US005948694A

United States Patent [19]

Reber et al.

[11] **Patent Number: 5,948,694**

[45] **Date of Patent: Sep. 7, 1999**

[54] **MOLECULAR DETECTION APPARATUS**

[75] Inventors: **William L. Reber**, Schaumburg, Ill.; **Michael K. Stenstrom**, Los Angeles, Calif.; **Cary D. Perttunen**, Shelby Township, Mich.

[73] Assignee: **Motorola, Inc.**, Schaumburg, Ill.

[21] Appl. No.: **08/838,491**

[22] Filed: **Apr. 7, 1997**

[51] **Int. Cl.**[6] **G01N 33/543**; G01N 1/14; G01N 21/00; G01N 21/29

[52] **U.S. Cl.** **436/518**; 436/805; 436/810; 422/50; 422/55; 422/56; 422/58; 422/82.05; 422/310

[58] **Field of Search** 436/518, 805, 436/810; 422/50, 56, 58, 82.05, 310; 210/493.5; 435/278.1, 810

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Primary Examiner—James C. Housel
Assistant Examiner—S. Devi
Attorney, Agent, or Firm—Jeffrey G. Toler; James E. Gauger

[57] **ABSTRACT**

A molecular detection apparatus comprises a molecular receptor (**20**), a detection element (**22**) responsive to the molecular receptor (**20**), and a substrate (**24**) which supports the detection element (**22**). The molecular detection apparatus further includes a grasping member (**26**) and an elongated member (**30**) to couple the grasping member (**26**) to the substrate (**24**).

9 Claims, 4 Drawing Sheets

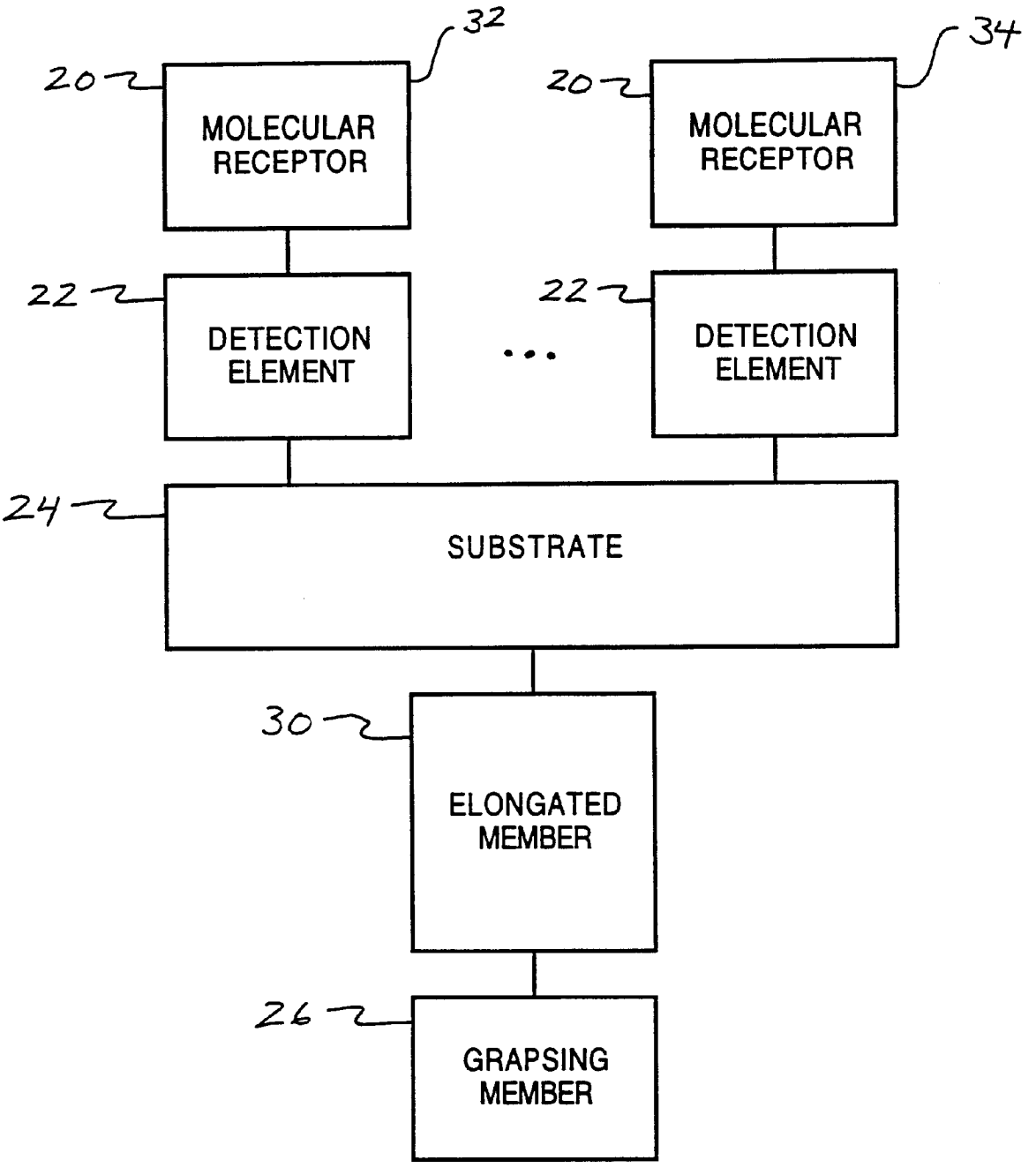

32
34
20
20
MOLECULAR RECEPTOR
MOLECULAR RECEPTOR
22
22
DETECTION ELEMENT
...
DETECTION ELEMENT
24
SUBSTRATE
30
ELONGATED MEMBER
26
GRAPSING MEMBER

FIG. 1

FIG. 2

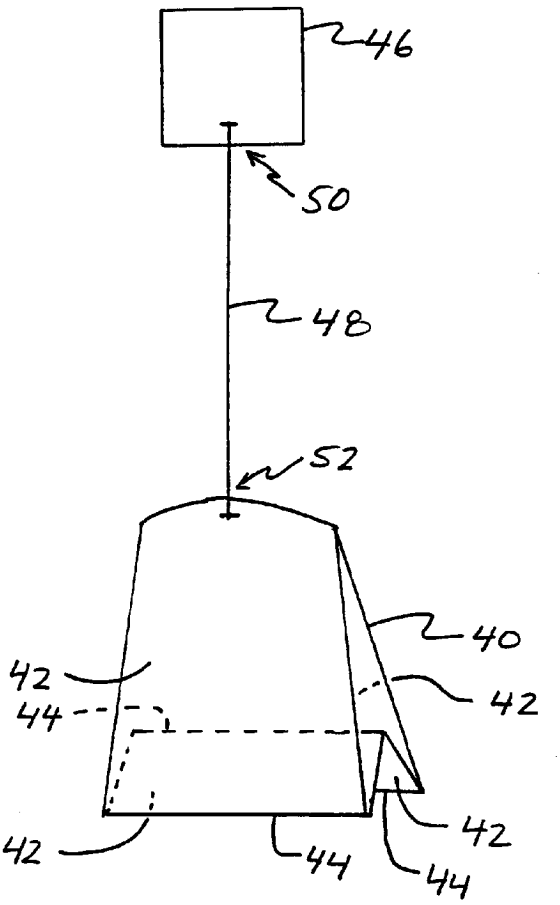


FIG. 3

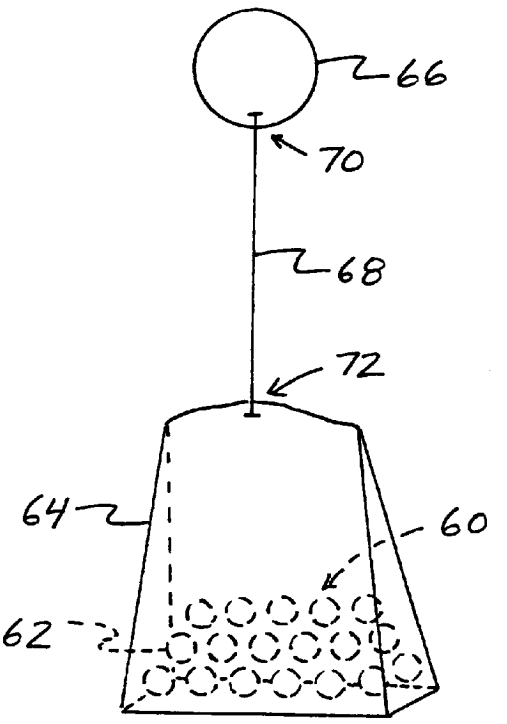


FIG. 4

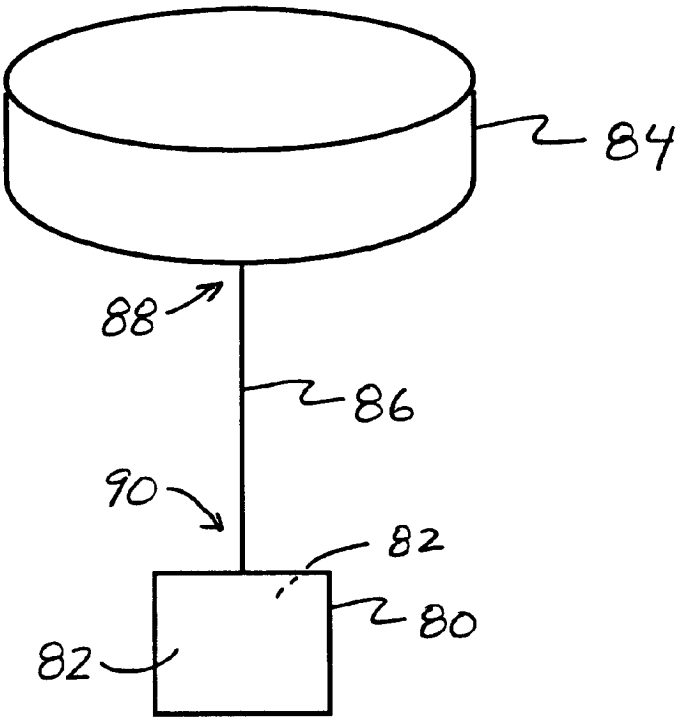
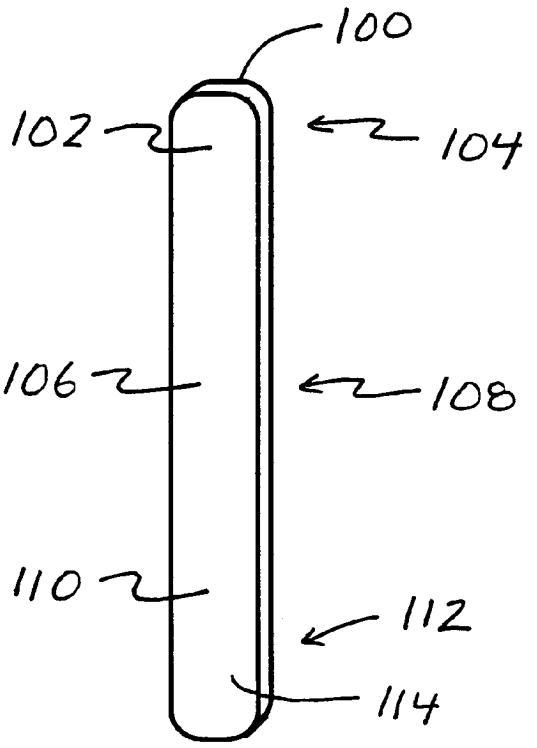


FIG. 5



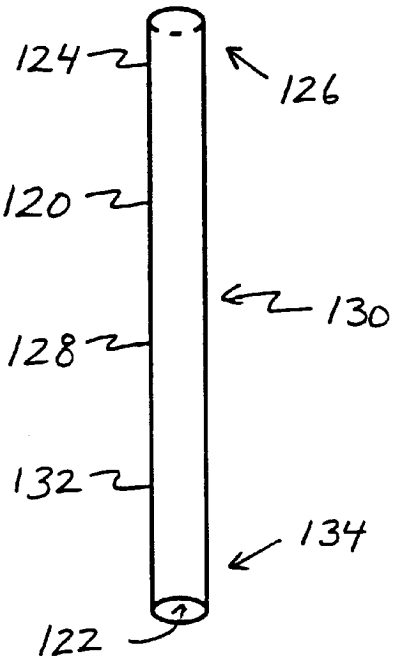


FIG. 6

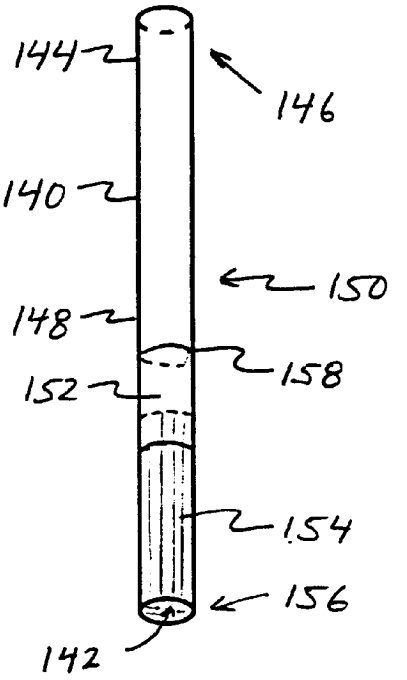


FIG. 7

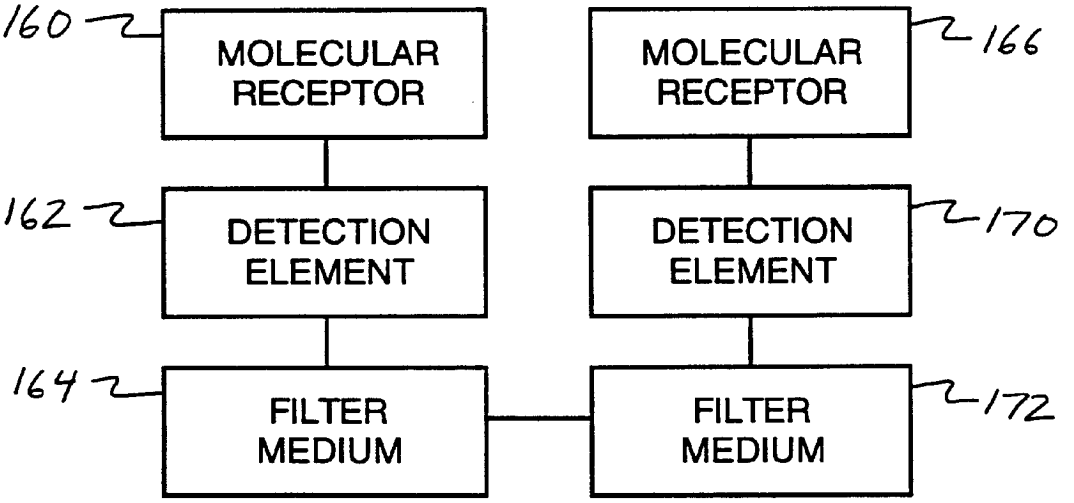


FIG. 8

MOLECULAR DETECTION APPARATUS

TECHNICAL FIELD

The present invention relates to molecular detection devices.

BACKGROUND OF THE INVENTION

Lawrence Berkeley National Laboratory has announced and published methods and systems for direct colorimetric detection of receptor-ligand interaction using a polymerized bilayer sensor. The sensor comprises a plurality of sensor molecules fabricated into a thin film. Each sensor molecule includes a molecular receptor which binds to a molecule of interest, such as *E. coli* 0157:H7. The backbone of the sensor molecule includes a colorimetric detection element in the form of a long diacetylene lipid. Exposure to ultraviolet light links the molecular receptor with the colorimetric detection element by activating a triple bond within the diacetylene lipids. A blue-tinted polydiacetylene (PDA) film results from this step.

The PDA film is sensitive to changes on its surface as manifested by the wavelength of light transmitted thereby. For example, when *E. coli* 0157:H7 toxins bind to the surface of the sensor, the backbone chain of PDA reorganizes to produce a red tint. The colorimetric reaction from blue to red is visible by a naked eye.

In another application, a synthetic membrane based on polydiacetylenes is formed to have influenza virus binding sites on its surface. The color of the membrane changes from blue to red in response to a binding event of a sample of influenza virus to the binding sites.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention is pointed out with particularity in the appended claims. However, other features of the invention may become more by referring to the following detailed description in conjunction with the accompanying drawings in which:

FIG. **1** is a block diagram of a molecular detection apparatus in accordance with the present invention;

FIG. **2** illustrates a first embodiment of a molecular detection apparatus in accordance with the present invention;

FIG. **3** illustrates a second embodiment of a molecular detection apparatus in accordance with the present invention;

FIG. **4** illustrates a third embodiment of a molecular detection apparatus in accordance with the present invention;

FIG. **5** illustrates a fourth embodiment of a molecular detection apparatus in accordance with the present invention;

FIG. **6** illustrates a fifth embodiment of a molecular detection apparatus in accordance with the present invention;

FIG. **7** illustrates a sixth embodiment of a molecular detection apparatus in accordance with the present invention; and

FIG. **8** is a block diagram that illustrates another embodiment of a molecular detection apparatus in accordance with the present invention.

DETAILED DESCRIPTION OF A PREFERRED EMBODIMENT

FIG. **1** is a block diagram of a molecular detection apparatus in accordance with the present invention. The

molecular detection apparatus includes at least one molecular receptor **20** specific to at least one molecule which is to be detected. Examples of types of molecules which can be detected include, but are not limited to: polynucleotides such as DNA strands and RNA strands; pathogens such as coliforms, viruses, bacteria, *E. coli,* malaria, and parasites; proteins; and enzymes. The at least one molecular receptor **20** can include at least one ligand specific to a desired molecule to be detected.

The molecular detection apparatus further includes at least one detection element **22** responsive to the at least one molecular receptor **20**. Each detection element **22** provides an indication of a molecular recognition event from its respective molecular receptor **20**. In a preferred embodiment, each detection element **22** includes a visual detection element which produces a visual indication in response to a binding event between the molecular receptor **20** and a molecule. The visual indication allows an individual to determine the existence of the molecule by visually inspecting the detection element **22**.

In a preferred embodiment, each detection element **22** includes a colorimetric detection element which changes color in response to a molecular recognition event. The colorimetric detection element can exhibit a first color such as blue when the molecular receptor is absent of a molecule bound thereto, and can exhibit a second color such as red when a molecule is bound to the molecular receptor. The colorimetric detection element can include a diacetylene lipid as described earlier.

The molecular detection apparatus further includes a substrate **24** which supports the detection element **22** and the molecular receptor **20**. The substrate **24** can have a variety of forms, and can be formed using a variety of materials. Examples of materials from which the substrate **24** is formed include, but are not limited to, paper, plastic, and glass. Examples of forms of the substrate **24** include, but are not limited to, a planar form, a non-planar form, a cylindrical form, a hollowed form, and a bead form.

Preferably, the substrate **24** has a surface which promotes adsorption. The substrate **24** can be formed of an adsorptive material, or the surface can be coated with an adsorptive material. The adsorptive material is beneficial in capturing molecules, such as viruses, at the surface of the substrate **24**. Optionally, the surface of the substrate **24** can be charged to attract oppositely-charged molecules thereto.

The substrate **24** can be formed using an organic polymer whose charge, molecular weight, and length is managed. The organic polymer can be manufactured to be food grade in order to be consumable.

The at least one molecular receptor **20** and the at least one detection element **22** can have the form of a film disposed on a surface of the substrate **24**. For example, the at least one molecular receptor **20** and the at least one detection element **22** can be included in a PDA film as described earlier. A monolayer support can be interposed between the substrate **24** and the detection element **22**.

The at least one molecular receptor **20** and the at least one detection element **22** can be patterned on the substrate **24** to form an image viewable when molecules bind to the at least one molecular receptor **20**. Optionally, the substrate **24** has a background color, such as blue, similar to the first color of the at least one detection element **22** when bound molecules are absent from the at least one molecular receptor **20**. In this case, the pattern of the at least one detection element **22** is substantially unnoticeable in the absence of molecules bound thereto. The pattern of the at least one molecular

receptor **20** becomes apparent as its color changes in response to molecules binding thereto. The pattern of the image can include an icon, textual information, and/or graphical information indicative of a condition of detecting the molecules.

A grasping member **26** allows an individual to grasp the molecular detection apparatus. The grasping member **26** can include a container cap, a tag, a tab, a handle, a rod, or a stick which can be grasped by a hand of the individual.

The molecular detection apparatus further includes an elongated member **30** which couples the grasping member **26** to the substrate **24**. The elongated member **30** has a length dimension greater than each of its width dimensions. Examples of the elongated member **30** include, but are not limited to: a flexible line such as a string, a cord, a thread, or a wire; and a rigid, semi-rigid, or resilient member such as a rod, a stick, or a tube. The elongated member **30** can be formed of a variety of materials, including but not limited to, paper, plastic, metal, and fabric. The elongated member **30** can be solid, hollow, or stranded. Further, the elongated member **30** can be either telescoping or otherwise extendible to have a smaller footprint in storage.

At a position along the length dimension, the elongated member **30** can be partitioned into a first half and a second half, wherein the grasping member **26** is coupled at the first half and the substrate **24** is coupled at the second half. Further, the grasping member **26** can be coupled at or near a first end of the elongated member **30**. Similarly, the substrate **24** can be coupled at or near a second end of the elongated member **30**.

In some embodiments, the grasping member **26** and the elongated member **30** are provided by a unitary member. For example, a single stick can provide both the grasping member **26** and the elongated member **30**. Similarly, the elongated member **30** and the substrate **24** can be provided by a unitary member. Here, for example, a single stick can provide both the elongated member **30** and the substrate **24** to support the detection element **22**.

It is noted that the at least one molecular receptor **20** can include a first molecular receptor **32** for detecting a first molecule and a second molecular receptor **34** for detecting a second molecule, where the first molecule differs from the second molecule. In general, the at least one molecular receptor **20** can include a plurality of different molecular receptors.

FIG. **2** illustrates a first embodiment of a molecular detection apparatus in accordance with the present invention. The molecular detection apparatus includes a substrate **40** which supports a film of at least one detection element and at least one molecular receptor. The at least one detection element and the at least one molecular receptor are coated onto at least one surface **42** of the substrate **40**. The substrate **40** can include at least one fold **44** to provide a greater surface area for supporting detection elements and molecular receptors. As illustrated, the at least one fold **44** can include a plurality of concertina folds.

The substrate **40** can be formed of paper, plastic, or an organic polymer, for example. Optionally, the substrate **40** is formed of a permeable material which allows a fluid to flow therethrough. The permeable material can include either a porous material or a perforated material to allow a fluid, such as a liquid or a gas, to flow therethrough.

The molecular detection apparatus includes a grasping member in the form of a tag **46**. The tag **46** can be formed of a sheet of material such as paper or plastic. Although illustrated to have the shape of a square, the tag **46** can have any shape in general.

An elongated member having the form of a flexible line **48** couples the tag **46** to the substrate **40**. The flexible line **48** can be formed of thread, string, wire, or any thin cord. The flexible line **48** includes a first end **50** and a second end **52**. The tag **46** is coupled to the flexible line **48** near the first end **50**. The substrate **40** is coupled to the flexible line **48** near the second end **52**.

The flexible line **48** can be coupled to the tag **46** and the substrate **40** in a variety of ways. The flexible line **48** can be tied to either or both of the tag **46** and the substrate **40**. Alternatively, the flexible line **48** can be adhered to either or both of the tag **46** and the substrate **40**. As another alternative, the flexible line **48** can be fastened to either or both of the tag **46** and the substrate **40** using a fastener such as a staple.

FIG. **3** illustrates a second embodiment of a molecular detection apparatus in accordance with the present invention. The molecular detection apparatus includes a plurality of substrates **60** each supporting at least one detection element and at least one molecular receptor. Each of the substrates **60** has the form of bead **62**. The at least one detection element and the at least one molecular receptor are coated onto an external surface of each bead **62**. Each bead **62** can be formed of plastic or an organic polymer, for example.

The molecular detection apparatus includes a container **64** which contains the substrates **60**. Preferably, the container **64** includes a permeable portion to allow fluid to flow therethrough while simultaneously retaining the substrates **60** therein. The container **64** can be formed of a porous sheet of material such as filter paper or another filter medium. Alternatively, the container **64** can be formed of a perforated sheet of material having openings sized smaller than the substrates **60**.

The molecular detection apparatus includes a grasping member in the form of a tag **66**. The tag **66** can be formed of a sheet of material such as paper or plastic. Although illustrated to have the shape of a circle, the tag **66** can have any shape in general.

An elongated member having the form of a flexible line **68** couples the tag **66** to the substrates **60** via the container **64**. The flexible line **68** can be formed of thread, string, wire, or any thin cord. The flexible line **68** includes a first end **70** and a second end **72**. The tag **66** is coupled to the flexible line **68** near the first end **70**. The container **64** is coupled to the flexible line **68** near the second end **72**.

The flexible line **68** can be coupled to the tag **66** and the container **64** in a variety of ways. The flexible line **68** can be tied to either or both of the tag **66** and the container **64**. Alternatively, the flexible line **68** can be adhered to either or both of the tag **66** and the container **64**. As another alternative, the flexible line **68** can be fastened to either or both of the tag **66** and the container **64** using a fastener such as a staple.

FIG. **4** illustrates a third embodiment of a molecular detection apparatus in accordance with the present invention. The molecular detection apparatus includes a substrate **80** which supports a film of at least one detection element and at least one molecular receptor. The at least one detection element and the at least one molecular receptor are coated onto at least one surface **82** of the substrate **80**.

The molecular detection apparatus includes a grasping member in the form of a container cap **84**. The container cap **84** can have the form of a cap, a lid, or a cover for a container such as a bottle, a jar, or a can.

An elongated member **86** couples the container cap **84** to the substrate **80**. The elongated member **86** can be formed of

a flexible line, a semi-rigid line, or a rigid line. In preferred embodiments, the elongated member **86** is formed of either a thread, a string, a wire, a thin cord, or a plastic rod or stick. Optionally, at least one detection element and at least one molecular receptor are coated onto an external surface of the elongated member **86**.

The container cap **84** is coupled at or near a first end **88** of the elongated member **86**. The substrate **80** is coupled at or near a second end **90** of the elongated member **86**. The elongated member **86** can be tied, adhered, or fastened to either or both of the container cap **84** and the substrate **80**.

FIG. **5** illustrates a fourth embodiment of a molecular detection apparatus in accordance with the present invention. The molecular detection apparatus includes a unitary member having the form of a stick **100**. The stick **100** can be formed of materials including but not limited to paper, plastic, wood, and glass. The stick **100** can be either solid or hollowed.

The stick **100** provides a grasping member **102** at or near a first end **104**, an elongated member **106** at a midsection **108**, and a substrate **110** at or near a second end **112**. The substrate **110** is disposed at an exterior surface of the stick **100**. The substrate **110** includes a planar portion **114** at which a film of at least one detection element and at least one molecular receptor is supported. The at least one detection element and the at least one molecular receptor are coated onto the planar portion **114** of the substrate **110**.

Preferably, the stick **100** is coated with or formed from an adsorptive material. Optionally, the substrate **110** has grooves in its external surface to increase a surface area at which molecular receptors and detection elements are supported.

FIG. **6** illustrates a fifth embodiment of a molecular detection apparatus in accordance with the present invention. The molecular detection apparatus includes a unitary member having the form of a stick **120** with a hollow portion **122**. As illustrated, the hollow portion **122** can extend throughout the length of the stick **120**. Additionally, either or both of the ends of the stick **120** can be sealed. The stick **120** can be formed of materials including but not limited to paper, plastic, wood, and glass. If desired, the stick **120** can be telescoping to have a smaller footprint in storage.

The stick **120** provides a grasping member **124** at or near a first end **126**, an elongated member **128** at a midsection **130**, and a substrate **132** at or near a second end **134**. The substrate **132** can be disposed at an exterior surface, an interior surface, or both surfaces of the stick **120**. At least one detection element and at least one molecular receptor are supported by a portion of the substrate **132**.

FIG. **7** illustrates a sixth embodiment of a molecular detection apparatus in accordance with the present invention. The molecular detection apparatus includes a unitary member having the form of a stick **140** with a hollow portion **142**. It is preferred that the stick **140** be formed of a transparent or a translucent material such as plastic or glass. The stick **140** provides a grasping member **144** at or near a first end **146**, an elongated member **148** at a midsection **150**, and a substrate **152** disposed within the hollow portion **142**. If desired, the stick **140** can be telescoping to have a smaller footprint in storage.

A film of at least one detection element and at least one molecular receptor can be supported by the substrate **152**. In this case, the detection element is positioned to be viewable from a location exterior to the stick **140**. A wick **154** is disposed within the hollow portion **142** at or near a second end **156** of the stick **140**. By capillary action, the wick **154** communicates a sample of a fluid from the second end **156** to the substrate **152**. Molecules in the sample specific to the molecular receptor cause a visual indication in the detection element. The visual indication may be viewed through the stick **140** by an individual.

Alternatively, a solution of liposomes having the at least one detection element and the at least one molecular receptor can be disposed within the hollow portion **142**. The solution can be contained anywhere from the first end **146** to the midsection **150**. A breakable seal **158** contains the solution within the hollow portion **142**. Once the wick **154** receives a sample of a fluid from the second end **156**, the seal **158** can be broken to allow interaction between the sample and the solution. The seal **158** can be broken by squeezing or bending the portion of the stick **140** containing the solution. Molecules in the sample specific to the molecular receptor cause a visual indication in the detection element. The visual indication may be seen through the stick **140** by an individual.

The embodiments described with reference to FIGS. **2–7** are amenable for use in detecting predetermined molecules in a fluid. Here, an individual can grasp the molecular detection apparatus by the grasping member. While grasping the grasping member, the individual inserts a portion of the molecular detection apparatus into the fluid. Typically, the molecular detection apparatus is inserted so that the molecular receptors are immersed by the fluid. The individual can move, stir, or repeatedly dunk the molecular detection apparatus within the fluid to increase the likelihood of contacting the predetermined molecules. Thereafter, the individual removes the molecular detection apparatus from the fluid. The individual visually inspects the detection elements for the presence of the predetermined molecules in the fluid.

In one example, the fluid can include water in a container such as a cup or a bottle. An individual may wish to determine whether a pathogen is present in the water. Here, the individual can utilize a molecular detection apparatus having molecular receptors specific to the pathogen. The individual inserts the molecular detection apparatus into the container to visually detect the presence or absence of the pathogen.

The embodiment described with reference to FIG. **4** is advantageous in detecting molecules using a cap which seals a container of fluid. Shaking and mixing of the fluid during transportation of the container increases the likelihood of the molecules being adsorbed and detected by the molecular detection apparatus. A user can remove the cap from the container and inspect the detection elements to determine a condition of the fluid.

The embodiment described with reference to FIG. **7** is advantageous in that the molecular receptors and the detection elements come into contact only with a small sample of the fluid absorbed by the wick. Hence, the molecular receptors and the detection elements do not contact a portion of the fluid which is to be consumed.

FIG. **8** is a block diagram of another embodiment of a molecular detection apparatus. The molecular detection apparatus comprises a first molecular receptor **160**, a first detection element **162** responsive to the first molecular receptor **160**, and a first filter medium **164** associated with the first detection element **162**. The molecular detection apparatus further comprises a second molecular receptor **166**, a second detection element **170** responsive to the second molecular receptor **166**, and a second filter medium **172** associated with the first filter medium **164**. The second

filter medium **172** can be coupled to or attached to the first filter medium **164** to form a filter having a larger area.

The first molecular receptor **160** is utilized to detect a first type of molecule, and the second molecular receptor **166** is utilized to detect a second type of molecule. The first type of molecule differs from the second type of molecule. In general, the molecular detection apparatus can include any plurality of molecular receptors, detection elements, and filter media to detect any plurality of different molecules.

The molecular detection apparatus is utilized to detect predetermined molecules in a fluid which communicates therethrough. For example, a liquid such as water can be passed through the molecular detection apparatus to detect pathogens therein. The filter media are sized to accommodate a desired quantity of fluid. For example, the filter media can be sized for personal quantities of water, or for up to hundreds of liters and beyond.

If desired, a characteristic of the first filter medium **164** can differ from the second filter medium **172** so that a different amount of fluid is exposed to each. For example, the first filter medium can have a different porosity than the second filter medium, a different thickness than the second filter medium, and/or a different area than the second filter medium. By varying amounts of fluid exposed to different filter medium (and hence to different molecular receptors), more fluid can be sampled to detect rarer molecules than for more common molecules.

Thus, there has been described herein several embodiments including preferred embodiments of a molecular detection apparatus.

Because the various embodiments of the present invention utilize an elongated member to couple a grasping member to a molecular sensor, they provide a significant improvement in facilitating ease of use of an apparatus to detect predetermined molecules in a fluid.

Additionally, the various embodiments of the present invention pattern a plurality of detection elements in the form of an image to better communicate a condition of a fluid to a user.

It will be apparent to those skilled in the art that the disclosed invention may be modified in numerous ways and may assume many embodiments other than the preferred form specifically set out and described above.

Accordingly, it is intended by the appended claims to cover all modifications of the invention which fall within the true spirit and scope of the invention.

What is claimed is:

1. A molecular detection apparatus comprising:

an elongate member having a hollow portion and an end;

a molecular receptor disposed within the hollow portion;

a visual detection element responsive to the molecular receptor, the visual detection element viewable through the elongate member;

a wick disposed within the hollow portion, at least a portion of the wick disposed between the molecular receptor and the end of the elongate member; and

a breakable seal which separates the molecular receptor from the wick.

2. The molecular detection apparatus of claim **1** wherein the molecular receptor and the visual detection element are included in a solution of liposomes.

3. The molecular detection apparatus of claim **1** wherein the molecular receptor comprises a ligand.

4. The molecular detection apparatus of claim **1** wherein the visual detection element comprises a colorimetric detection element.

5. A molecular detection apparatus comprising:

an extendible, elongate member having a hollow portion and an end;

a molecular receptor disposed within the hollow portion;

a visual detection element responsive to the molecular receptor, the visual detection element viewable through the elongate member; and

a wick disposed within the hollow portion, at least a portion of the wick disposed between the molecular receptor and the end of the elongate member.

6. The molecular detection apparatus of claim **5** wherein the elongate member is telescoping.

7. The molecular detection apparatus of claim **5** wherein the molecular receptor and the visual detection element are included in a solution of liposomes.

8. The molecular detection apparatus of claim **5** wherein the molecular receptor comprises a ligand.

9. The molecular detection apparatus of claim **5** wherein the visual detection element comprises a colorimetric detection element.

* * * * *