f_1|$, where $f_n$ and $f_1$ are the resonance frequencies of the analyte with a refractive index of $n$ and air, respectively. We observed a linear relationship between the refractive index of the medium and the resonance frequency in both cases. The sensitivity of the I-design and Fano meta-atom chips was 80 and 39 GHz/RIU, respectively. This indicates that the sensitivity of the I-designed meta-atoms is approximately 2 times higher than that of the Fano meta-atoms, even though the number of arrays is less.

The THz measurements using a picoliter-order volume of solutions have been demonstrated using different concentrations of ethanol-water solution, including 0 (pure water; $n = 2.2$), 20, 40, and 80 vol%. In the measurements, the microchannel was covered using a 500 µm thick quartz plate to prevent the evaporation of solutions, and a solution of ∼50 nl was manually dripped using a microsyringe into one of the water storage vessels fabricated at both sides of the microchannel. Then, the solution was automatically drawn into the microchannel via capillary action and measured. The actual volume of the sample, defined as the volume of microchannel along the meta-atoms, was 85 pl. Herein, we cleaned the chip and repeated the
Figure 4. (a) Measured and (b) simulated THz transmittance spectra of I-designed meta-atoms with different space size between the central and outer strips. (c) Numerical simulation of THz electric field around the gap regions at their resonance frequencies as a function of the spaces.

Figure 5. Calculated resonance frequency shifts (GHz) versus varied refractive index ($n$) in I-design and Fano meta-atom chips.

measurements 10 times to evaluate the reproducibility. After the measurements, we calculated the averaged THz transmittance spectra of the solutions: $T_{ave}(\omega) = E_{amp}(\omega) / E_{ref}(\omega)$, where $E_{amp}(\omega)$ and $E_{ref}(\omega)$ are the frequency-dependent THz amplitudes when the microchannel was filled with and without a solution sample, respectively. To extract the transmittance peak and resonance frequency of each solution sample, the
differentiated THz transmittance spectrum \( \left( \frac{dT_{\text{ave}}}{df} \right) \) was calculated, and the frequency point where the value becomes zero was determined as a resonance frequency. All the solution samples were measured at room temperature. Figure 6(a) shows the averaged THz transmittance spectra obtained using the I-design meta-atom chip. When the chip was empty \((n = 1.0)\), the resonance frequency was observed at 0.54 THz, and it was shifted to 0.42 THz after filling the microchannel with pure water \((0 \text{ vol%)}\). The frequency shift, defined as the ‘total shift’, was approximately 120 GHz (figure S5(a) in supplementary material). The shift is attributed to the increase in the capacitance because of the substitution of higher dielectric materials into the microchannel. In addition, the resonance frequencies shifted to higher values with an increase in the concentrations due to the decrease in the refractive index of the solution in the microchannel owing to the increase in the amount of ethanol [57, 58]. Similar tendencies were also found in those measured using the compatible 5 × 5 arrays of the Fano meta-atom chip, showing the total shift of approximately 50 GHz (figures S5(b) and (c) in supplementary material). This shows that the sensitivity of the I-design meta-atom chip is better than that of the Fano meta-atom chip, which is consistent with the calculated sensitivities as shown in figure 5. Plots of the resonance frequency shifts \( (\Delta f') \) as a function of the concentration of the ethanol-water solutions are shown in figure 6(b). Herein, \( \Delta f' \equiv |f_e - f_w| \), where \( f_e \) and \( f_w \) are the resonance frequencies of the ethanol-water samples with different concentrations and pure water, respectively. The error bar in figure 6(b) represents the standard error. The solid curves represent the polynomial-fits to the data points, calculated by commercial software, Origin 2022. The shifts in both resonance frequencies increased with an increase in ethanol concentrations and reached a maximum at 80 and 60 vol% for the I-design and Fano meta-atom chips, respectively. The I-design meta-atom chip showed higher frequency shifts than the Fano resonance meta-atom chip, which was saturated at a lower concentration. These differences in the frequency shift are attributed to the difference in the distribution of the THz electric field around the gap regions at the respective resonance frequencies. The effective sensing area was 0.10 \( \lambda_{\text{THz}} \times 0.57 \lambda_{\text{THz}} \) \((0.057 \lambda_{\text{THz}}^2)\) and 0.57 \( \lambda_{\text{THz}} \times 0.57 \lambda_{\text{THz}} \) \((0.325 \lambda_{\text{THz}}^2)\) for the I-design and compatible Fano meta-atom chips, respectively. This indicates that the I-design meta-atom chip can be miniaturized by 7 times while maintaining its high sensitivity. The definition of the effective sensing area is described in section S3 of supplementary material.

To further evaluate the sensitivity, we prepared glucose-water solutions with low concentrations \((0, 1, 2, \text{ and } 10 \text{ mg l}^{-1})\) and measured their average THz transmittance spectra, as shown in figure 7(a). The samples showed a similar tendency: the resonance frequency shifted to a higher value with an increase in the glucose concentrations. To clarify the frequency shifts, we calculated the differentiated THz transmittance spectra \( \left( \frac{dT_{\text{ave}}}{df} \right) \) as shown in figure 7(b) and plotted the resonance frequency shifts as a function of the concentration of the glucose-water solutions as shown in figure 7(c). The error bar in figure 7(c) represents the standard error. Even the 1 mg l\(^{-1}\) glucose-water solution was sensitively detected, which is difficult to achieve using existing chips [49, 50]. Such high sensitivity could be achieved with the I-design meta-atom chip owing to the effective interactions between the THz electric-filed and the solution samples. The amount of glucose detected in the measurement using 1 mg l\(^{-1}\) of the glucose-water solution was estimated by the molar mass.
Figure 7. (a) The averaged terahertz (THz) transmittance spectra of glucose water solutions at different concentrations measured using the I-designed meta-atom chip. (b) The differentiated spectra of (a). (c) The plots of the resonance frequency shift as a function of concentration of the glucose water solutions. The error bar represents the standard error.

Figure 8. (a) Measured THz transmittance and (b) differentiated spectra of fresh mineral-water solutions at different hardness. (c) Differentiated spectra of old sample.

of glucose (180.156 g mol$^{-1}$) and the volume of the microchannel in contact with meta-atoms. For an 85 pl solution in the actual volume, 472 amol of glucose could be sensitively detected. Thus, the I-design meta-atom chip could improve the sensitivity and effective sensing area by approximately one order of magnitude compared to the Fano resonance meta-atom chip [50].

As a simple example of ion sensing, we used commercial mineral water (Contrex, hardness of 1468 mg l$^{-1}$) as a solution sample. We used two samples: fresh and old samples. The old sample has been maintained at room temperature for two years. Five samples of different hardness were prepared for the old and fresh samples by diluting them 1, 2, 10, 20, and 40 mg l$^{-1}$. Figures 8(a) and (b) show the measured THz transmittance and differentiated spectra, respectively. For the fresh samples, the relationship between the resonance frequency shift and the hardness of the solutions is similar to that in the case of ethanol- and glucose-water solutions. We repeated the same measurement and analysis for the old sample, and the differentiated spectra are shown in figure 8(c). Unlike the result of the fresh sample (figure 8(b)), no resonance frequency shift was observed even with a change in hardness. Since the mineral components of hard water tend to crystallize and precipitate, it is considered that the old sample had extremely low hardness or was almost pure water. The quantitative measurements of minerals in the fresh and old Contrex samples by using a commercial total hardness photometer (HI-97735, Hanna Instruments Ltd) showed that the total hardness ($CaCO_3$) in the old sample was found to be reduced to approximately 2.8% of that in the fresh sample, suggesting this possibility. Details are described in section S6 of supplementary material. The quantitative analysis of mineral components using the developed chip can be employed in food quality control.

Figure 9 compares recently reported THz-microfluidic sensors [58–62] for measuring solutions in terms of the sensitivity (mol), effective sensing area (mm$^2$), and actual volume of solutions. The maximum sensitivity was calculated as the product of the molar concentration of the solution and the sensor area (i.e. mole number). The size of the plot depends on the actual volume of solutions required for sensing, i.e. the volume of the solution filled in the sensor area. Many THz sensors have limitations, particularly in their effective sensing areas, due to the diffraction limit of far-field THz waves. In contrast, the proposed I-design
Figure 9. Comparison of recently reported THz sensors for measuring small amount of solutions, with focus on the sensitivity, effective sensing area, and actual volume of solutions. The size of the plot depends on the actual volume of the solution. Inset shows a $15 \times$ magnification of the region surrounded by the gray dotted line.

meta-atom chip showed higher sensitivity at the amol level with a significantly smaller effective sensing area and actual volume owing to the near-field measurement technique. Although our previously reported chips have high sensitivity and compactness, the proposed I-design chip has improved the sensitivity and effective sensing area by approximately one order of magnitude.

4. Conclusions

In summary, we proposed and developed an NLOC-based compact THz-microfluidic chip with only five units of I-design meta-atoms and showed the possibility of attomole-level sensing using a picoliter-order volume of solutions in a sub-wavelength effective sensing area. By optimizing the numbers of arrayed I-design meta-atoms, we observed a resonance response using $1 \times 5$ arrays, which correspond to an effective sensing area of $0.10 \lambda_{THz} \times 0.57 \lambda_{THz}^2$ (where $\lambda_{THz}$ is the center wavelength of 0.4 THz in the broadband spectra of the generated THz waves), when the central meta-atom was irradiated with a point THz source. The sensitivity of the chip was evaluated using ethanol- and glucose-water solutions and commercial mineral water at different concentrations. We succeeded in detecting 472 amol of solutes in an 85 pl solution. Compared with our previous THz-microfluidic chip with $5 \times 5$ arrays of Fano meta-atoms [50], the developed chip improves the effective sensing area by approximately one order of magnitude while maintaining high sensitivity. This indicates that the use of I-design meta-atom in the near-field THz excitation mode is more suitable for developing compact and highly sensitive THz chips. This technique would accelerate future biosensing technologies, including the use of THz waves, and contribute to the development of novel THz-microfluidic sensor chips, such as THz lab-on-a-chip and THz micro-total analysis systems.

Data availability statement

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

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