TOPICAL REVIEW

Virus recognition with terahertz radiation: drawbacks and potentialities

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Abstract

Virus sensing is earning great interest for recognition of dangerous and widely spread diseases, such as influenza A (virus subtypes H1N1, H3N2 etc), severe acute respiratory syndrome, Middle East respiratory syndrome etc. Many molecular and biological techniques have been developed and adopted for virus detection purposes. These techniques show some drawbacks concerning long collection time and data analysis, sensitivity, safety, costs etc. Therefore, new sensing approaches have been proposed for overcoming these limitations. In this short-review, we explore the emerging and challenging terahertz radiation technology and its applications to virus high-sensitivity remote-sensing devices.

1. Introduction

A virus is a pathogenic agent that is able to replicate only inside host living cells, parasitizing the cellular biosynthetic system. Its diameter typically ranges between ∼20 and ∼300 nm [1–3]. When a host cell is infected, an avalanche effect arises because the infecting virus forces the replication of its genetic material. Virus infection can spread in many ways, for instance by coughing and sneezing [4, 5], by ingesting infected food and/or water [6, 7], by sexual contact [8–10], by punctures of blood-sucking insects [11] etc. Therefore, rapid and effective techniques for virus sensing and recognition are becoming of vital importance. A fast and accurate monitoring can help to prevent wide transmission, spreading of viral infection and to carry out timely therapeutic treatment, disease control and surveillance. Nowadays, this is a crucial point, especially during the Covid-19 pandemic situation that is affecting our lives. This emergency, in fact, has imposed a severe burden on society and has led to the urgent need of effective virus diagnostic methods. Actually, many molecular and biological techniques are conventionally used. They include reverse transcription polymerase chain reaction (RT-PCR) [6, 12], reverse transcription loop-mediated isothermal amplification (RT-LAMP) [13, 14] and CRISPR–Cas13-based SHERLOCK system [15, 16]. In addition to those techniques, microfluidic biosensors are also considered [17–20]. In box 1 we report a brief summary concerning the most conventional molecular virus-detection techniques.
Box 1: Molecular techniques for virus detection

Nucleic acid and protein based methods are the most common molecular techniques for virus recognition. Nucleic acid based methods investigate virus nucleotide sequences or genes in biological patient’s samples (fluids, washes, aspirates etc) [21]. Protein based methods, instead, look at viral protein antigens and antibodies, created by the immune system, in response to a viral infection [22].

**Nucleic acid testing.** The RT-PCR combines two techniques: the RT and PCR [6, 12]. The RT allows to recognize the genetic information. A RNA single strand transcription is made and a complementary strand (cDNA) is synthetized. The classic PCR instead, amplifies specific regions of cDNA, making them detectable [21]. Branched-chain DNA (bDNA) assay [23, 24] detects and quantifies nucleic acid targets. The main difference with RT-PCR is the direct measurement of RNA or DNA molecules at physiological levels by amplifying signals, rather than by amplifying sequences. As a general observation, bDNA shows a lower sensitivity than the RT-PCR technique [25].

**Protein testing.** Protein testing exploits the type-specific antibody response produced in response to the viral infection, looking for antibodies in blood serum or plasma [21]. Among protein testing, serological tests have been largely used in many virus types detection, from herpes simplex virus [26], to varicella-zoster virus [27], zika virus (ZIKV) [28] and severe acute respiratory syndrome-CoV-2 [29–31]. The effective result of these tests hardly depends on the immune system response. Therefore, the antibodies quantity imposes a limit of detection during the measurement. enzyme-linked immunosorbent assay (ELISA) [32, 33] is a biochemical test for the detection of antibody-antigen binding reaction. The presence of the antigen can be detected, with the help of an antibody-enzyme complex and a chromogen. A chromogenic substrate, in fact, yields a visible color change or fluorescence when interacting with the enzyme.

However, the above mentioned assays are time-consuming, labor-intensive and no reagent-free [21, 25]. Therefore, a complementary, fast, sensitive and non-invasive alternative is highly desirable. In the following sections, an overview concerning the most promising terahertz (THz) technology approaches virus monitoring and detection will be presented and discussed.

2. THz spectroscopy

In the last decades, technology has experienced a wide diffusion of customizable and flexible THz systems for spectroscopic and imaging applications [34–38]. These systems found challenging applications in many science fields, like biology and medicine [37, 39–41], gas sensing [42, 43], material science [44, 45], chemical analysis and identification [46, 47] etc. THz radiation is largely appealing for biomedical issues because its low photon energy (4 meV @ 1 THz [48]) and its high penetration in anhydrous targets enable nondestructive and non-ionizing sensing. This is in contrast with other optical techniques, including ultraviolet or x-rays, where the high energy photons (> >eV) can cause direct biological damage on the sample [48–50]. In addition, many rotational and vibrational energy levels are located within the THz spectral range [48, 51] providing chemical specificity to imaging experiments, which can be efficiently done in label-free and non-contact modes [34, 37, 52]. However, THz radiation suffers from poor spatial resolution due to its large wavelength (λ = 300 µm @ 1 THz) [53]. Detecting tiny microorganisms such as bacteria and viruses is very challenging because their lateral dimensions are strongly sub-diffraction [25]. In addition, the extreme sensitivity of THz radiation to polar molecules, specifically water, limits THz waves penetrability from tens to hundred microns in hydrated samples, preventing wide technological spread in biological fields [35, 48, 51, 52]. Regardless of these constraints, several THz investigations have been performed on biological materials [39, 52, 54]. For instance, Lee et al [50] exploiting THz spectroscopy for measuring THz absorbance of H9N2 virus sample, in the spectral range from 0.2 to 2 THz. As it can be seen in figure 1 the freeze-dried pellet virus sample absorption is practically identical to the substrate, showing no identifiable spectral features.

Authors assigned the case to superposition of many protein vibration modes and inhomogeneous broadening of absorption features [50]. This suggests that the weak THz detection sensitivity and low chemical specificity are the main obstacles for THz sensing applications in pathogenic monitoring.

Interestingly, Sun and coauthors [55] used their THz-time domain spectroscopy (THz-TDS) system in transmission mode to assess an indirect virus detection modality. They investigated the binding properties of H9 HA protein and its specific human monoclonal antibody F10. H9 HA protein is the main surface glycoprotein of the Avian influenza (AI) virus and F10 is its specific antibody. Sun and the authors
Figure 1. Absorbance vs frequency of H9N2 virus freeze-dried pellet (pink) and control (black) samples [50].

Figure 2. Absorption coefficient vs ratio of binding sites (RBS) for H9 HA-F10 (red) and H9 HA-irmAb (blue) samples, compared to H9 NA sample [55]. RBS takes into account H9 HA protein and antibody concentrations.

demonstrated that THz spectroscopy is sensitive to the antibody-antigen reaction, by looking at the changes in the hydration shell around H9 HA molecules, in absence or in presence of F10. They measured the absorption coefficient for three different samples in liquid phase (~μm thickness): H9 HA, H9 HA with F10 (specific antibody) and H9 HA with irmAb (non specific antibody). Figure 2 shows the absorption coefficient vs ratio of binding sites (that takes into account both protein and antibody concentrations) for the three samples [55]. The absorption coefficients for H9 HA and H9 HA-irmAb show a non monotonous behavior indicating a hydration shell formation. The H9 HA-F10 sample, instead, present a monotonous behavior with no evidence of hydration. This trend highlights the consequence of binding sites of the antibody-antigen reaction on the protein configuration. Thus, using the capabilities of THz spectroscopy for probing antibody-antigen binding, the optical properties provide a sensitive approach to monitor the H9 HA-F10 interaction. The concentration detection limit was 15 μg ml\(^{-1}\), compared to 113 μg ml\(^{-1}\), determined by ELISA assay. THz spectroscopy approach resulted then ~7.5-fold more sensitive compared to standard ELISA [32, 33].

Although a more extensive research should be performed, previous results [50], suggest that a direct virus THz detection is very difficult due to the virus low THz absorption coefficient and the absence of specific THz spectral features. On the contrary, indirect methods can be successfully used to investigate antibody-antigen reactions, as reported by Sun and coauthors [55]. Those results also suggest that efficient devices, for example based on graphene [56] or on micro-fluidic chips [57], and novel materials like meta-
and nano-materials should be developed for increasing sensitivity and chemical specificity of THz radiation in this vibrating research field [56]. As reported by Zhou et al [56], graphene exhibits very fascinating electrical and optical properties, with the possibility to increase the sensitivity by graphene plasmonics and also it can be efficiently used for detecting biomolecules. Moreover, micro-fluidic chips [57] are of great interest because they allow to use extremely small liquid volumes, limiting the strong water absorption in the THz range. In addition, molecules can be trapped within a very small region in the micro-fluidic channels, providing very concentrated measurements.

3. Meta- and nano-materials

Metamaterial based chips are artificially structured devices with a wide variety of metallic structures with sub-wavelength [56, 58–62]. They gained popularity because of their operational simplicity, compactness and point-of-care suitability. They show attractive electromagnetic properties, mostly related to the excitations of surface plasmon polaritons (SPPs) [63–65], including the capability to extremely localize and enhance the electric field associated to the incoming radiation [50]. Sample deposition on metamaterial devices produces a variation in their dielectric properties, changing the SPPs propagation and interaction with the electromagnetic radiation [64]. In particular, THz metamaterials chips may have single- or multi-resonance frequencies $f_n^0$ exploiting their frequency shift $\Delta f$ due to sample deposition. $f_n^0$ strictly depend on the unit cell geometry and on the substrate refractive index [25, 50, 66–68]. The local dielectric changes caused by virus, proteins, nucleic acids and other biological samples can be efficiently detected by using metamaterials. Indeed, as very thin water layers (∼20 μm) are needed, the limitations imposed by the strong water absorption coefficient in the THz range can be easily overcome [69].

Sample discrimination takes into account (1) the resonance frequency shift $\Delta f$ and (2) the relative variation of optical response (OR) (typically transmittance, absorbance or reflectance) at the resonance frequencies $f_n^0$. This variation is generically labeled with $\Delta OR = OR_{SUB} - OR_{SAMP}$, where $OR_{SUB}$ and $OR_{SAMP}$ are the substrate and sample optical responses at the initial and final (after the interaction) resonance frequencies, respectively [25, 50].

The sensitivity of these metamaterial devices is commonly defined through:

(a) in refractive index unit (RIU) [70]

$$S_1 = \frac{\Delta f}{\Delta n} \left[ \frac{\text{GHz}}{\text{RIU}} \right],$$  \hspace{1cm} (1)

(b) in virus surface number density unit

$$S_2 = \frac{\Delta f}{N_{av}} \left[ \frac{\text{GHz} \cdot \mu m^2}{\text{particle}} \right].$$  \hspace{1cm} (2)

Being the sensitivity in equations (1) and (2) proportional to $\Delta f$, an appropriate design of the metamaterial unit cell area is crucial to enhance the detection capability, shifting the resonant peaks to the desired modes [71]. Many shapes and substrate refractive indexes have been proposed to efficiently fabricate these devices. For instance, periodically repeated split-rings resonators [25], rectangular slots [50], planar Jerusalem crosses [64], H-shaped graphene resonators [70] have been proposed. In figure 3, a schematic picture of the metamaterial unit cell used in [25, 50, 64, 70] is reported.

Recently, nanostructures such as nanogaps have been embedded in metamaterials by nanolithography. Researchers demonstrated that the reduction of the substrate refractive index and the gap width leads to an improvement of sensitivity [69, 72]. However, the sensor specification can be only obtained with functionalization: the biomolecules and/or other biological components are anchored on the meta- and nano-materials. For example, functionalized metamaterials [73–75] with alkanethiol molecules of well-ordered covalent bonded monolayers, or surface chemical modification using silane and silanol chemistries [76–78], CO$_2$-H modification, anchoring and/or decorating with antigens [79], have been proposed. Moreover, gold nanoparticles (GNPs) have been used, in the THz spectral range, also in combination with metamaterial chips [56, 80]. Ahmadivand et al [80] exploited GNPs to effectively detect ZIKV-envelope proteins at low concentration, with a 100-fold enhanced sensitivity.

Hong et al [69] proposed their hybrid slot antenna with silver mono-dimensional nanowires. They demonstrated a 2.5-fold sensitivity enhancement, compared to the one without silver nanowires on it.

All these advances in material technology set the scene for extremely promising performance of THz biosensors.
FIGURE 3. Different geometries of metamaterial unit cell found in literature. (a) Split-rings resonator \cite{25}. (b) Rectangular slot \cite{50}. (c) Planar Jerusalem Cross \cite{64}. (d) H-shaped resonator \cite{70}.

FIGURE 4. H9N2 Transmittance vs frequency at four sample concentrations. (a) Buffer (0 mg ml$^{-1}$), (b) 0.10 mg ml$^{-1}$, (c) 0.14 mg ml$^{-1}$ and (d) 0.28 mg ml$^{-1}$ \cite{50}.

Park et al \cite{25} fabricated THz split-ring resonators (see figure 3(a)) by e-beam lithography and photolithography. Their metamaterials were prepared both on quartz and on silicon substrate, followed by metal evaporation of Cr (3 nm) and Au (97 nm). They used them for detecting small MS2 and PRD1 viruses (30 and 60 nm, respectively), at low density. They analyzed a 40 $\mu$m thick layer for both viruses and obtained information on the viruses dielectric constant ($\varepsilon_r$), lacking in literature.

Successively, the same group performed measurements on both viruses, changing their density and the metamaterial gap widths. They demonstrated that the resonance frequency shift increases with virus surface density until saturation and the sensitivity is higher for smaller metamaterial gap widths (200 nm instead of 3 $\mu$m).

Lee et al \cite{50} fabricated rectangular nano-antennas (see figure 3(b)) by e-beam lithography, using a silicon wafer patterned with gold (150 nm). They tested their device with periodic rectangular slots for sensing AI virus subtypes: H1N1, H5N2 and H9N2. Authors demonstrated that each virus sample produces a different transmission change and resonance frequency shift, with respect to substrate only. This opens the
Figure 5. Resonance frequency shift ($\Delta f$) and transmittance changes ($\Delta T$) as a function of H9N2 sample concentration [50].

Table 1. Complex refractive indexes used by [50, 64, 70] for modeling H1N1, H5N2, H9N2 virus types.

| Virus type | Refractive index (N) | ($\alpha,\beta$) |
|------------|---------------------|-----------------|
| H1N1       | $N = n + 1.4ik$     | (1,1.4)         |
| H5N2       | $N = n + ik$        | (1,1)           |
| H9N2       | $N = 1.2n + 1.4ik$  | (1.2,1.4)       |

Figure 6. How changes in $\alpha$ and $\beta$ values yield resonance frequency shifts ($\Delta F$) and absorption differences ($\Delta A$). 
(a) $1.0 < \alpha < 1.4$, $\beta = 1.4$. (b) $\Delta F$ and $\Delta A$ as a function of $\alpha$. $\Delta F$ linearly changes with $\alpha$ and $\Delta A$ keeps constant.
(c) $1.0 < \beta < 2.0$, $\alpha = 1.2$. (d) $\Delta F$ and $\Delta A$ as a function of $\beta$. $\Delta A$ linearly changes with $\alpha$ and $\Delta F$ keeps constant. Reprinted with permission by [64].
way to discrimination among different virus types, by looking at $\Delta OR$ and $\Delta f$. Moreover, Lee et al [50] studied H9N2 transmittance, by varying its concentration. Four different concentration values have been chosen (buffer and three virus increasing concentrations). A linear decrease in transmittance value was found, at the resonance frequency, as the concentration increased (see figure 4).

Figure 5 shows resonance frequency (green triangles) and transmittance changes (pink circles) as a function of virus concentration [50]. Note that $\Delta T$ linearly changes as a function of sample concentration (see figures 4 and 5), while $\Delta f$ keeps constant [50].

Finally, Hong et al [69] manufactured their hybrid slot antennas on quartz substrate garnishing them with silver nanowires (with 20 nm diameter and 1–5 $\mu$m length). They tested their metamaterial on PRD1 virus droplets. Authors observed sensitivity enhancement due to the presence of nanowires. The hybrid chip exhibit a $\sim$2.5 factor enhanced sensitivity $S$, if compared to the bare chip ($S \sim 33$ GHz·$\mu$m$^2$/particle instead of $\sim 13$ GHz·$\mu$m$^2$/particle). This value can be further improved by performing multi drop-casting and by changing geometrical factors and used substrate materials.

Some groups [50, 64, 70] performed finite-difference time-domain simulations on various metamaterial unit cell geometries. Three AI virus samples (H1N1, H5N2 and H9N2) have been modeled as $\sim \mu$m thick layers, composed by homogeneous dielectric clads. Each virus complex refractive index $N$ has been written as follows:

$$ N = \alpha n + i \beta k,$$

where $\alpha$ and $\beta$ are frequency independent parameters. $(\alpha, \beta)$ pairs are distinctive of different viruses and their concentrations. $n$ and $k$ are the real and imaginary part of $\tilde{n} = \sqrt{\tilde{\epsilon}}$, respectively [50, 64]. In particular, viruses have been described using the parameters listed in table 1.

Lee and collaborators [50] found a great accordance between experimental and simulated data on the three virus types. H1N1 and H5N2 share the same $\Delta f$, while H1N1 and H9N2 the same $\Delta T$. This finding is directly related to the $(\alpha, \beta)$ values. $\alpha$ is responsible of resonance frequency shift, while $\beta$ of transmittance changes. Therefore, as H1N1 and H5N2 share the same $\alpha$, they will experience the same $\Delta f$. The same applies for $\beta$ and $\Delta T$. 

Figure 7. (a) Absorption response of unload chip and three Avian Influenza (AI) virus models (H5N2, H1N1, H9N2) as a function of frequency. (b) Absorption changes ($\Delta A$) and frequency shifts ($\Delta f$) for the three virus modeled subtypes. (c) Resonance frequency shift by increasing the sample thickness. (d) Resonance frequency shift saturation curve as a function of sample thickness. Reprinted with permission by [64].
Cheng and coauthors \[64\], with their Planar Jerusalem Cross structures (figure 3(c)) confirmed Lee et al \[50\] results by varying \((\alpha, \beta)\) pairs and looking at resonance frequency shifts and absorption changes. They modeled their 5 \(\mu\)m thick samples and the results are reported in figure 6. In figure 6(a) they kept \(\beta = 1.4\) and varied \(\alpha\) between 1.0 and 1.4. They demonstrated that, as \(\alpha\) increases, the resonance frequency linearly decreases, therefore the resonance frequency shift \(\Delta F\) linearly increases, while absorption \((\Delta A)\) values remain almost constant (see figure 6(b)). The opposite trend has been verified for \(\beta\), as shown in figures 6(c) and (d).

In figure 7(a) the simulated absorption response for three AI virus types is reported. The viruses are modeled by different \((\alpha, \beta)\) values, as reported in table 1. The histogram in figure 7(b) shows absorption differences and resonance frequency shifts. Thereby, all these virus models confirm the efficient discrimination by looking at \(\Delta F\) and \(\Delta A\). Finally, more interestingly, Cheng et al \[64\] simulated how the increasing sample thickness (from 1 to 8 \(\mu\)m) affects the resonance frequency shift. They found a saturation effect (see figures 7(c) and (d)), verifying the saturation-thickness behavior exploited by Park et al \[25\] in their measurements.

4. Conclusion and perspectives

The demand for large-scale tools to detect viruses in quick and effective modalities has grown and is continuously increasing, in the light of pandemic events of the last two decades. Although many molecular techniques (RT-PCR, bDNA, RT-LAMP etc.) are currently available and successfully used, they are still complex and difficult to apply on a large-scale. In this framework, THz technology has some characteristics that make it suitable for biosensing applications, such as pathogens, complementing or enhancing conventional solutions. This short review emphasizes the possibility to sense and identify viruses with THz radiation. In the first part, we focused on traditional THz sensing, such as THz-TDS, which does not reach a good sensitivity to monitor and/or discriminate the virus presence, unless indirect investigations are preferred. In the second part of this review, we dealt with the effective THz virus sensing using meta- and nano-sensors. Both experiments and simulations were reported to demonstrate the great potentialities of virus detection with metamaterial chips. Different unit cells geometries were studied in order to push over the detection limit. Meta- and nano-materials, operating in the THz regime, are an emerging alternative with a great potential for high-speed and on-site virus detection. The recent technological improvements in manufacturing techniques promise to extend the performances of meta- and nano-sensors, achieving sensitivity values much higher than traditional/conventional tools. Consequently, this research topic, although started merely few years ago, has grown and reached a discrete maturity, and it is destined to hold a relevant position in the future.

Data availability statement

No new data were created or analyzed in this study.

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References

[1] Harrap K A 1972 The structure of nuclear polyhedrosis viruses: II. The virus particle Virology 50 124–32

[2] Li-Fang H, Alling D, Popkin T, Shapiro M, Alter H J and Purcell R H 1987 Determining the size of non-a, non-b hepatitis virus by filtration J. Infectious Dis. 156 636–40

[3] Rossmann M G 2013 Structure of viruses: a short history Q. Rev. Biophys. 46 133
[50] Lee D-K et al 2017 Nano metamaterials for ultrasensitive terahertz biosensing Sci. Rep. 7 1–6
[51] Lee Y-S 2009 Principles of Terahertz Science and Technology vol 170 (Boston: Springer) [https://doi.org/10.1007/978-0-387-09540-0]
[52] Yang X, Zhao X, Yang K, Liu Y, Liu Y, Fu W and Luo Y 2016 Biomedical applications of terahertz spectroscopy and imaging Trends Biotechnol. 34 810–24
[53] Abbe E 1873 Beiträge zur theorie des mikroskops und der mikroskopischen wahrnehmung Archiv für Mikroskopische Anatomie 9 413–68
[54] Ajito K and Ueno Y 2011 THz chemical imaging for biological applications IEEE Trans. Terahertz Sci. Technol. 1 293–300
[55] Sun Y, Zhong J, Zhang C, Zuo J and Emma P-M 2015 Label-free detection and characterization of the binding of hemagglutinin protein and broadly neutralizing monoclonal antibodies using terahertz spectroscopy J. Biomed. Opt. 20 037006
[56] Zhou R, Wang C, Wendao X and Xie L 2019 Biological applications of terahertz technology based on nanomaterials and nanostructures Nanoscale 11 3445–57
[57] Tang Q, Liang M, Yi L, Wong P K, Wilmink G J, Zhang D D and Xin H 2016 Microfluidic devices for terahertz spectroscopy of live cells toward lab-on-a-chip applications Sensors 16 476
[58] Chen X and Fan W 2017 Ultrasensitive terahertz metamaterial sensor based on spoof surface plasmon Sci. Rep. 7 1–8
[59] Wendao X, Xie L and Ying Y 2017 Mechanisms and applications of terahertz metamaterial sensing: a review Nanoscale 9 13864–78
[60] Samy Saadeelkin A, Hameed M F O, Elkaramany E M A and Obaya S S A 2019 Highly sensitive terahertz metamaterial sensor IEEE Sens. J. 19 7993–9
[61] Ahmadvand A, Gerislioglu B, Ahuja R and Mishra Y K 2020 Terahertz plasmonics: the rise of toroidal metadevices towards immunobiosensing Mater. Today 32 108–30
[62] Diaz M B and Jáuregui López I 2020 Terahertz sensing based on metasurfaces Adv. Opt. Mater. 8 1900721
[63] Zhang Y and Han Z 2015 Spoof surface plasmon based planar antennas for the realization of terahertz hotspots Sci. Rep. 5 18606
[64] Cheng D, Xia H, Huang X, Zhang B, Liu G, Shu G, Fang C, Wang J and Luo Y 2018 Terahertz biosensing metamaterial absorber for virus detection based on spoof surface plasmon polaritons Int. J. RF Micro. Computer-Aided Eng. 28 e21448
[65] Yang W X, Zhang H C, Ma H F, Jiang W X and Cui T J 2019 Concept, theory, design and applications of spoof surface plasmon polaritons at microwave frequencies Adv. Opt. Mater. 7 1800421
[66] Limaj O, Nucara A, Lupi S, Ortoli M, Di Gaspare A, Palange E and Carelli P 2011 Scaling the spectral response of metamaterial dipolar filters in the terahertz Opt. Commun. 284 1690–3
[67] D’Apuzzo F et al 2015 Resonating terahertz response of periodic arrays of subwavelength apertures Plasmonics 10 45–50
[68] D’Apuzzo F et al 2017 Terahertz and mid-infrared plasmons in three-dimensional nanoporous graphene Nat. Commun. 8 14885
[69] Hong J T, Jun S W, Cha S H, Park J Y, Lee S, Shin G A and Ahn Y H 2018 Enhanced sensitivity in THz plasmonic sensors with silver nanowires Sci. Rep. 8 1–8
[70] Keshavarz A and Yafapour Z 2019 Sensing Avian influenza viruses using terahertz metamaterial reflector IEEE Sens. J. 19 5161–6
[71] Xia X, Sun Y, Yang H, Wang L and Gu C 2008 The influences of substrate and metal properties on the magnetic response of metamaterials at terahertz region J. Appl. Phys. 104 033505
[72] Chen X et al 2013 Atomic layer lithography of wafer-scale nanogap arrays for extreme confinement of electromagnetic waves Nat. Commun. 4 1–7
[73] Tantaktiti F, Burk-Rafel J, Cheng F, Egnaichth R, Owen T, Hoffman M, Weiss D N and Ratner D M 2012 Nanoscale clustering of carbohydrate thios in mixed self-assembled monolayers on gold Langmuir 28 6950–9
[74] Xiaojun W, Quan B, Pan X, Xinlong X, Xinchao L, Changzhi G and Wang Li 2013 Alkanethiol-functionalized terahertz metamaterial as label-free, highly-sensitive and specific biosensor Biosens. Bioelectron. 42 626–31
[75] Lee H J, Lee J H and Jung H I 2011 A symmetric metamaterial element-based RF biosensor for rapid and label-free detection Appl. Phys. Lett. 99 163703
[76] Terracciano M, Rea I, Politi J and De Stefano L 2013 Optical characterization of aminosilane-modified silicon dioxide surface for biosensing J. Eur. Opt. Soc.-Rap. Publications 8 13075
[77] De Stefano L, Oliviero G, Amato J, Borbone N, Picciiali G, Mayol Y, Rendina I, Terracciano M and Rea I 2013 Aminosilane functionalizations of mesoporous oxidized silicon for oligonucleotide synthesis and detection J. R. Soc. Interface 10 20130160
[78] Terracciano M, Galstyan V, Rea I, Casalino M, De Stefano I and Sberveglieri G 2017 Chemical modification of TiO2 nanotube arrays for label-free optical biosensing applications Appl. Surf. Sci. 419 235–40
[79] Bhardwaj S K, Bhardwaj N, Kumar V, Bhatt D, Azouz A, Bhaumik J, Kim K H and Deep A 2021 Recent progress in nanomaterial-based sensing of airborne viral and bacterial pathogens Environ. Int. 146 106183
[80] Ahmadvand A, Gerislioglu B, Tomitaka A, Manickam P, Kausnik H, Bhanvati S, Nair M and Pala N 2018 Extreme sensitive metasensor for targeted biomarkers identification using colloidal nanoparticles-integrated plasmonic unit cells Biomed. Optics Express 9 373–86