

SERS SENSORS

Cross Reference to Related Application(s)

- 5 The present disclosure claims the benefit of Singapore Patent Application No. 10201801989P filed on 9 March 2018, which is incorporated in its entirety by reference herein.

Technical Field

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The present disclosure generally relates to surface-enhanced Raman spectroscopy (SERS) sensors. More particularly, the present disclosure describes various embodiments of a SERS sensor and a method of manufacturing the SERS sensor.

15 Background

Surface-enhanced Raman spectroscopy or scattering (SERS) is a surface-sensitive technique that enhances Raman scattering by molecules adsorbed on rough metal surfaces or by nanostructures. Raman scattering is the inelastic scattering of a photon by molecules which are excited to higher energy levels. SERS can be used as an analytical technique to provide single molecule-resolved signal and to fingerprint the Raman spectrum. Due to its ultrasensitive response and multiplexing capabilities, SERS has received considerable attention for a wide range of chemical and biological sensing applications, such as food safety-relevant monitoring.

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Current research on SERS has been more focused on the fabrication of metal nanostructures on solid surfaces, such as silicon wafer, glass slide, quartz, and roughened silver electrode. Some commercial SERS products available in the market include Klarite substrates, Q-SERS substrates, and MatoS substrates. Klarite substrates have a gold-coated textured silicon surface consisting of inverted square pyramid subunits. Q-SERS substrates have gold particles irregularly distributed on glass. MatoS substrates have stochastic nanopatterns created by ultra-short pulse

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laser on glass. These SERS products have rigid substrates that impose difficulties for practical application involving complex multiple steps in the sampling process, such as sample extraction / dissolution, centrifuge and transfer steps. Other difficulties include rigorous manufacturing conditions, such as vacuum environment, time-consuming production steps, and clean room environment, which are impractical for mass production at affordable cost.

Flexible SERS paper sensors have emerged as an alternative to address such problems. *Hoppmann, Eric P., et al (Highly sensitive and flexible inkjet printed SERS sensors on paper)* disclose an example of a flexible SERS paper sensor with gold nanoparticles deposited on the paper. Although this may address the impracticalities of rigid substrates, such paper sensors may not be sufficiently sensitive.

Therefore, there is a need to provide improved SERS sensors that address or alleviate at least one of the aforementioned problems / disadvantages.

Summary

According to a first aspect of the present disclosure, there is a SERS sensor comprising: a flexible substrate; and 3D nanomaterials deposited on the flexible substrate by a printing process, the 3D nanomaterials comprising anisotropic nanostructures formed of a metallic material, wherein each anisotropic nanostructure comprises a plurality of pointed end portions extending from a central core portion.

According to a second aspect of the present disclosure, there is a method of manufacturing a SERS sensor. The method comprises: preparing a flexible substrate; preparing 3D nanomaterials comprising anisotropic nanostructures formed of a metallic material, each anisotropic nanostructure comprising a plurality of pointed end portions extending from a central core portion; and performing a printing process to deposit the 3D nanomaterials on the flexible substrate to thereby form the SERS sensor.

An advantage of one or more aspects of the present disclosure is that the anisotropic nanostructures offer enhanced SERS sensitivity and better SERS assay performance due to the pointed end portions which act as efficient nanoantennas. Additionally, the use of flexible substrates offers higher surface areas and in turn further increase the SERS sensitivity. Due to the enhanced SERS sensitivity, the SERS sensor can be used for direct sampling of analytes from sample surface, thus reducing risk of analyte contamination which would compromise the SERS performance.

SERS sensors according to the present disclosure are thus disclosed herein. Various features, aspects, and advantages of the present disclosure will become more apparent from the following detailed description of the embodiments of the present disclosure, by way of non-limiting examples only, along with the accompanying drawings.

Brief Description of the Drawings

Figure 1 is an illustration of a SERS sensor.

Figure 2 is a flowchart illustration of a method of manufacturing a SERS sensor.

Figure 3A to Figure 3E are illustrations of various flexible substrates of the SERS sensor.

Figure 4A and Figure 4B are illustrations of various nanostructures of the SERS sensor.

Figure 5A to Figure 5D are illustrations of various printing processes in the method of manufacturing the SERS sensor.

Figure 6A to Figure 6C are illustrations of results of experiments performed on SERS sensors with paper substrates to detect malachite green.

Figure 7A and Figure 7B are illustrations of results of experiments performed on SERS sensors with plastic and metallic substrates to detect malachite green.

5 Figure 8A to Figure 8C are illustrations of results of experiments performed on SERS sensors with paper substrates to detect thiram.

Figure 9A and Figure 9B are illustrations of results of experiments performed on SERS sensors to detect thiram on an apple.

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Detailed Description

For purposes of brevity and clarity, descriptions of embodiments of the present disclosure are directed to SERS sensors in accordance with the drawings. While
15 aspects of the present disclosure will be described in conjunction with the embodiments provided herein, it will be understood that they are not intended to limit the present disclosure to these embodiments. On the contrary, the present disclosure is intended to cover alternatives, modifications and equivalents to the embodiments described herein, which are included within the scope of the present
20 disclosure as defined by the appended claims. Furthermore, in the following detailed description, specific details are set forth in order to provide a thorough understanding of the present disclosure. However, it will be recognized by an individual having ordinary skill in the art, i.e. a skilled person, that the present disclosure may be practiced without specific details, and/or with multiple details arising from
25 combinations of aspects of particular embodiments. In a number of instances, well-known systems, methods, procedures, and components have not been described in detail so as to not unnecessarily obscure aspects of the embodiments of the present disclosure.

30 In embodiments of the present disclosure, depiction of a given element or consideration or use of a particular element number in a particular figure or a reference thereto in corresponding descriptive material can encompass the same, an

equivalent, or an analogous element or element number identified in another figure or descriptive material associated therewith. The use of "/" herein, in a figure, or in associated text is understood to mean "and/or" unless otherwise indicated. The recitation of a particular numerical value or value range herein is understood to
5 include or be a recitation of an approximate numerical value or value range.

References to "an embodiment / example", "another embodiment / example", "some embodiments / examples", "some other embodiments / examples", and so on, indicate that the embodiment(s) / example(s) so described may include a particular
10 feature, structure, characteristic, property, element, or limitation, but that not every embodiment / example necessarily includes that particular feature, structure, characteristic, property, element or limitation. Furthermore, repeated use of the phrase "in an embodiment / example" or "in another embodiment / example" does not necessarily refer to the same embodiment / example.

15 The terms "comprising", "including", "having", and the like do not exclude the presence of other features / elements / steps than those listed in an embodiment. Recitation of certain features / elements / steps in mutually different embodiments does not indicate that a combination of these features / elements / steps cannot be
20 used in an embodiment. As used herein, the terms "a" and "an" are defined as one or more than one. The use of "/" in a figure or associated text is understood to mean "and/or" unless otherwise indicated.

In representative or exemplary embodiments of the present disclosure, there is a
25 surface-enhanced Raman spectroscopy or scattering (SERS) sensor 100 as shown in Figure 1. The SERS sensor 100 includes a flexible or pliable substrate 102. The flexible substrate 102 is supple enough to bend freely or repeatedly without breaking. The SERS sensor 102 further includes three-dimensional (3D) nanomaterials 104 deposited on the flexible substrate 102 by a printing process. The 3D nanomaterials
30 104 include anisotropic nanostructures 106 formed of a metallic material, such as gold. The metallic material may alternatively be silver or a hybrid of several metallic materials. The anisotropic nanostructures 106 may include nanostars 106a and/or

nanocubes 106b. As can be seen from the nanostars 106a and nanocubes 106b, each anisotropic nanostructure 106 has a plurality of pointed end portions 108 extending from a central core portion 110. The pointed end portions 108 represent sharp tips / corners of the anisotropic nanostructures 106 which can collectively
5 function as efficient nanoantennas for the 3D nanomaterials 104. Although nanostars 106a and nanocubes 106b are described as examples of the anisotropic nanostructures 106 having the pointed end portions 108 extending from the central core portions 110, it will be appreciated that the anisotropic nanostructures 106 can have other shapes / forms as will be readily understood by the skilled person.

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Nanomaterials have any dimension within the nanoscale which is defined as dimensions ranging from 1 to 100 nm, or having internal structure or surface structure in the nanoscale. Nanomaterials are classified into zero-dimensional (0D), one-dimensional (1D), two-dimensional (2D), or three-dimensional (3D). 0D
15 nanomaterials include nanostructures such as spherical nanoparticles. 1D nanomaterials include nanostructures such as nanotubes, nanorods, and nanowires. 2D nanomaterials exhibiting plate-like shapes and include nanostructures such as graphene, nanofilms, and nanolayers. 3D nanomaterials have nanostructures extending in all three dimensions such as bundles of nanowires / nanotubes, and
20 multi-nanolayers. In various embodiments herein, the 3D nanomaterials 104 include nanostructures 106 that can form the surface morphology as SERS-active components.

With reference to Figure 2, there is a method 200 of manufacturing the SERS sensor
25 100. The method 200 includes a step 202 of preparing the flexible substrate 102. The flexible substrate 102 may be formed of one of paper, plastic, and metallic materials. The method 200 further includes a step 204 of preparing the 3D nanomaterials 104 including the anisotropic nanostructures 106 which may be formed of a metallic material such as gold. The metallic material may alternatively be
30 silver or a hybrid of several metallic materials. The method 200 further includes a step 206 of performing a printing process to deposit the 3D nanomaterials 104 on the flexible substrate 102 to thereby form the SERS sensor 100.

In the step 202 of preparing the flexible substrate 102, the flexible substrate 102 is selected from different types / materials as SERS-active material supports. The flexible substrate 102 is obtained from readily available commercial sources. In one embodiment as shown in Figure 3A, the flexible substrate 102 is a plastic substrate 102a including polyethylene terephthalate (PET) film. The plastic substrate 102a has a flat and smooth surface that is optionally treated with chemicals. In another embodiment as shown in Figure 3B, the flexible substrate 102 is a metallic substrate 102b including aluminum foil. The metallic substrate 102b has a flat and smooth surface that is optionally treated with chemicals.

In some embodiments, the flexible substrate 102 is a paper substrate 102c which is mainly formed of a cellulose material. The paper substrate 102c may include one of copy paper, filter paper, and chromatography paper. In one embodiment as shown in Figure 3C, the paper substrate 102c includes copy paper 102c1 which has a relative flat surface rougher than that of the plastic substrate 102a and metallic substrate 102b. The copy paper 102c1 includes standard paper used in offices, such as A4-sized printing / photocopier paper. In another embodiment as shown in Figure 3D, the paper substrate 102c includes filter paper 102c2 which has a partially-permeable or porous surface. As filter papers 102c2 are commonly used as air filters and coffee filters, they are readily available from commercial sources. In another embodiment as shown in Figure 3E, the paper substrate 102c includes chromatography paper 102c3 which has a partially-permeable or porous surface and is commonly used to separate colored chemicals or substances.

Unlike the plastic substrate 102a and metallic substrate 102b, the paper substrate 102c is treated with chemicals prior to depositing the 3D nanomaterials 104 on the paper substrate 102c. The step 202 of preparing the paper substrate 102c includes silanizing the paper substrate 102c. The paper substrate 102c is cut into strips of dimensions 15 x 20 mm, and then dried in an oven at 103 °C for 2 hours to remove moisture. Said silanizing includes immersing the paper substrate 102c in a toluene solvent including phenyltriethoxysilane. Depending on the material of the paper

substrate 102, the paper substrate 102c is immersed in different concentrations of phenyltriethoxysilane in the toluene solvent. Said silanizing further includes incubating the paper substrate 102c after said immersing. For example, the paper substrate 102c is incubated at 50 °C for 11 hours or overnight. Said silanizing further includes rinsing the paper substrate 102c with ethanol after said incubating. This facilitates the displacement of weakly bound silane molecules and the hydrolysis of residual alkoxy groups in silane layers. Said silanizing further includes thermal curing the paper substrate 102c after said rinsing. For example, the paper substrate 102c is thermally cured in an oven at 130 °C for 2 hours to facilitate condensation of hydrogen-bonded silanols to thereby form siloxane bonds. Accordingly, the surface of the paper substrate 102c is functionalized with siloxane molecules and the paper substrate 102c is silanized.

Prior to the step 204 of preparing the 3D nanomaterials 104, the anisotropic nanostructures 106 constituting the 3D nanomaterials 104 were first synthesized using various methods known to the skilled person. As shown in transmission electronic microscope (TEM) images in Figure 4A, gold nanostructures 106 were synthesized in the form of anisotropic nanostars 106a and anisotropic nanocubes 106b. For comparison, isotropic nanostructures 106 were also synthesized in the form of big isotropic nanospheres 106c and small isotropic nanospheres 106d.

The anisotropic gold nanostars 106a were synthesized using a seeded growth method. Specifically, multiple branched polycrystalline gold nanostar particles 106a were synthesized. The gold nanostars 106a have a mean overall size of 80.8 ± 8.6 nm (variation of approximately 10% from the mean) and a mean core size of 33 nm (variation of approximately 5.6% from the mean). The anisotropic gold nanocubes 106b were synthesized using seed-mediated synthesis. In the seed-mediated synthesis, single-crystalline gold nanospheres were formed and said forming included a 2-time growth-dissolution cycle to obtain high quality single-crystalline gold nanoparticle seeds. Subsequently, the as-formed nanospheres were used as the seeds to reduce gold ions (Au^{3+}) in a confined environment so as to form cubic

nanoparticles or nanocubes 106b. The gold nanocubes 106b have a mean edge size of 73.7 ± 3.7 nm (variation of approximately 5% from the mean).

The isotropic gold nanospheres (big) 106c were synthesized using seed-mediated synthesis. Single-crystalline gold nanospheres were formed in the seed-mediated synthesis. Subsequently, the as-formed nanospheres were used as seeds to reduce the gold ions (Au^{3+}) on their surfaces to grow to a bigger size. The big nanospheres 106c have a quasispherical form and a mean size of 61.5 ± 4.4 nm (variation of approximately 7.2% from the mean). The isotropic gold nanospheres (small) 106d were synthesized as citrate-capped gold nanospheres using the Turkevich method. The type of gold spherical particles is polycrystalline in nature, uniform, and monodispersed. The small nanospheres 106d have a mean size of 13.1 ± 0.7 nm (variation of approximately 5.1% from the mean).

Surface modification was performed for all synthesized gold nanostructures 106a-d. Specifically, the step 204 of preparing the 3D nanomaterials 104 includes modifying the gold nanostructures 106a-d with a thiolated polyethylene glycol (PEG) derivative, such as polyethylene glycol methyl ether thiol (SH-PEG-methoxyl) or polyethylene glycol 2-mercaptoethyl ether acetic acid (SH-PEG-carboxyl / SH-PEG-COOH). For example, SH-PEG-methoxyl is used to chemically react with and modify the anisotropic nanostars 106a and isotropic small nanospheres 106d, and SH-PEG-carboxyl is used to chemically react with and modify the anisotropic nanocubes 106b and isotropic big nanospheres 106c. Chemical reactions from the PEG derivative functionalizes the surfaces of the gold nanostructures 106a-d. The PEG-modified gold nanostructures 106a-d are then stored in a fridge at 4 °C.

Figure 4B illustrates an extinction spectrum graph 400 of extinction intensity against wavelength for each of the gold nanostructures 106a-d. The graph 400 shows the ultraviolet-visible spectra (UV-Vis) absorption measurement results. Each of the gold nanostructures 106a-d has a peak wavelength that corresponds to the maximum extinction intensity. The peak wavelength is wavelength at which the gold nanostructures 106a-d absorb the most incident light. The peak wavelengths for the

gold nanostructures 106a-d are 682 nm, 576 nm, 541 nm, and 523 nm, respectively. Notably, the anisotropic nanostars 106a has the highest peak wavelength.

In the step 206 of performing a printing process to deposit the 3D nanomaterials 104 on the flexible substrate 102, the printing process is associated with inkjet printing, drop casting, or gravure printing. In some embodiments, the printing process is associated with inkjet printing using an anisotropic ink including the nanostructures 106, specifically the anisotropic nanostars 106a / nanocubes 106b. The anisotropic ink is formulated with certain properties. For example, the anisotropic ink has a surface tension of approximately 53 mN/m and a viscosity of approximately 2.05 cP at 150 rpm. The surface tension may be measured using a force tensiometer such as the KSV Sigma 701, and the viscosity may be measured using a cone / plate rheometer such as the Brookfield LVDV-II+ Pro. Said inkjet printing may be performed using a Dimatix Materials Printer DMP-2831 machine 500 as shown in Figure 5A. The 3D nanomaterials 104 may be inkjet-printed on the flexible substrate 102 such as a plastic substrate 102a (e.g. PET film) or paper substrate 102c (e.g. copy paper). The flexible substrate 102, such as PET film, may be subjected to a prior ultraviolet ozone treatment for 10 minutes. Comparing to drop casting and gravure printing, inkjet printing is able to achieve the highest spatial or pattern resolution of approximately 50 μm , highest volume control at approximately 10^{-12} liters, and high pattern versatility. However, inkjet printing requires formulation of the anisotropic ink, has the highest cost, has the slowest printing speed in the order of hours, and control of the density of the nanostructures 106 in the 3D nanomaterials 104 is challenging. For example, an image 502 was inkjet-printed with the anisotropic ink containing anisotropic gold nanostars 106a onto the copy paper substrate 102c1 (office A4 paper) with good quality, as can be seen in Figure 5A. The visible dark pattern of the image 502 can generate decent Raman signals from the copy paper substrate 102c1.

In some embodiments, the printing process is associated with drop casting using a patterned ink barrier including the nanostructures 106 on its surface. In one embodiment, drop casting is performed with the assistance of wax printing. With

reference to Figure 5B, a wax printer 504, such as the Xerox ColorQube 8570, is first used to fabricate the patterned ink barrier by wax printing. The patterned ink barrier includes the nanostructures 106 and is subsequently heat-treated in an oven at 130 °C with a controlled baking time. This results in the final template for drop-cast
5 patterned ink surface a reproducible way. With the aid of wax patterned surface, drop casting is able to achieve higher SERS sensing performance, as compared to inkjet printing, and with good reproducibility.

In another embodiment, drop casting is performed without the assistance of wax
10 printing. Specifically, drop casting without pre-wax printing was done by directly pipetting the 3D nanomaterials 104 onto the flexible substrate 102. Comparing to inkjet printing and gravure printing, drop casting is able to achieve high volume control at approximately 10^{-6} liters, does not require formulation of ink, has the lowest cost, has the fastest printing speed in the order of seconds, and there is ease
15 of control of the density of the nanostructures 106 in the 3D nanomaterials 104. However, drop casting achieves the lowest spatial or pattern resolution (approximately 0.5 mm for drop casting with the assistance of wax printing) and low pattern versatility. Figure 5C illustrates scanning electron microscope (SEM) images of drop-casted SERS sensors 100, the first image 506 having anisotropic gold
20 nanocubes 106b on a copy paper substrate 102c1, and the second image 508 having anisotropic gold nanostars 106a on a chromatography paper substrate 102c3. Notably, the SEM images were taken after coating a thin layer (approximately 2 nm) of platinum nanoparticles on the paper substrates 102c.

25 In some embodiments, the printing process is associated with gravure printing using a metallic plate having a predefined pattern, wherein the 3D nanomaterials 104 are printed on the flexible substrate 102 according to the predefined pattern. With reference to Figure 5D, Ink patterning on the metallic plate was performed using a gravure printer 510, such as the K Printing Proofer KPP printing machine, so that the
30 metallic plate is customized with the predefined pattern which has a pattern resolution of 300 lines per inch. Comparing to inkjet printing and drop casting, gravure printing is able to achieve high spatial or pattern resolution of approximately

85 μm , high volume control at approximately 10^{-6} liters, medium pattern versatility, and does not require ink formulation. Moreover, the printing speed is fast in the order of minutes and the control of the density of the nanostructures 106 in the 3D nanomaterials 104 is more moderate. However, gravure printing requires fabrication of the customized metallic plate as a template for depositing the 3D nanomaterials 104 on the flexible substrates 102 to form the SERS sensors 100. Said depositing can be done using the gravure printer 510 at speed 1, roller reading of 0.2 mm, and blade reading of 5.05 mm. This deposition method is efficient and has potential for high-throughput mass production of the SERS sensors 100.

The various printing processes for depositing the 3D nanomaterials 104 on the flexible substrate 102 offer advantages of mass production, low cost, high precision ink distribution, and good control of SERS sensing performance with fast Raman readings. To evaluate the SERS sensors 100, various experiments were performed on different SERS sensors 100 manufactured by the method 200. The SERS sensors 100 have different combinations of flexible substrates 102, 3D nanomaterials 104, and printing processes. Raman spectra and SERS intensity of the SERS sensors 100 were measured in these experiments. The Raman spectra was measured using a Renishaw Raman microscope equipped with a 785 nm laser at less than 5 mW power, 10 seconds exposure, and 1x accumulation. The SERS sensors 100 were tested using on-focus plane.

With reference to Figure 6A to Figure 6C, an experiment was performed to demonstrate the capability of the SERS sensors 100 with paper substrates 102c to detect an analyte, specifically a pesticide malachite green oxalate.

In Figure 6A, the experiment was performed on a first SERS sensor 100a having anisotropic gold nanostars 106a deposited on a chromatography paper substrate 102c3, and on a second SERS sensor 100b having isotropic gold small nanospheres 106d deposited on a chromatography paper substrate 102c3. The nanostars 106a and small nanospheres 106d were modified with SH-PEG-methoxyl, and were deposited on the respective chromatography paper substrates 102c3 by drop casting

with the assistance of wax printing. The chart 600 shows the Raman spectra of the SERS sensors 100ab for detecting 100 μM of malachite green. Specifically, the chart lines 602 and 604 represent the Raman spectra of the first SERS sensor 100a with and without malachite green, respectively. Notably, in the chart line 602, the peak intensity occurred at Raman shift 1618 cm^{-1} . The chart lines 606 and 608 represent the Raman spectra of the second SERS sensor 100b with and without malachite green, respectively. The chart 605 shows the SERS intensities of the first SERS sensor 100a in comparison to the concentration of malachite green. The assistance of wax printing in the drop casting can achieve a detection limit of 1 μM , but without wax printing which helps to create a more confined test area, the detection limit can only reach 100 μM . The chart 610 shows the SERS intensities of the SERS sensors 100ab at Raman shift 1618 cm^{-1} in comparison with a plain chromatography paper substrate 102c3 without the 3D nanomaterials 104. Specifically, the bar 612 represents the SERS intensity of the plain chromatography paper substrate 102c3. The SERS intensity from the bar 612 may be interpreted as the background noise. The bars 614 and 616 represent the SERS intensities of the second SERS sensor 100b and first SERS sensor 100a, respectively. The first SERS sensor 100a generated a SERS intensity of approximately 15 K while the second SERS sensor 100b generated an almost zero SERS intensity after consideration of the background noise determined from the plain chromatography paper substrate 102c3. Evidently, the first SERS sensor 100a with the anisotropic nanostars 106a is more effective than the second SERS sensor 100b with the isotropic small nanospheres 106d.

In Figure 6B, the experiment was performed on a first SERS sensor 100a having anisotropic gold nanostars 106a deposited on a chromatography paper substrate 102c3, and on a second SERS sensor 100b having isotropic gold small nanospheres 106d deposited on a chromatography paper substrate 102c3. The nanostars 106a and small nanospheres 106d were modified with SH-PEG-methoxyl, and were deposited on the respective chromatography paper substrates 102c3 by gravure printing. The chart 620 shows the Raman spectra of the SERS sensors 100ab for detecting 1 mM of malachite green. Specifically, the chart lines 622 and 624 represent the Raman spectra of the first SERS sensor 100a with and without

malachite green, respectively. Notably, in the chart line 622, the peak intensity occurred at Raman shift 1618 cm^{-1} . The chart lines 626 and 628 represent the Raman spectra of the second SERS sensor 100b with and without malachite green, respectively. The chart 630 shows the SERS intensities of the SERS sensors 100ab at Raman shift 1618 cm^{-1} in comparison with a plain chromatography paper substrate 102c3 without the 3D nanomaterials 104. Specifically, the bar 632 represents the SERS intensity of the plain chromatography paper substrate 102c3. The bars 634 and 636 represent the SERS intensities of the second SERS sensor 100b and first SERS sensor 100a, respectively. The first SERS sensor 100a generated an enhanced SERS intensity compared to that of the second SERS sensor 100b by a factor of approximately 108. Evidently, the first SERS sensor 100a with the anisotropic nanostars 106a is more effective than the second SERS sensor 100b with the isotropic small nanospheres 106d.

In Figure 6C, the experiment was performed on a first SERS sensor 100a having anisotropic gold nanostars 106a deposited on a copy paper substrate 102c1, and on a second SERS sensor 100b having isotropic gold small nanospheres 106d deposited on a copy paper substrate 102c1. The nanostars 106a and small nanospheres 106d were modified with SH-PEG-methoxyl, and were deposited on the respective copy paper substrates 102c1 by inkjet printing. The copy paper substrates 102c1 were silanized prior to said inkjet printing. The chart 640 shows the Raman spectra of the SERS sensors 100ab for detecting 1 mM of malachite green. Specifically, the chart lines 642 and 644 represent the Raman spectra of the first SERS sensor 100a with and without malachite green, respectively. Notably, in the chart line 642, the peak intensity occurred at Raman shift 1618 cm^{-1} . The chart lines 646 and 648 represent the Raman spectra of the second SERS sensor 100b with and without malachite green, respectively. The chart 650 shows the SERS intensities of the SERS sensors 100ab at Raman shift 1618 cm^{-1} in comparison with a plain copy paper substrate 102c1 without the 3D nanomaterials 104. Specifically, the bar 652 represents the SERS intensity of the plain copy paper substrate 102c1. The bars 654 and 656 represent the SERS intensities of the second SERS sensor 100b and first SERS sensor 100a, respectively. The first SERS sensor 100a generated an

enhanced SERS intensity compared to that of the second SERS sensor 100b by a factor of approximately 10. Evidently, the first SERS sensor 100a with the anisotropic nanostars 106a is more effective than the second SERS sensor 100b with the isotropic small nanospheres 106d.

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With reference to Figure 7A and Figure 7B, an experiment was performed to demonstrate the capability of the SERS sensors 100 with plastic and metallic substrates 102ab to detect the pesticide malachite green oxalate.

10 In Figure 7A, the experiment was performed on a first SERS sensor 100a having anisotropic gold nanostars 106a deposited on an aluminum foil substrate 102b, and on a second SERS sensor 100b having isotropic gold small nanospheres 106d deposited on an aluminum foil substrate 102b. The nanostars 106a and small nanospheres 106d were modified with SH-PEG-methoxyl, and were deposited on
15 the respective aluminum foil substrates 102b by drop casting. The chart 700 shows the Raman spectra of the SERS sensors 100ab for detecting 100 μM of malachite green. Specifically, the chart lines 702 and 704 represent the Raman spectra of the first SERS sensor 100a with and without malachite green, respectively. Notably, in the chart line 702, the peak intensity occurred at Raman shift 1618 cm^{-1} . The chart
20 lines 706 and 708 represent the Raman spectra of the second SERS sensor 100b with and without malachite green, respectively. The chart 710 shows the SERS intensities of the SERS sensors 100ab at Raman shift 1618 cm^{-1} in comparison with a plain aluminum foil substrate 102b without the 3D nanomaterials 104. Specifically, the bar 712 represents the SERS intensity of the plain aluminum foil substrate 102b.
25 The SERS intensity from the bar 712 may be interpreted as the background noise. The background noise is very low / nearly zero, indicating that the aluminum foil substrate 102b is suitable for use for a SERS sensor 100 with minimal interference. The bars 714 and 716 represent the SERS intensities of the second SERS sensor 100b and first SERS sensor 100a, respectively. The first SERS sensor 100a
30 generated an enhanced SERS intensity compared to that of the second SERS sensor 100b by a factor of approximately 71. Evidently, the first SERS sensor 100a

with the anisotropic nanostars 106a is more effective than the second SERS sensor 100b with the isotropic small nanospheres 106d.

In Figure 7B, the experiment was performed on a first SERS sensor 100a having anisotropic gold nanostars 106a deposited on a PET film substrate 102a, and on a second SERS sensor 100b having isotropic gold small nanospheres 106d deposited on a PET film substrate 102a. The nanostars 106a and small nanospheres 106d were modified with SH-PEG-methoxyl, and were deposited on the respective PET film substrates 102a by drop casting. The chart 720 shows the Raman spectra of the SERS sensors 100ab for detecting 100 μ M of malachite green. Specifically, the chart lines 722 and 724 represent the Raman spectra of the first SERS sensor 100a with and without malachite green, respectively. Notably, in the chart line 722, the peak intensity occurred at Raman shift 1618 cm^{-1} . The chart lines 726 and 728 represent the Raman spectra of the second SERS sensor 100b with and without malachite green, respectively. The chart 730 shows the SERS intensities of the SERS sensors 100ab at Raman shift 1618 cm^{-1} in comparison with a plain PET film substrate 102a without the 3D nanomaterials 104. Specifically, the bar 732 represents the SERS intensity of the plain PET film substrate 102a. The bars 734 and 736 represent the SERS intensities of the second SERS sensor 100b and first SERS sensor 100a, respectively. The first SERS sensor 100a generated an enhanced SERS intensity compared to that of the second SERS sensor 100b by a factor of approximately 91. The PET film substrate 102a contributes to the significantly strong SERS intensity due to its hydrophobic surface that minimizes the spread of hydrophilic ink droplets. Evidently, the first SERS sensor 100a with the anisotropic nanostars 106a is more effective than the second SERS sensor 100b with the isotropic small nanospheres 106d.

With reference to Figure 8A to Figure 8C, an experiment was performed to demonstrate the capability of the SERS sensors 100 with paper substrates 102c to detect another analyte, specifically a pesticide thiram.

In Figure 8A, the experiment was performed on a first SERS sensor 100a having anisotropic gold nanocubes 106b deposited on a copy paper substrate 102c1, and on a second SERS sensor 100b having isotropic gold big nanospheres 106c deposited on a copy paper substrate 102c1. The nanocubes 106b and big nanospheres 106c were modified with SH-PEG-carboxyl, and were deposited on the respective copy paper substrates 102c1 by drop casting. The copy paper substrates 102c1 were silanized prior to said drop casting. The chart 800 shows the Raman spectra of the SERS sensors 100ab for detecting 100 μM of thiram. Specifically, the chart lines 802 and 804 represent the Raman spectra of the first SERS sensor 100a with and without thiram, respectively. Notably, in the chart line 802, there are two peak intensities that occurred at Raman shifts 931 cm^{-1} and 1383 cm^{-1} . The chart lines 806 and 808 represent the Raman spectra of the second SERS sensor 100b with and without thiram, respectively. The charts 810 and 820 show the SERS intensities of the SERS sensors 100ab at Raman shifts 931 cm^{-1} and 1383 cm^{-1} , respectively. The bars 812 and 822 represent the SERS intensities of the second SERS sensor 100b, and the bars 814 and 824 represent the SERS intensities of the first SERS sensor 100a. The first SERS sensor 100a generated an enhanced SERS intensity compared to that of the second SERS sensor 100b by a factor of approximately 12. Evidently, the first SERS sensor 100a with the anisotropic nanocubes 106b is more effective than the second SERS sensor 100b with the isotropic big nanospheres 106c.

In Figure 8B, the charts 830 and 840 show the Raman spectra of the SERS sensor 100a, having anisotropic gold nanocubes 106b deposited on a silanized copy paper substrate 102c1, for detecting thiram in different concentrations ranging from 10 nM to 1 mM. The lowest detection limit of thiram is 10 nM which is lower than its maximum residue limit of 21 μM . Evidently, the SERS sensor 100a is able to detect thiram at concentration as low as 10 nM.

In Figure 8C, the chart 850 show the Raman spectra of the SERS sensor 100a, having anisotropic gold nanocubes 106b deposited on a silanized copy paper substrate 102c1, as well as of a conventional rigid MatoS SERS sensor for detecting

thiram in a 0.5 μL (100 μM) thiram solution. Specifically, the chart lines 852 and 854 represent the Raman spectra of the first SERS sensor 100a with and without thiram, respectively. Notably, in the chart line 852, the peak intensity occurred at Raman shift 1383 cm^{-1} . The chart lines 856 and 858 represent the Raman spectra of the MatoS SERS sensor with and without thiram, respectively. The chart 860 shows the SERS intensities of the SERS sensor 100a and MatoS SERS sensor at Raman shift 1383 cm^{-1} . The bars 862 and 864 represent the SERS intensities of the second MatoS SERS sensor and first SERS sensor 100a, respectively. The first SERS sensor 100a generated an enhanced SERS intensity compared to that of the MatoS SERS sensor by a factor of approximately 80. Evidently, the first SERS sensor 100a is more effective than the conventional rigid MatoS SERS sensor.

With reference to Figure 9A and Figure 9B, an experiment was performed to demonstrate the capability of the SERS sensors 100 to detect thiram extracted from an apple 900.

In Figure 9A, the experiment was performed on a first SERS sensor 100a having anisotropic gold nanocubes 106b deposited on a copy paper substrate 102c1 by drop casting. The nanocubes 106b were modified with SH-PEG-carboxyl and the copy paper substrate 102c1 was silanized prior to said drop casting. The apple 900 contains thiram in a 0.5 μL (100 μM) thiram solution. The first SERS sensor 100a was used in a "swap-and-test" mode (direct mode) to sample the thiram from the apple 900. Specifically, the first SERS sensor 100a sampled the thiram by directly contacting the apple 900. The chart 910 shows the Raman spectra of the first SERS sensor 100a for detecting the thiram. The chart lines 912 and 914 represent the Raman spectra of the first SERS sensor 100a with and without thiram, respectively, the latter serving as a control line. Notably, in the chart line 912, the peak intensity occurred at Raman shift 1383 cm^{-1} .

In Figure 9B, the experiment was performed on a second SERS sensor 100b having anisotropic gold nanocubes 106b deposited on a chromatography paper substrate 102c3 by drop casting. The nanocubes 106b were modified with SH-PEG-carboxyl.

The apple 900 contains thiram in a 0.5 μL (20 μM) thiram solution. The second SERS sensor 100b was used in a “swap-and-test” mode (indirect mode) to sample the thiram from the apple 900. Specifically, a piece of plain chromatography paper 902 samples the thiram by directly contacting the apple 900. The thiram sample is then delivered from the plain chromatography paper 902 to the second SERS sensor 100b by a microfluidic channel for final testing. The chart 920 shows the Raman spectra of the second SERS sensor 100b for detecting the thiram. The chart lines 922 and 924 represent the Raman spectra of the second SERS sensor 100b with and without thiram, respectively, the latter serving as a control line. Notably, in the chart line 922, the peak intensity occurred at Raman shift 1383 cm^{-1} .

From the Raman spectra in Figure 9A and Figure 9B, it can be seen that the SERS sensors 100 can be used for direct sampling of analytes from any sample surface including a curved surface such as of the apple 900. The SERS sensors 100 can be used in the “swap-and-test” mode in either direct mode or indirect mode.

As can be seen from the results of the various experiments, anisotropic nanostars 106a and nanocubes 106b offer significantly enhanced SERS sensitivity and better SERS assay performance than lower dimension nanostructures, such as isotropic nanospheres. The SERS sensitivity and performance is due to the pointed end portions 108 of the anisotropic nanostars 106a and nanocubes 106b. The pointed end portions 108 at as efficient nanoantennas to concentrate localized electromagnetic field at the edge of each pointed end portion 108, giving rise to multiple intrinsic SERS hot spots within a single nanostructure 106. This leads to significantly enhanced SERS response relative to lower dimension nanostructures. Additionally, the use of flexible substrates 102 for the SERS sensors 100, such as paper, offers higher surface areas and in turn further increase the SERS sensitivity. This was demonstrated in the experiment shown in Figure 8C.

The various printing processes for depositing the 3D nanomaterials 104 on the flexible substrate 102 are low cost and scalable for mass production of SERS sensors 100. These printing processes are compatible with the different types of

flexible substrates 102, including paper, PET film, and aluminum foil. Such printing processes can thus meet large scale fabrication demand and at much lower cost, compared to conventional processes which require rigorous manufacturing conditions such as vacuum / clean room environment. Particularly, gravure printing
5 shows the highest potential for mass production among the other printing processes.

The SERS sensors 100 described herein offer direct sampling of analytes, enabling sensing manners such as “swab-and-test”, “dip-and-test”, and “in packaging sensing” with minimal preparation steps on the analytes. By direct sampling, the analytes
10 need not be transferred from the sample surface to the SERS sensor 100 via some communication channel which could contaminate the analytes and compromise the SERS performance. Various experiments have been performed to evaluate the SERS performance of the SERS sensors 100 for certain analytes including pesticides malachite green oxalate and thiram. The evaluation of the SERS sensors
15 100 show that the SERS sensors 100 are applicable in a wide range of areas including, but not limited to, food safety, forensic science, aquaculture, biomedical, and environmental monitoring.

In the foregoing detailed description, embodiments of the present disclosure in
20 relation to SERS sensors are described with reference to the provided figures. The description of the various embodiments herein is not intended to call out or be limited only to specific or particular representations of the present disclosure, but merely to illustrate non-limiting examples of the present disclosure. The present disclosure serves to address at least one of the mentioned problems and issues associated
25 with the prior art. Although only some embodiments of the present disclosure are disclosed herein, it will be apparent to a person having ordinary skill in the art in view of this disclosure that a variety of changes and/or modifications can be made to the disclosed embodiments without departing from the scope of the present disclosure. Therefore, the scope of the disclosure as well as the scope of the following claims is
30 not limited to embodiments described herein.

Claims

1. A surface-enhanced Raman spectroscopy (SERS) sensor comprising:
a flexible substrate; and
5 anisotropic ink printed on the flexible substrate, the anisotropic ink comprising 3D anisotropic gold nanostars deposited on the flexible substrate, wherein the gold nanostars in the anisotropic ink are modified with a thiolated polyethylene glycol (PEG) derivative.
- 10 2. The SERS sensor according to claim 1, wherein the flexible substrate is formed of one of paper, plastic, and metallic materials.
3. The SERS sensor according to claim 2, wherein the flexible substrate is a plastic substrate comprising polyethylene terephthalate (PET) film.
- 15 4. The SERS sensor according to claim 2, wherein the flexible substrate is a metallic substrate comprising aluminum foil.
5. The SERS sensor according to claim 2, wherein the flexible substrate is a paper
20 substrate comprising one of copy paper, filter paper, and chromatography paper.
6. The SERS sensor according to claim 5, wherein the paper substrate is silanized.
7. The SERS sensor according to any one of claims 1 to 6, wherein the thiolated
25 PEG derivative is SH-PEG-methoxyl or SH-PEG-carboxyl.
8. The SERS sensor according to any one of claims 1 to 7, wherein the anisotropic ink is printed using one of inkjet printing, drop casting, and gravure printing.
- 30 9. The SERS sensor according to claim 8, wherein said drop casting is assisted by wax printing.

10. A method of manufacturing a surface-enhanced Raman spectroscopy (SERS) sensor, the method comprising:

preparing a flexible substrate;

preparing anisotropic ink comprising 3D anisotropic gold nanostars,;

5 modifying the gold nanostars in the anisotropic ink with a thiolated polyethylene glycol (PEG) derivative; and

printing the anisotropic ink on the flexible substrate, thereby depositing the modified gold nanostars on the flexible substrate and forming the SERS sensor.

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11. The method according to claim 10, wherein the flexible substrate is formed of one of paper, plastic, and metallic materials.

12. The method according to claim 11, wherein the flexible substrate is a plastic
15 substrate comprising polyethylene terephthalate (PET) film.

13. The method according to claim 11, wherein the flexible substrate is a metallic substrate comprising aluminum foil.

20 14. The method according to claim 11, wherein the flexible substrate is a paper substrate comprising one of copy paper, filter paper, and chromatography paper.

15. The method according to claim 14, said preparing of the paper substrate comprising silanizing the paper substrate.

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16. The method according to claim 15, said silanizing of the paper substrate comprising:

immersing the paper substrate in a toluene solvent comprising phenyltriethoxysilane;

30

incubating the paper substrate after said immersing;

rinsing the paper substrate with ethanol after said incubating; and

thermal curing the paper substrate after said rinsing.

17. The method according to any one of claims 10 to 16, wherein the thiolated PEG derivative is SH-PEG-methoxyl or SH-PEG-carboxyl.

18. The method according to any one of claims 10 to 17, wherein said printing of
5 the anisotropic ink comprises inkjet printing using the anisotropic ink.

19. The method according to any one of claims 10 to 17, wherein the said printing of the anisotropic ink comprises drop casting using a patterned ink barrier comprising the anisotropic ink on its surface.

10

20. The method according to claim 19, wherein the patterned ink barrier is fabricated by wax printing.

21. The method according to any one of claims 10 to 17, wherein said printing of
15 the anisotropic ink comprises gravure printing using a metallic plate comprising a predefined pattern, wherein the metallic anisotropic nanostructures are printed on the flexible substrate according to the predefined pattern.