Device and system for collecting and analyzing vapor condensate, particularly exhaled breath condensate, as well as method of using the same

CROSS-REFERENCING

This application claims the benefit of provisional application serial nos. 62/218,455 filed on September 14, 2015, 62/293,188, filed on February 9, 2016, 62/305,123, filed on March 8, 2016, 62/369,181, filed on July 31, 2016 and of PCT application serial no. PCT/US16/46437, filed on August 20, 2016, which POT application claims the benefit of provisional application serial nos. 62/202,989, filed on August 10, 2015, 62/218,455 filed on September 14, 2015, 62/293,188, filed on February 9, 2016, 62/305,123, filed on March 8, 2016, and 62/369,181, filed on July 31, 2016, all of which applications are incorporated herein in their entireties for all purposes.

FIELD

The present invention is related to the field of bio/chemical sampling, sensing, assays and applications.

BACKGROUND

In bio/chemical vapor condensate sample analysis, particularly exhaled breath condensate (EBC), there is a need for the methods and devices that can simplify the sample collection and measurement processes, that can accelerate the process (e.g. binding, mixing reagents, etc.) and quantify the parameters (e.g. analyte concentration, the sample volume, etc.),that can handle samples with small volume, that allow an entire assay performed in less than a minute, that allow an assay performed by a smartphone (e.g. mobile phone), that allow nonprofessional to perform an assay her/himself, and that allow a test result to be communicated locally, remotely, or wirelessly to different relevant parties. The present invention relates to the methods, devices, and systems that can address these needs.

SUMMARY

The following brief summary is not intended to include all features and examples of the present disclosure. The present disclosure is related to the field of bio/chemical sensing, assays and applications. Particularly, the present disclosure is related to collecting a small amount of a

vapor condensate sample (e.g. the exhaled breath condensate (EBC) from a subject of a volume as small as 10 fL (femto-Liter) in a single drop), preventing or significantly reducing an evaporation of the collected vapor condensate sample, analyzing the sample, analyzing the sample by mobile-phone, and performing such collection and analysis by a person without any professionals.

In one aspect, the present disclosure refers to a device for collecting and analyzing vapor condensate (VC) sample, comprising:

a collection plate and a cover plate, wherein:

i. the plates are movable relative to each other into different configurations;

ii. one or both plates are flexible;

iii. each of the plates has, on its respective surface, a sample contact area for contacting a vapor condensate (VC) sample that contains an analyte;

iv. one or both of the plates comprise spacers that are fixed with a respective plate, wherein the spacers have a predetermined substantially uniform height and a predetermined constant inter-spacer distance and wherein at least one of the spacers is inside the sample contact area;

wherein one of the configurations is an open configuration, in which: the two plates are either completely or partially separated apart, the spacing between the plates is not regulated by the spacers, and the VC sample is deposited on one or both of the plates; and

wherein another of the configurations is a closed configuration which is configured after the VC sample deposition in the open configuration; and in the closed configuration: at least a part of the VC sample is between the two plates and in contact with the two plates, and has a highly uniform thickness that is regulated by the spacers and the two sample surfaces of the plates and is equal to or less than 30 μm with a small variation.

In another aspect, the present disclosure refers to a system for rapidly analyzing a vapor condensation sample using a mobile communication device comprising:

(a) a device as disclosed herein; and

(b) a mobile communication device comprising:

i. one or a plurality of cameras for detecting a signal and/or imaging the vapor condensate sample; and

ii. electronics, signal processors, hardware and software for receiving and/or processing the detected signal and/or the image of the vapor condensate sample and for remote communication.

In another aspect, the present disclosure refers to a method for rapidly analyzing an analyte in a sample using a mobile phone, comprising:

(a) depositing a sample on the device as disclosed herein;

(b) assaying an analyte in the sample deposited on the device to generate a result; and

(c) communicating the result from the mobile communication device to a remote location from the mobile communication device.

In another aspect, the present disclosure refers to a method for analyzing an analyte in a vapor condensate sample comprising:

obtaining a device as disclosed herein;

depositing the vapor condensate sample onto one or both plates of the device;

placing the plates in the closed configuration and applying an external force over at least part of the plates; and

analyzing the analyte in the layer of uniform thickness while the plates are in the closed configuration.

In another aspect, the present disclosure refers to a method for analyzing an analyte in a vapor condensate sample, wherein the method comprises:

(a) obtaining the device as disclosed herein wherein the spacers have:

i. a pillar shape with substantially uniform cross-section and a flat top surface;

ii. a ratio of the width to the height equal to or larger than one;

iii. a predetermined constant inter-spacer distance that is in the range of 10 µm to 200 µm; and

iv. a filling factor equal to 1% or larger; and

(b) depositing a sample on one or both of the plates when the plates are configured in the open configuration;

(c), after (b), using the two plates to compress at least part of the sample into the layer of substantially uniform thickness that has an average value equal to or less than 30 µm with a variation of less than 10%, wherein the compressing comprises:

bringing the two plates together; and

conformable pressing, either in parallel or sequentially, an area of at least one of the plates to press the plates together to a closed configuration, wherein the conformable pressing generates a substantially uniform pressure on the plates over the at least part of the sample, and the pressing spreads the at least part of the sample laterally between the sample contact surfaces of the plates, and wherein the closed configuration is a configuration in which the spacing between the plates in the layer of uniform thickness region is regulated by the spacers; and

(d) analyzing the analyte in the layer of uniform thickness while the plates are the closed configuration;

wherein the filling factor is the ratio of the spacer contact area to the total plate area;

wherein a conformable pressing is a method that makes the pressure applied over an area is substantially constant regardless the shape variation of the outer surfaces of the plates; and

wherein the parallel pressing applies the pressures on the intended area at the same time, and a sequential pressing applies the pressure on a part of the intended area and gradually move to other area.

BRIEF DESCRIPTION OF THE DRAWINGS

The skilled artisan will understand that the drawings, described below, are for illustration purposes only. The drawings are not intended to limit the scope of the present teachings in anyway. The drawings may not be in scale. In the figures that present experimental data points, the lines that connect the data points are for guiding a viewing of the data only and have no other means.

Fig. 1 An illustration of certain aspects of an exemplary device and methods of collecting exhaled breath condensate (EBC) using a SiEBCA (Single-drop EBC Collector/Analyzer).

Fig. 2 An illustration of different formations of EBC at closed configuration of SiEBCA depends on spacer height. In closed configureation-1: If spacer height is smaller than average height of EBC at open configuration: at closed configuration, EBC become a continuous thin film contacting both collection and cover plates and may have air isolated pockets. In the closed condiguraiton-2: If spacer height is larger than average height of EBC at open configuration; at closed configuration EBC become isolated puddle(s) that contact both collection and cover plates, and that are larger but fewer than that at the open configuration.

Fig. 3. An illustration of an embodiment of the devices and the methods of a SiEBCA (Single-drop EBC Collector/Analyzer).

Fig. 4. An illustration of a SiEBCA with both "open spacer' and "enclosed spacer", where the open spacer is a post (pillar) while the enclosed spacer is a ring spacer (d) and a four chamber grid spacer (e).

Fig. 5. The surface wetting properties for an untreated and a treated (for better wetting than untreated surface) surface of a collection plate.

Fig. 6. Methods of pressing the plates of SiEBCA by human hand.

Fig. 7. Experimental data of EBC Droplets sizes and density on the collection plate (untreated PMMA film) at an "open configuration" (e.g. only the collection plate without the cover plate.

Fig. 8. Experimental data of EBC formation on the collection plate which is a surface treated PMMA film) at a plate open configuration.

CLAIMS

1. A device for collecting and analyzing vapor condensate (VC) sample, comprising: a collection plate and a cover plate, wherein:

i. the plates are movable relative to each other into different configurations;

ii. one or both plates are flexible;

iii. each of the plates has, on its respective surface, a sample contact area for contacting a vapor condensate (VC) sample that contains an analyte;

iv. one or both of the plates comprise spacers that are fixed with a respective plate, wherein the spacers have a predetermined substantially uniform height and a predetermined constant inter-spacer distance and wherein at least one of the spacers is inside the sample contact area;

wherein one of the configurations is an open configuration, in which: the two plates are either completely or partially separated apart, the spacing between the plates is not regulated by the spacers, and the VC sample is deposited on one or both of the plates; and

wherein another of the configurations is a closed configuration which is configured after the VC sample deposition in the open configuration; and in the closed configuration: at least a part of the VC sample is between the two plates and in contact with the two plates, and has a highly uniform thickness that is regulated by the spacers and the two sample surfaces of the plates and is equal to or less than 30 μm with a small variation.

2. The device of claim 1, wherein the device further comprises a dry reagent coated on one or both of the plates.

3. The device of claim 2, wherein the dry binding site comprises a capture agent.

4. The device of claim 2, wherein the dry binding site comprises an antibody or a nucleic acid.

5. The device of claim 2, wherein the releasable dry reagent is a cell stain.

6. The device of claim 1, wherein the device further comprises, on one or both plates, a releasable dry reagent and a release time control material that delays the time that the releasable dry regent is released into the sample.

7. The device of claim 6, wherein the releasable dry reagent is a labeled reagent.

8. The device of claim 6, wherein the releasable dry reagent is a fluorescently labeled reagent.

9. The device of claim 6, wherein the releasable dry reagent is a fluorescently labeled antibody.

10. The device of claim 1, wherein the device further comprises, on one or both plates, a dry binding site that has a predetermined area, wherein the dry binding site binds to and immobilizes the analyte in the sample.

11. The device of claim 6, wherein the release time control material delays the time that the releasable dry reagent starts to be released into the sample by at least 3 seconds.

12. The device of claim 1, wherein the device further comprises, on one or both plates, one or a plurality of dry binding sites and/or one or a plurality of reagent sites.

13. The device of claim 1, wherein the sample is exhale breath condensate.

14. The device of claim 1, wherein the sample is a vapor from a biological sample, an environmental sample, a chemical sample, or a clinical sample.

15. The device of claim 1, wherein the analyte comprises a molecule (e.g., a protein, peptides, DNA, RNA, nucleic acid, or other molecules), cells, tissues, viruses, or nanoparticles with different shapes.

16. The device of claim 1, wherein the analyte comprises volatile organic compounds

(VOCs).

17. The device of claim 1, wherein the analyte comprises nitrogen, oxygen, CO_2, H_2O, or inert gases.

18. The device of claim 1, wherein the analyte is stained.

19. The device of claim 1, wherein on one of the surfaces that contacts the sample, it further comprises an enclosure-spacer that encloses a partial or entire VC sample deposited on the collection plate.

20. The device of claim 1, wherein the highly uniform thickness has a value equal to or less than 0.5 um.

21. The device of claim 1, wherein the highly uniform thickness has a value in the range of 0.5 um to 1 um.

22. The device of claim 1, wherein the highly uniform thickness has a value in the range of 1 um to 2 um.

23. The device of claim 1, wherein the highly uniform thickness has a value in the range of 2 um to 10 um.

24. The device of claim 1, wherein the highly uniform thickness has a value in the range of 10 um to 20 um.

25. The device of claim 1, wherein the highly uniform thickness has a value in the range of 20 um to 30 um.

26. The device of claim 1, wherein the thickness of the at least a part of VC sample at the closed configuration is larger than the thickness of VC sample deposited on the collection plate at the open configuration.

27. The device of claim 1, wherein the thickness of the at least a part of the VC sample at the closed configuration is less than the thickness of the VC sample deposited on the

collection plate at the open configuration.

28. The device of claim 1, wherein the spacers are fixed on the plate by directly embossing the plate or injection molding of the plate.

29. The device of claim 1, wherein a material of the plate and the spacers is selected from the group consisting of polystyrene, PMMA, PC, COC, COP, and another plastic.

30. The device of claim 1, wherein the inter-spacer distance is in the range of 1 um to 200 um.

31. The device of claim 1, wherein the inter-spacer distance is in the range of 200 um to 1000 um.

32. The device of claim 1, wherein the VC sample is an exhaled breath condensate from a human or an animal.

33. The device of claim 1, wherein the spacers regulating the layer of uniform thickness have a filling factor of at least 1 %, wherein the filling factor is a ratio of a spacer area in contact with the layer of highly uniform thickness to a total plate area in contact with the layer of highly uniform thickness.

34. The device of claim 1, wherein for spacers regulating the layer of highly uniform thickness, Young's modulus of the spacers times a filling factor of the spacers is equal to or larger than 10 MPa, wherein the filling factor is the ratio of a spacer area in contact with the layer of highly uniform thickness to a total plate area in contact with the layer of highly uniform thickness.

35. The device of claim 1, wherein for a flexible plate, a thickness of the flexible plate times a Young's modulus of the flexible plate is in the range of 60 to 750 GPa-um.

36. The device of claim 1, wherein for a flexible plate, a fourth power of the interspacer-distance (ISD) divided by a thickness of the flexible plate (h) and a Young's modulus (E) of the flexible plate, $ISD^4/(hE)$, is equal to or less than 10^6 um^3/GPa.

37. The device of claim 1, wherein one or both plates comprises a location marker, either on a surface of or inside the plate, that provides information of a location of the plate.

38. The device of claim 1, wherein one or both plates comprises a scale marker, either on a surface of or inside the plate, that provides information of a lateral dimension of a structure of the sample and/or the plate.

39. The device of claim 1, wherein one or both plates comprises an imaging marker, either on surface of or inside the plate, that assists imaging of the sample.

40. The device of claim 1, wherein the spacers function as a location marker, a scale marker, an imaging marker, or any combination thereof.

41. The device of claim 1, wherein the average thickness of the layer of uniform thickness is about equal to a minimum dimension of the analyte in the sample.

42. The device of claim 1, wherein the inter-spacer distance is in the range of 1 μm to 50 μm.

43. The device of claim 1, wherein the inter-spacer distance is in the range of 50 μm to 120 μm.

44. The device of claim 1, wherein the inter-spacer distance is in the range of 120 μm to 200 μm.

45. The device of claim 1, wherein the inter-spacer distance is substantially periodic.

46. The device of claim 1, wherein the spacers are pillars with a cross-sectional shape selected from the group consisting of round, polygonal, circular, square, rectangular, oval, elliptical, and any combination of the same.

47. The device of claim 1, wherein the spacers have a pillar shape and have a substantially flat top surface, wherein, for each spacer, a ratio of the lateral dimension of the spacer to its height is at least 1.

48. The device of claim 1, wherein for each spacer, a ratio of the lateral dimension of the spacer to its height is at least 1.

49. The device of claim 1, wherein a minimum lateral dimension of the spacer is less than or substantially equal to the minimum dimension of the analyte in the sample.

50. The device of claim 1, wherein a minimum lateral dimension of the spacer is in the range of 0.5 µm to 100 µm.

51. The device of claim 1, wherein a minimum lateral dimension of the spacer is in the range of 0.5 µm to 10 µm.

52. The device of claim 1, wherein the spacers have a density of at least 100/mm^2.

53. The device of claim 1, wherein the spacers have a density of at least 1000/mm^2.

54. The device of claim 1, wherein at least one of the plates is transparent.

55. The device of claim 1, wherein at least one of the plates is made from a flexible polymer.

56. The device of claim 1, wherein, for a pressure that compresses the plates, the spacers are not compressible and/or, independently, only one of the plates is flexible.

57. The device of claim 1, wherein the flexible plate has a thickness in the range of 10 µm to 200 µm.

58. The device of claim 1, wherein the small variation is less than 30 %.

59. The device of claim 1, wherein the small variation is less than 10 %.

60. The device of claim 1, wherein the small variation is less than 5 %.

61. The device of claim 1, wherein the collection and cover plates are connected and are configured to be changed from the open configuration to the closed configuration by folding the plates.

62. The device of claim 1, wherein the collection and cover plates are connected by a hinge and are configured to be changed from the open configuration to the closed configuration by folding the plates along the hinge.

63. The device of claim 1, wherein the collection and cover plates are connected by a hinge that is a separate material to the plates, and are configured to be changed from the open configuration to the closed configuration by folding the plates along the hinge.

64. The device of claim 1, wherein the collection and cover plates are made in a single piece of material and are configured to be changed from the open configuration to the closed configuration by folding the plates.

65. The device of claim 1, wherein the layer of highly uniform thickness of the sample is uniform over a lateral area that is at least 100 um^2.

66. The device of claim 1, wherein the layer of highly uniform thickness of the sample is uniform over a lateral area that is at least 1 mm^2.

67. The device of claim 1, wherein the device is configured to analyze the sample in 60 seconds or less.

68. The device of claim 1, wherein at the closed configuration, the final sample thickness device is configured to analyze the sample in 60 seconds or less.

69. The device of claim 1, wherein the device further comprises, on one or both of the plates, one or a plurality of amplification sites that are each capable of amplifying a signal from the analyte or a label of the analyte when the analyte or label is within 500 nm from the amplification site.

70. The device of claim 1, wherein at the closed configuration, the final sample thickness device is configured to analyze the sample in 10 seconds or less.

71. The device of claim 1, wherein the collection or cover plate further comprises, on its surface, a first predetermined assay site and a second predetermined assay site, wherein

the distance between an edge of the first predetermined assay site and an edge of the second predetermined assay site is substantially larger than the thickness of the layer of highly uniform thickness when the plates are in the closed position, wherein at least a part of the layer of highly uniform thickness is over the predetermined assay sites, and wherein the sample has one or a plurality of analytes that are capable of diffusing in the sample.

72. The device of claim 1, wherein the collection or cover plate has, on its surface, at least three analyte assay sites, and the distance between the edges of any two neighboring assay sites is substantially larger than the thickness of the layer of highly uniform thickness when the plates are in the closed position, wherein at least a part of the layer of highly uniform thickness is over the assay sites, and wherein the sample has one or a plurality of analytes that are capable of diffusing in the sample.

73. The device of claim 1, wherein the collection or cover plate has, on its surface, at least two neighboring analyte assay sites that are not separated by a distance that is substantially larger than the thickness of the layer of highly uniform thickness when the plates are in the closed position, wherein at least a part of the layer of highly uniform thickness is over the assay sites, and wherein the sample has one or a plurality of analytes that are capable of diffusing in the sample.

74. The device of claim 1, wherein the device further comprises a detector that is an optical detector for detecting an optical signal.

75. The device of claim 1, wherein the device further comprises a detector that is an electrical detector for detecting an electrical signal.

76. The device of claim 1, wherein the thickness of the at least a part of the VC sample at the closed configuration is less than the thickness of the VC sample deposited on the collection plate at the open configuration.

77. A system for rapidly analyzing a vapor condensation sample using a mobile communication device comprising:

(a) a device of claim 1; and

(b) a mobile communication device comprising:

i. one or a plurality of cameras for detecting a signal and/or imaging the vapor condensate sample; and

ii. electronics, signal processors, hardware and software for receiving and/or processing the detected signal and/or the image of the vapor condensate sample and for remote communication.

78. The system of claim 77, further comprising:

(d) a housing configured to hold the sample and to be mounted to the mobile communication device.

79. The system of claim 78, wherein the housing comprises optics for facilitating the imaging and/or signal processing of the sample by the mobile communication device, and a mount configured to hold the optics on the mobile communication device.

80. The system of claim 78, wherein an element of the optics in the housing is movable relative to the housing.

81. The system of claim 77, wherein the system further comprises a light source from either the mobile communication device or an external source.

82. The system of claim 77, wherein one of the plates has a binding site that binds the analyte, wherein at least part of the uniform sample thickness layer is over the binding site, and is substantially less than the average lateral linear dimension of the binding site.

83. The system of claim 77, wherein the mobile communication device is configured to communicate test results to a medical professional, a medical facility or an insurance company.

84. The system of claim 77, wherein the mobile communication device is further configured to communicate information on a test and a subject with a medical professional, a medical facility or an insurance company.

85. The system of claim 77, wherein the mobile communication device is further configured to communicate information of a test to a cloud network, and the cloud network is configured to process the information to refine a test result.

86. The system of claim 77, wherein the mobile communication device is further configured to communicate information of a test and a subject to a cloud network, the cloud network is configured to process the information to refine a test result, and the refined test results is sent back the subject.

87. The system of claim 77, wherein the mobile communication device is configured to receive a prescription, diagnosis or a recommendation from a medical professional.

88. The system of claim 77, wherein the mobile communication device is configured with hardware and software to:

(a) capture an image of the sample;

(b) analyze a test location and a control location in the image; and

(c) compare a value obtained from analysis of the test location to a threshold value that characterizes the rapid diagnostic test.

89. The system of claim 77, wherein at least one of the plates comprises a storage site in which assay reagents are stored.

90. The system of claim 77, wherein at least one of the cameras reads a signal from the device.

91. The system of claim 77, wherein the mobile communication device communicates with a remote location via a wifi or cellular network.

92. The system of claim 77, wherein the mobile communication device is a mobile phone.

93. A method for rapidly analyzing an analyte in a sample using a mobile phone, comprising:

(a) depositing a sample on the device of claim 1;

(b) assaying an analyte in the sample deposited on the device to generate a result; and

(c) communicating the result from the mobile communication device to a remote location from the mobile communication device.

94. The method of claim 93, wherein the analyte comprises a molecule (e.g., a protein, peptides, DNA, RNA, nucleic acid, or other molecule), cells, tissues, viruses, or nanoparticles with different shapes.

95. The method of claim 93, wherein the analyte comprises white blood cell, red blood cell and platelets.

96. The method of claim 93, wherein the method comprises:

analyzing the result at the remote location to provide an analyzed result; and

communicating the analyzed result from the remote location to the mobile communication device.

97. The method of claim 93, wherein the analyzing is done by a medical professional at a remote location.

98. The method of claim 93, wherein the mobile communication device receives a prescription, diagnosis or a recommendation from a medical professional at the remote location.

99. The method of claim 93, wherein the thickness of the at least a part of VC sample at the closed configuration is larger than the thickness of VC sample deposited on the collection plate at the open configuration.

100. The method of claim 93, wherein the assaying step comprises detecting the analyte in the sample.

101. The method of claim 93, wherein the analyte is a biomarker.

102. The method of claim 93, wherein the analyte is a protein, nucleic acid, cell, or

metabolite.

103. The method of claim 93, wherein the assay done in step (b) is a binding assay or a biochemical assay.

104. A method for analyzing an analyte in a vapor condensate sample comprising:

obtaining a device of claim 1;

depositing the vapor condensate sample onto one or both plates of the device;

placing the plates in the closed configuration and applying an external force over at least part of the plates; and

analyzing the analyte in the layer of uniform thickness while the plates are in the closed configuration.

105. A method for analyzing an analyte in a vapor condensate sample, wherein the method comprises:

(a) obtaining the device of claim 1 wherein the spacers have:

i. a pillar shape with substantially uniform cross-section and a flat top surface;

ii. a ratio of the width to the height equal to or larger than one;

iii. a predetermined constant inter-spacer distance that is in the range of 10 µm to 200 µm; and

iv. a filling factor equal to 1% or larger; and

(b) depositing a sample on one or both of the plates when the plates are configured in the open configuration;

(c), after (b), using the two plates to compress at least part of the sample into the layer of substantially uniform thickness that has an average value equal to or less than 30 µm with a variation of less than 10%, wherein the compressing comprises:

bringing the two plates together; and

conformable pressing, either in parallel or sequentially, an area of at least one of the plates to press the plates together to a closed configuration, wherein the conformable pressing generates a substantially uniform pressure on the plates over

the at least part of the sample, and the pressing spreads the at least part of the sample laterally between the sample contact surfaces of the plates, and wherein the closed configuration is a configuration in which the spacing between the plates in the layer of uniform thickness region is regulated by the spacers; and

(d) analyzing the analyte in the layer of uniform thickness while the plates are the closed configuration;

wherein the filling factor is the ratio of the spacer contact area to the total plate area;

wherein a conformable pressing is a method that makes the pressure applied over an area is substantially constant regardless the shape variation of the outer surfaces of the plates; and

wherein the parallel pressing applies the pressures on the intended area at the same time, and a sequential pressing applies the pressure on a part of the intended area and gradually move to other area.

106. The method of claim 105, wherein the analyzing step comprises counting the analyte in the sample.

107. The method of claim 106, wherein an imaging and the counting is done by:

i. illuminating the cells in the layer of uniform thickness;
ii. taking one or more images of the cells using a CCD or CMOS sensor;
iii. identifying cells in an image of the one or more images using a computer; and
iv. counting a number of cells in an area of the image.

108. The method of claim 105, wherein the method further comprises removing the external force after the plates are in the closed configuration; and imaging the analytes in the layer of uniform thickness while the plates are the closed configuration; and counting a number of analytes or the labels in an area of the image.

109. The method of claim 105, wherein the method comprises removing the external force after the plates are in the closed configuration; and measuring optical signal in the layer of uniform thickness while the plates are in the closed configuration.

110. The method of claim 105, wherein the inter-spacer distance is in the range of 20 µm to 200 µm.

111. The method of claim 105, wherein the inter-spacer distance is in the range of 5 µm to 20 µm.

112. The method of claim 105, wherein a product of the filling factor and a Young's modulus of the spacer is 2 MPa or larger.

113. The method of claim 105, wherein the surface variation is less than 50 nm.

114. The method of claim 105, further comprising a step of calculating a concentration of the analyte in a relevant volume of the sample, wherein the calculation is based on the relevant volume of the sample defined by a predetermined area of a storage site, the thickness of the layer of uniform thickness at the closed configuration, and an amount of target entity detected.

115. The method of claim 104, wherein the external force is provided by human hand.

116. The method of claim 105, wherein the device further comprises a dry reagent coated on one or both plates.

117. The method of claim 105, wherein the layer of uniform thickness of the sample has a thickness uniformity of up to +/-5%.

118. The method of claim 105, wherein the spacers are pillars with a cross-sectional shape selected from round, polygonal, circular, square, rectangular, oval, elliptical, or any combination of the same.

119. The method of claim 105, wherein inter-spacer distance is approximately the minimum dimension of the analyte.

120. The method of claim 105, wherein one or both plate sample contact surfaces comprises one or a plurality of amplification sites that are each capable of amplifying a signal from the analyte or a label of the analyte when the analyte or label is within 500 nm

from an amplification site.

121. The method of claim 105, wherein the sample is exhale breath condensate.

122. The method of claim 105, wherein the sample is a vapor from a biological sample, an environmental sample, a chemical sample, or clinical sample.

123. The method of claim 105, wherein the analyte comprises a molecule (e.g., a protein, peptides, DNA, RNA, nucleic acid, or other molecules), cells, tissues, viruses, and nanoparticles with different shapes.

124. The method of claim 105, wherein the analyte comprises volatile organic compounds (VOCs).

125. The method of claim 105, wherein the analyte comprises nitrogen, oxygen, CO_2, H_2O, and inert gases.

126. The method of claim 105, wherein the analyte is stained.

127. The method of claim 105, wherein on one of the sample surface, it further comprises an enclosure-spacer that encloses a partial or entire VC samples deposited on the collection plate.

128. The method of claim 105, wherein the substantially uniform thickness has a value equal to or less than 0.5 µm.

129. The method of claim 105, wherein the substantially uniform thickness has a value in the range of 0.5 µm to 1 µm.

130. The method of claim 105, wherein the substantially uniform thickness has a value in the range of 1 µm to 2 µm.

131. The method of claim 105, wherein the substantially uniform thickness has a value in the range of 2 µm to 10 µm.

132. The method of claim 105, wherein the substantially uniform thickness has a value in the range of 10 µm to 20 µm.

133. The method of claim 105, wherein the substantially uniform thickness has a value in the range of 20 µm to 30 µm.