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Beebe et al.

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(54) **DEVICE AND METHOD FOR EXTRACTING A TARGETED FRACTION FROM A SAMPLE**

(58) **Field of Classification Search**
USPC 422/425, 503, 551; 435/287.9, 288.3; 436/526

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See application file for complete search history.

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 922 days.

This patent is subject to a terminal disclaimer.

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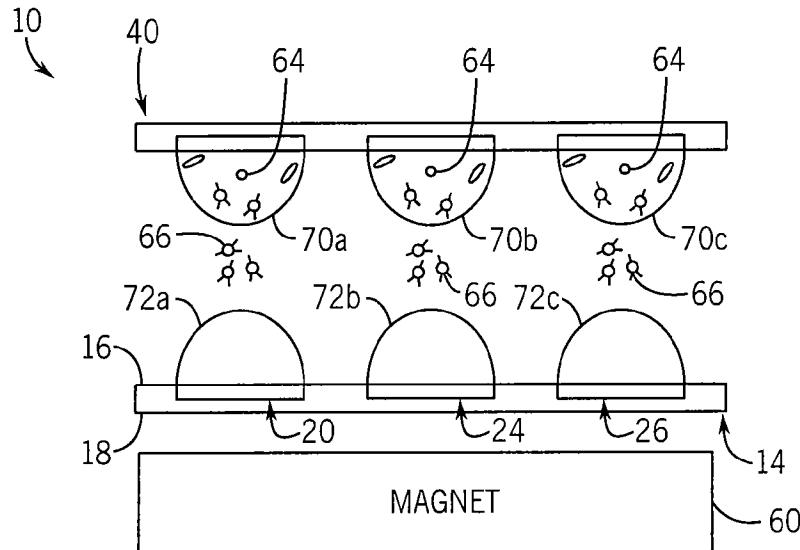
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(57) **ABSTRACT**

A device and a method for isolating a target from a sample are provided. The target is bound to solid phase substrate to form a target bound solid phase substrate. The device includes a first plate having a first region for receiving at least a portion of the sample. A second plate is spaced from the first plate by a distance and has a first region for receiving a reagent. A force attracts the target bound solid phase substrate toward the first region of the second plate such that the target bound solid phase substrate in the portion of the sample are drawn through the air gap and into the reagent by the force.

17 Claims, 6 Drawing Sheets



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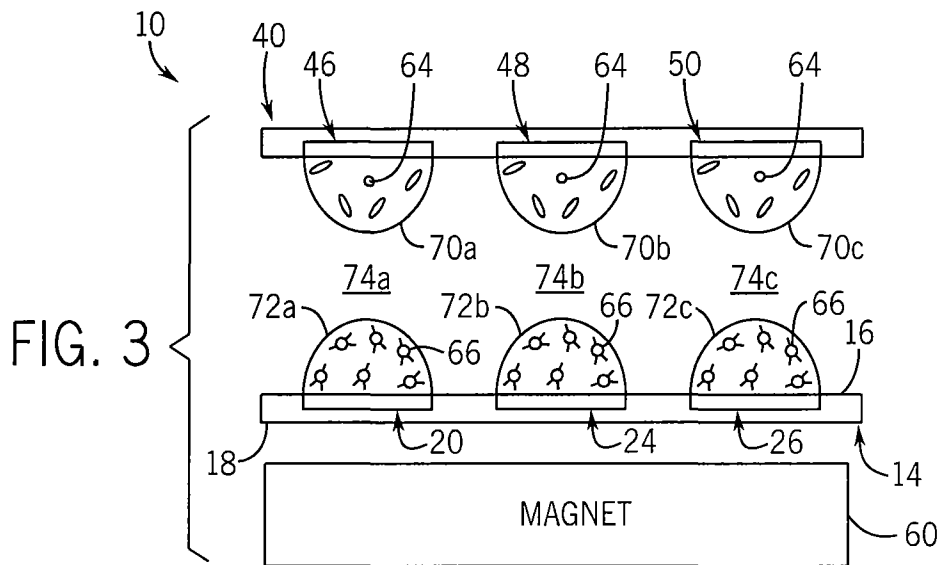
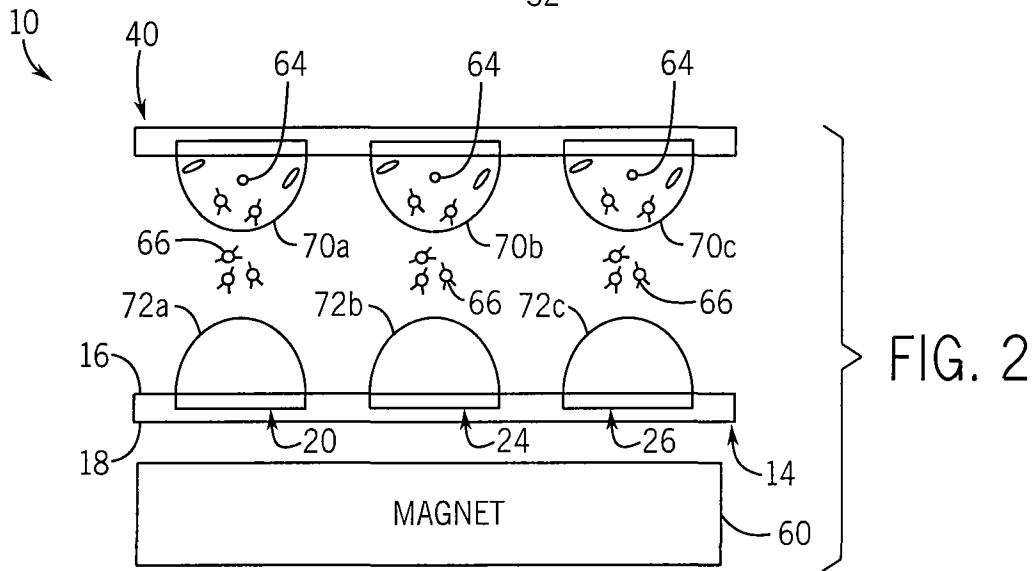
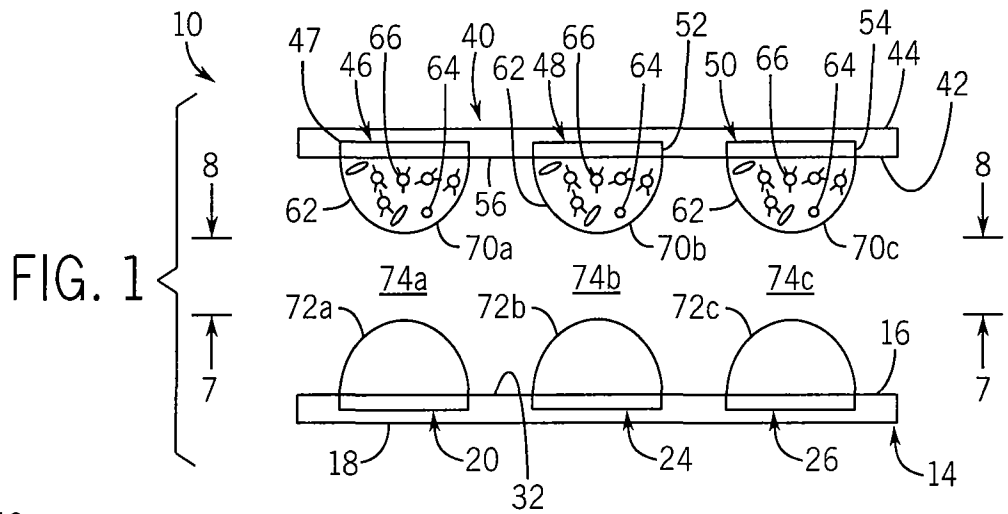
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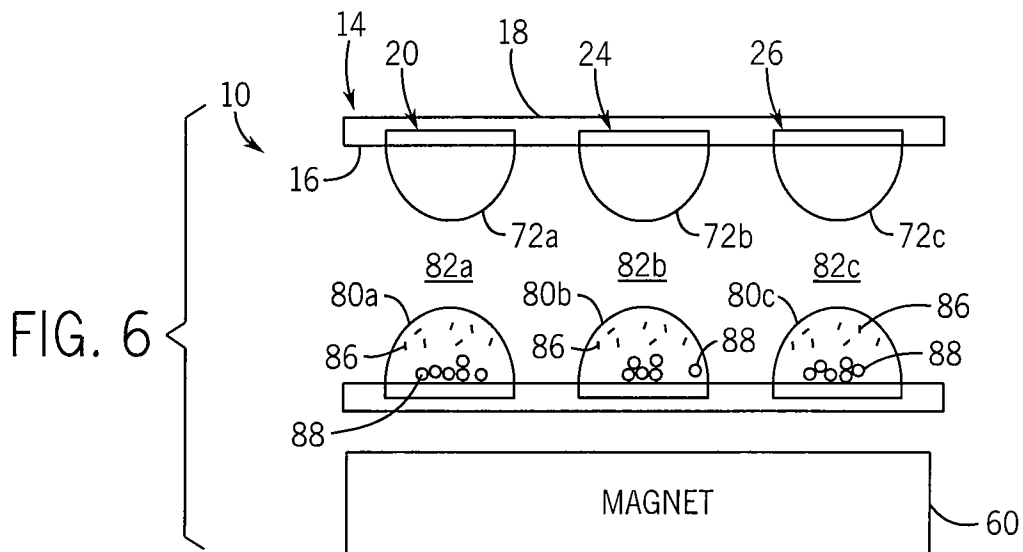
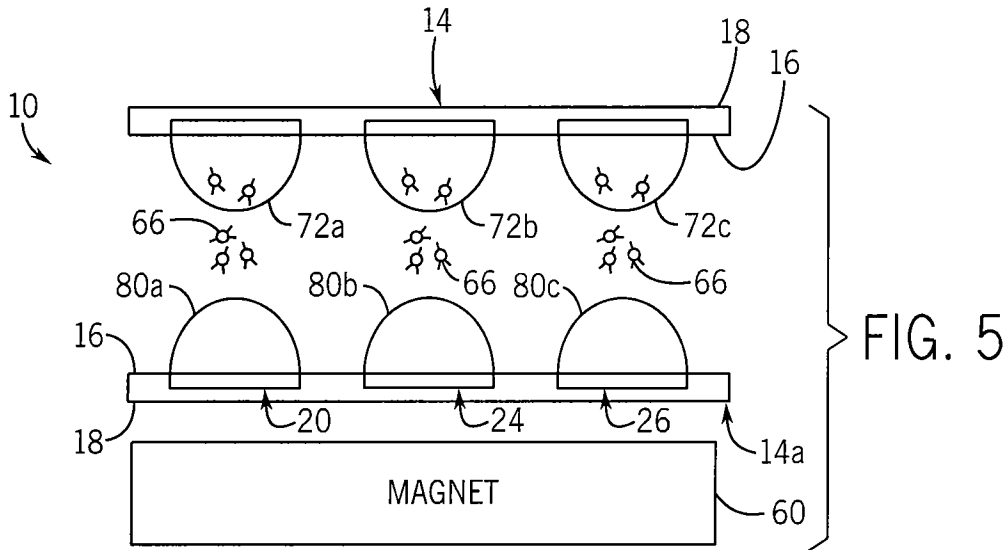
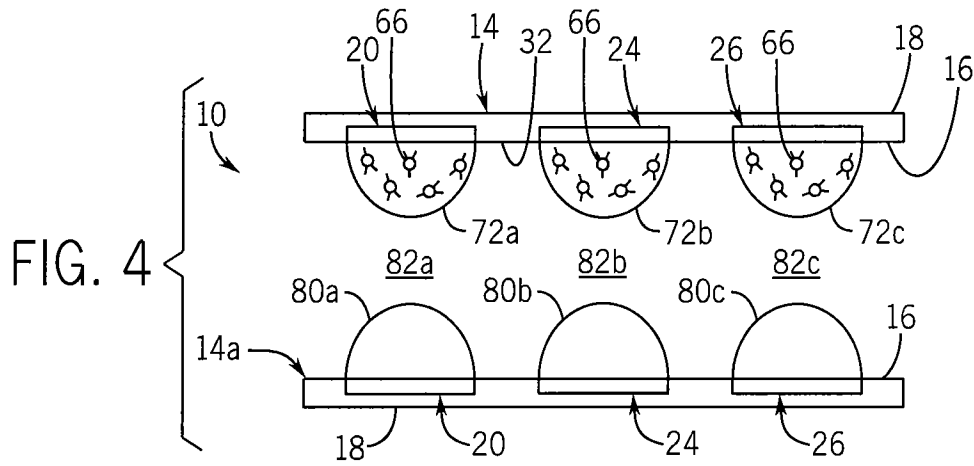
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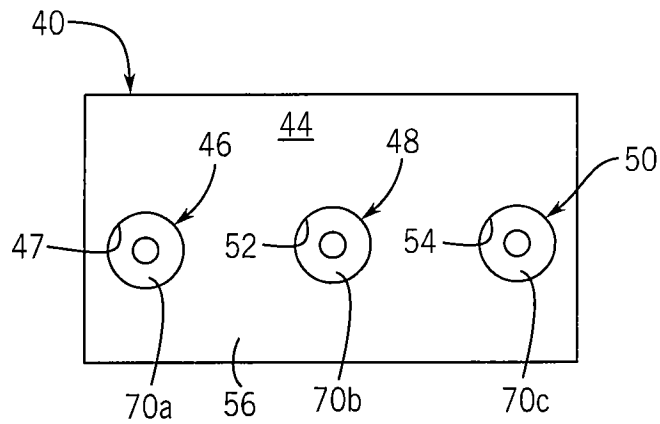


FIG. 7

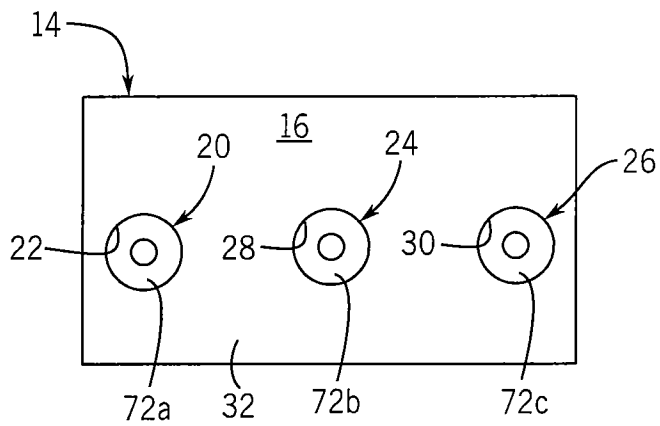


FIG. 8

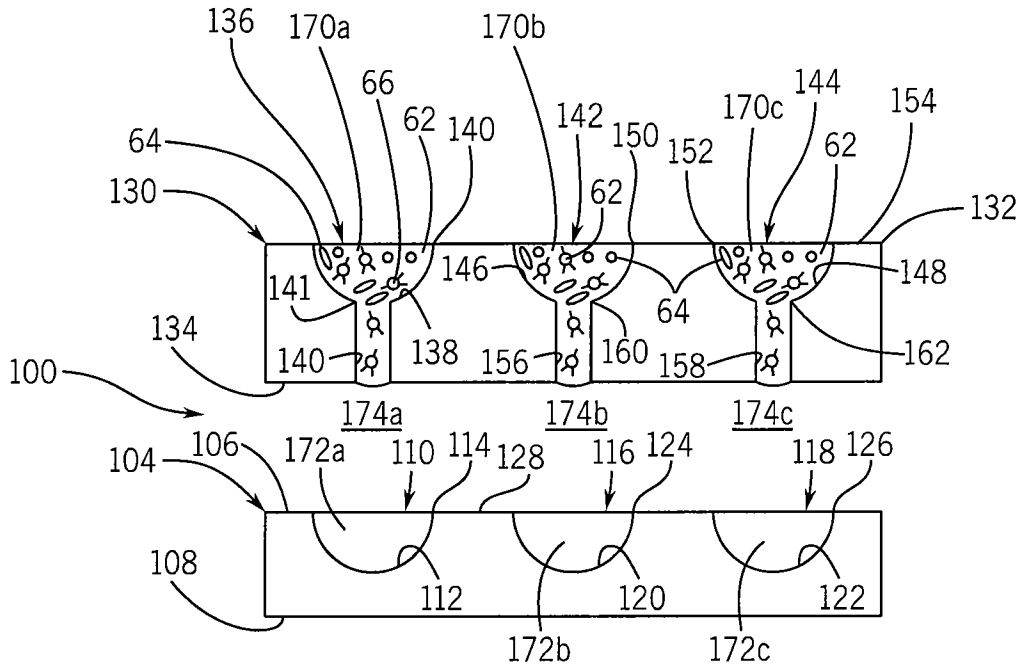


FIG. 9

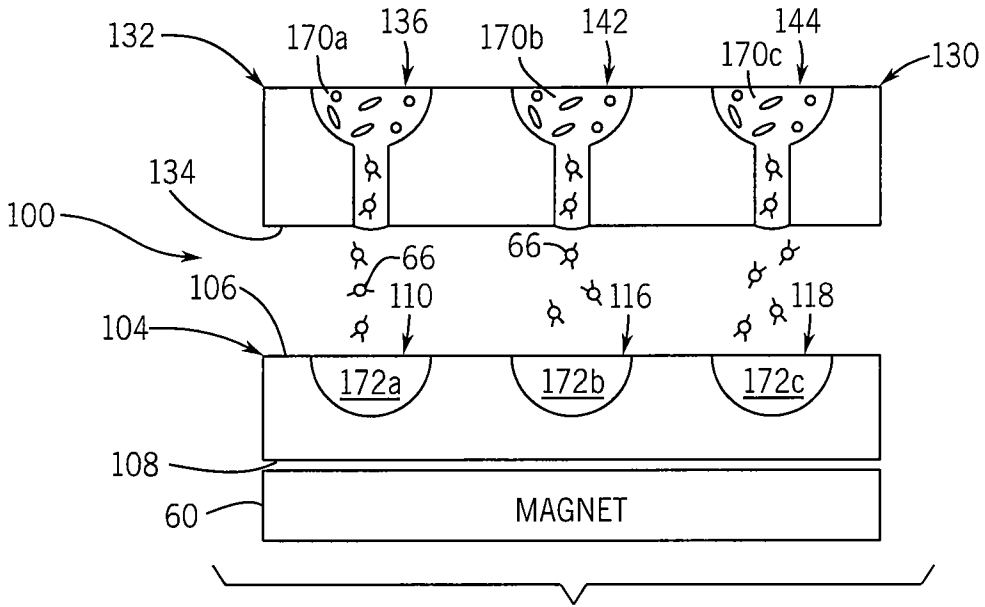


FIG. 10

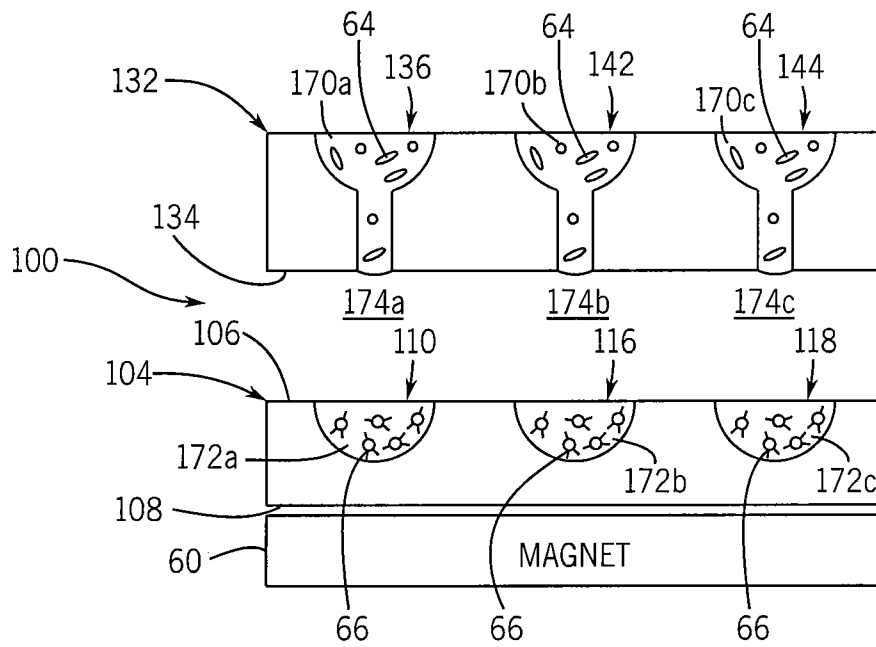


FIG. 11

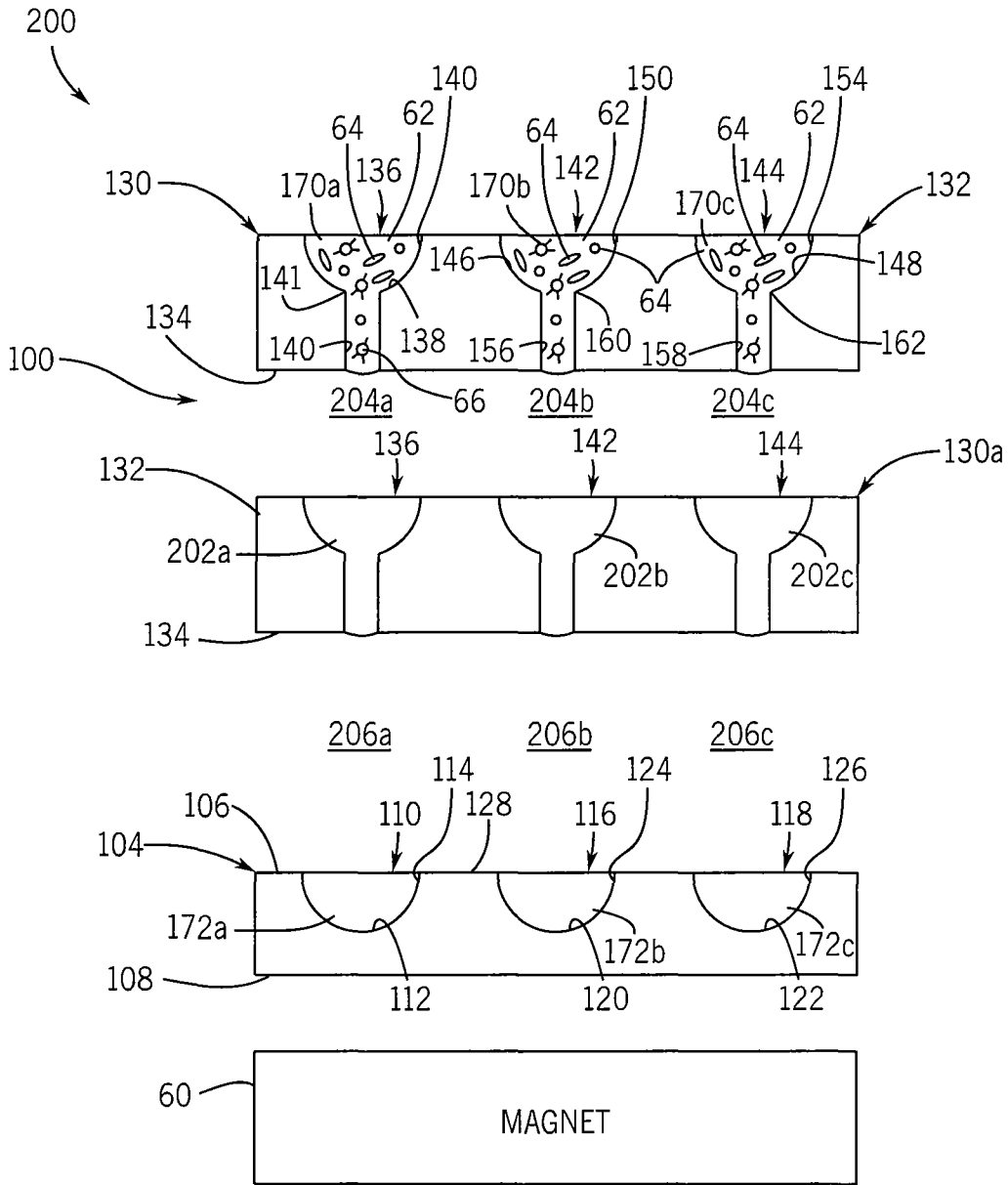


FIG. 12

DEVICE AND METHOD FOR EXTRACTING A TARGETED FRACTION FROM A SAMPLE

REFERENCE TO GOVERNMENT GRANT

This invention was made with government support under CA160344 awarded by the National Institutes of Health. The government has certain rights in the invention.

FIELD OF THE INVENTION

The present invention relates generally to the preparation of biological samples, and in particular, to a device for and a method of extracting a targeted fraction from a biological sample.

BACKGROUND AND SUMMARY OF THE INVENTION

Methods for isolating DNA, RNA, and proteins from complex biological samples are some of the most crucial steps in molecular biology. However, these methods are often overlooked within the biological sample processing workflow. As the throughput of downstream analytical techniques have increased, sample preparation methods have become a limiting factor in overall throughput. Many of the most used methods for sample preparation are very time consuming and can involve many steps including substrate binding, multiple wash steps, dilutions, or other processes that can result in loss of sample or dramatic increases in assay time.

The ability to use functionalized paramagnetic particles (PMPs) to isolate analyte of interest has expanded the utility of isolation methods across a range of platforms. One of PMPs advantages is that the particles are flexible for use in many system configurations since only a magnet is required for actuation and analyte isolation. The ways to isolate an analyte of interest from a given sample can further be divided into two basic methods. First, in the current primary method for using PMPs, the PMPs are held stationary while fluid is washed over the substrate to remove the background sample and any contaminants. Limitations of this popular method include the loss of the original input sample, allowing only a single effective isolation per sample, and the inefficiency of dilution-based sample preparation techniques, thereby necessitating multiple washes to effectively remove contaminants and leading to lengthy workflows. Second, recent work has demonstrated the ability to remove the PMPs from the original sample of interest using exclusion-based methods. These methods generally leverage gravitational forces or the dominance of surface tension at the microscale to position original samples and physically drag the PMPs out of the input sample along the surface of a device through some immiscible phase (e.g., air or oil) and into a second aqueous phase. These methods have been highly effective at isolating analyte with high specificity and selectivity. Further, these methods have been beneficial for their elegant workflow since isolation can be performed in a matter of seconds. Though effective, problems for these methods exist in the need for an immiscible fluid (oil) that can complicate both the fabrication and use of these techniques on larger scales and the function of 'dragging' particles along a surface which results in a friction-based loss of sample.

Therefore, it is a primary object and feature of the present invention to provide a device for and a method of extracting a targeted fraction from a biological sample.

It is a further object and feature of the present invention to provide a device for and a method of extracting a targeted fraction from a biological sample that is simple to fabricate and implement.

5 It is a still further object and feature of the present invention to provide a device for and a method of extracting a targeted fraction from a biological sample that reduces friction-based losses of the targeted fraction of prior devices/methods.

10 In accordance with the present invention, a device is provided for isolating a target from a sample. The target is bound to solid phase substrate to form target bound solid phase substrate. The device includes a first plate having a first surface and a first region for receiving at least a portion
15 of the sample. A second plate is spaced from the first plate by a distance and has a first region for receiving a reagent. The second plate includes a first surface directed toward the first surface of the first plate. A force is provided for attracting the target bound solid phase substrate toward the
20 first surface of the second plate. The portion of the sample received by first region of the first plate is spaced from the reagent by an air gap. The target bound solid phase substrate in the portion of the sample are drawn through the air gap and into the reagent by the force.

25 The first region of the first plate is defined by a portion of the first surface of the first plate wherein the first region of the first plate is hydrophilic and the first surface of the first plate external of the first region thereof is hydrophobic. In addition, the first region of the second plate is defined by a portion of the first surface of the second plate wherein the
30 first region of the second plate is hydrophilic and the first surface of the second plate external of the first region thereof is hydrophobic. Alternatively, the first plate may include a second surface and the first region of the first plate may include a recess in the second surface and a passageway
35 extending between the recess and the first surface of the first plate. Similarly, the first region of the second plate may include a recess in the first surface of the second plate. It is contemplated for the force to be a magnetic force and for the
40 second plate to include a second surface. The device may also include a magnet adjacent the second surface of the second plate for generating the magnetic force.

In accordance with a further aspect of the present invention, a device is provided for isolating a target from a
45 sample. The target is bound to solid phase substrate to form target bound solid phase substrate. The device includes a first sample receiving region for receiving at least a portion of the sample and a first reagent region for receiving a reagent. The first reagent region and the first sample region
50 are separated by an air gap. A force is provided for drawing the target bound solid phase substrate from the at least a portion of the sample, through the air gap and into the reagent.

A first plate includes the first sample receiving region and
55 a second plate includes the first reagent zone. The first plate includes a first surface and the first sample receiving region is defined by a portion of the first surface of the first plate. The first sample receiving region of the first plate is hydrophilic and the first surface of the first plate external of the
60 first sample receiving region thereof is hydrophobic. The second plate includes a first surface and the first reagent region is defined by a portion of the first surface of the second plate. The first reagent region of the first plate is hydrophilic and the first surface of the second plate external
65 of the first reagent region thereof is hydrophobic.

Alternatively, the first plate may include a second surface and the first sample receiving region of the first plate may

include a recess in the second surface and a passageway extending between the recess and the first surface of the first plate. In addition, the first reagent region of the second plate may include a recess in the first surface of the second plate. In accordance with a still further aspect of the present invention, a method is provided for isolating a target from a sample. The target is bound to solid phase substrate to form target bound solid phase substrate. The method includes the steps of providing the sample at a region of a first plate and providing a reagent at a region of a second plate. The target bound solid phase substrate is drawn from the sample, through an air gap and into the reagent with a force.

The step of drawing the target bound solid phase substrate may include the step of positioning a magnetic field adjacent the second plate. The first plate includes a first surface and the region of the first plate is defined by a portion of the first surface of the first plate. The second plate also includes a first surface and the region of the second plate is defined by a portion of the first surface of the first plate. Alternatively, the first plate may include first and second surfaces. The region of the first plate includes a recess in the second surface and a passageway extending between the recess and the first surface of the first plate. Similarly, the region of the second plate may include a recess in the first surface of the second plate.

BRIEF DESCRIPTION OF THE DRAWINGS

The drawings furnished herewith illustrate a preferred construction of the present invention in which the above advantages and features are clearly disclosed as well as others which will be readily understood from the following description of the illustrated embodiment.

In the drawings:

FIG. 1 is a cross-sectional view of a device in accordance with the present invention in an initial configuration;

FIG. 2 is a cross-sectional view of the device of the present invention in a second configuration;

FIG. 3 is a cross-sectional view of the device of the present invention in a third configuration;

FIG. 4 is a cross-sectional view of the device of the present invention in a fourth configuration;

FIG. 5 is an isometric view of a device of the present invention in a fifth configuration;

FIG. 6 is a cross-sectional view of the device of the present invention in a sixth configuration;

FIG. 7 is a cross-sectional view of the device of the present invention taken along line 7-7 of FIG. 1;

FIG. 8 is a cross-sectional view of the device of the present invention taken along line 8-8 of FIG. 1;

FIG. 9 is a cross-sectional view of an alternate embodiment of a device in accordance with the present invention in an initial configuration;

FIG. 10 is a cross-sectional view of the device of FIG. 9 in a second configuration;

FIG. 11 is a cross-sectional view of the device of FIG. 10 in a third configuration; and

FIG. 12 is a cross-sectional view of a still further embodiment of a device in accordance with the present invention in an initial configuration.

DETAILED DESCRIPTION OF THE DRAWINGS

Referring to FIGS. 1-8, a device for extracting and purifying a targeted fraction, such as an analyte, from complex biological samples, including cultured cells, tissue samples and other biological materials, in accordance with

the present invention is generally designated by the reference numeral 10. Device 10 includes lower plate 14, FIG. 8, having upper and lower surfaces 16 and 18, respectively. Except as hereinafter described, upper surface 16 of lower plate 14 is hydrophobic. Upper surface 16 of lower plate 14 includes first region 20 defined by edge 22 such that first region 20 has a generally circular configuration. However, other configurations are contemplated as being within the scope of the present invention. It is intended for first region 20 to retain a selected fluid thereon, as hereinafter described. As such, it is contemplated for first region 20 to be hydrophilic.

Upper surface 16 of lower plate 14 may further include second and third regions 24 and 26, respectively, defined by corresponding edges 28 and 30, respectively, such that second and third regions 24 and 26, respectively, have generally circular configurations. However, additional regions and/or other configurations of the regions are contemplated as being within the scope of the present invention. It is intended for second and third regions 24 and 26, respectively, to spatially retain selected fluids thereon, as hereinafter described. By way of example, it is contemplated for second and third regions 24 and 26, respectively, to be hydrophilic. Further, it is noted that the portion of upper surface 16 of lower plate 14 outside of first, second and third regions 20, 24 and 26, respectively, defines hydrophobic region 32.

Device 10 further includes an upper plate 40, FIG. 7, having upper and lower surfaces 42 and 44, respectively. Except as hereinafter described, lower surface 44 of upper plate 40 is hydrophobic. Lower surface 44 of upper plate 40 includes first region 46 defined by edge 47 such that first region 46 has a generally circular configuration. However, other configurations are contemplated as being within the scope of the present invention. It is intended for first region 46 to retain a selected fluid thereon, as hereinafter described. As such, it is contemplated for first region 46 to be hydrophilic.

Lower surface 44 of upper plate 40 may further include second and third regions 48 and 50, respectively, defined by corresponding edges 52 and 54, respectively, such that second and third regions 48 and 50, respectively, have generally circular configurations. It is noted that additional regions and/or other configurations are contemplated as being within the scope of the present invention. It is intended for second and third regions 48 and 50, respectively, to retain selected fluids thereon, as hereinafter described. As such, it is contemplated for second and third regions 48 and 50, respectively, to be hydrophilic. The portion of lower surface 44 of upper plate 40 outside of first, second and third regions 46, 48 and 50, respectively, defines hydrophobic region 56.

In the depicted embodiment, a single magnet 60 is supported below lower surface 18 of lower plate 14. It is noted, however, magnet 60 may be replaced by a plurality of magnets, each of which positioned below lower surface 18 of lower plate 14 and aligned with a corresponding hydrophilic region on upper surface 16 of lower plate 14. It is contemplated for magnet 60 to be axially movable between a first position wherein magnet 60 is adjacent to lower surface 18 of lower plate 14, FIGS. 2-3, and a second position axially spaced from lower surface 18 of lower plate 14, for reasons hereinafter described, FIG. 1.

It is intended to utilize device 10 to extract a targeted fraction, such as an analyte, DNA, RNA, proteins nucleic acids, whole cells and/or the like, from biological sample 62. As is known, biological sample 62 may include non-desired material 64 such as lysate, bodily fluids, forensic samples,

and/or biological contaminations. In order to prepare biological sample **62** for extraction of the fraction, an appropriate reagent is added to biological sample **62** and mixed such that the fraction binds to a solid phase substrate in the reagent to form fraction-bound solid phase substrate **66**. It is contemplated for the solid phase substrate to be attracted to a corresponding force. For example, the solid phase substrate may be a paramagnetic material attracted to a corresponding magnetic field. Other non-magnetic mechanisms such as gravity, optical force, ultrasonic actuation or the like are contemplated as being within the scope of the present invention.

Once mixed with the reagent, droplets **70a-70c** of biological sample **62** are deposited on first, second and third regions **46**, **48** and **50**, respectively, of lower surface **44** of upper plate **40**, in any conventional manner such as by a micropipette or like. It is contemplated for the volumes of droplets **70a-70c** to be generally equal. It can be appreciated that the hydrophilic nature of first, second and third regions **46**, **48** and **50**, respectively, act to pin droplets **70a-70c** thereon. In addition, hydrophobic region **56** of lower surface **44** of upper plate **40** further acts to retain droplets **70a-70c** on first, second and third regions **46**, **48** and **50**, respectively.

In addition, droplets **72a-72c** of one or more desired reagents (e.g. wash, secondary antibody, etc.) are deposited on first, second and third regions **20**, **24** and **26** of upper surface **16** of lower plate **14**. It is contemplated for the volumes of droplets **72a-72c** to be generally equal. It can be appreciated that the hydrophilic nature of first, second and third regions **20**, **24** and **26**, respectively, act to pin droplets **72a-72c** thereon. In addition, the hydrophobic region **32** of upper surface **16** of lower plate **14** further acts to retain droplets **72a-72c** on first, second and third regions **20**, **24** and **26**, respectively.

After depositing droplets **72a-72c** on first, second and third regions **20**, **24** and **26**, respectively, of lower plate **14**, upper plate **40** is positioned such that first, second and third regions **46**, **48** and **50**, respectively, of lower surface **44** of upper plate **40** are in registry with first, second and third regions **20**, **24** and **26**, respectively, of lower plate **14** such that droplets **70a-70c** are in registry with and spaced from droplets **72a-72c** by air gaps **74a-74c**, respectively. With upper plate **40** positioned, as heretofore described, magnet **60** is positioned adjacent lower surface **18** of lower plate **14** such that magnet **60** magnetically attracts fraction-bound solid phase substrate **66** in droplets **70a-70c** and draws fraction-bound solid phase substrate **66** toward upper surface **16** of lower plate **14**, FIG. 2. More specifically, the magnetic force generated by magnet **60** draws fraction-bound solid phase substrate **66** from droplets **70a-70c**, through air gaps **74a-74c**, respectively, and into droplets **72a-72c**, respectively, on first, second and third regions **20**, **24** and **26**, respectively, of upper surface **16** of lower plate **14**, FIG. 3. Any undesired (or unbound) material in droplets **70a-70c** is retained therein by surface tension. Thereafter, magnet **60** may be moved to a location spaced from lower plate **14** such that the magnetic force generated thereby no longer acts on fraction-bound solid phase substrate **66** in droplets **72a-72c**, thereby freeing fraction-bound solid phase substrate **66** within droplets **72a-72c**.

Referring to FIGS. 4-6, lower plate **40** (and hence, droplets **72a-72c**) may be repositioned so as to allow for further processing of fraction-bound solid phase substrate **66** in droplets **72-72a**. By way of example, lower plate **40** may be repositioned such that upper surface **16** of lower plate **14** may be directed downwardly toward upper surface **16** of a second lower plate **14a**. Second lower plate **14a** is identical

in structure to lower plate **14** such that the description heretofore of lower plate **14** is understood to describe second lower plate **14a** as if fully herein.

It is contemplated to provide droplets **80a-80c** of one or more desired reagents (e.g. wash, secondary antibody, etc.) on first, second and third regions **20**, **24** and **26** of upper surface **16** of second lower plate **14a**. It is contemplated for the volumes of droplets **80a-80c** to be generally equal. It can be appreciated that the hydrophilic nature of first, second and third regions **20**, **24** and **26**, respectively, of upper surface **16** of second lower plate **14a** act to pin droplets **80a-80c** thereon. In addition, the hydrophobic region **32** of upper surface **16** of second lower plate **14a** further acts to retain droplets **80a-80c** on first, second and third regions **20**, **24** and **26**, respectively, of upper surface **16** of second lower plate **14a**.

As described, first, second and third regions **20**, **24** and **26**, respectively, of second lower plate **14a** are in registry with first, second and third regions **20**, **24** and **26**, respectively, of lower plate **14** such that droplets **80a-80c** are in registry with and spaced from droplets **72a-72c** by air gaps **82a-82c**, respectively. With lower plate **14** and second lower plate **14a** positioned as described, magnet **60** is positioned adjacent lower surface **18** of second lower plate **14a** such that magnet **60** magnetically attracts fraction-bound solid phase substrate **66** in droplets **72a-72c** and draws fraction-bound solid phase substrate **66** toward upper surface **16** of second lower plate **14a**, FIG. 5. More specifically, the magnetic force generated by magnet **60** draws fraction-bound solid phase substrate **66** from droplets **72a-72c**, through air gaps **82a-82c**, respectively, and into droplets **80a-80c**, respectively, on first, second and third regions **20**, **24** and **26**, respectively, of upper surface **16** of second lower plate **14a**, FIG. 6. Any undesired (or unbound) material in droplets **72a-72c** is retained therein by surface tension. Thereafter, magnet **60** may be moved to a location spaced from second lower plate **14a** such that the magnetic force generated thereby no longer acts on fraction-bound solid phase substrate **66** in droplets **80a-80c**, thereby freeing fraction-bound solid phase substrate **66** within droplets **80a-80c**. Droplets **80a-80c**, and hence fraction-bound solid phase substrate **66** therein, are available for further processing, e.g. droplets **80a-80c** may be formed from elution buffers which disassociate target or fraction **86** from solid phase substrate **88**.

Referring to FIGS. 9-11, an alternate embodiment of a device for extracting and purifying a targeted fraction, such as an analyte, from complex biological samples, including cultured cells, tissue samples and other biological materials, in accordance with the present invention is generally designated by the reference numeral **100**. Device **100** includes lower plate **104** having upper and lower surfaces **106** and **108**, respectively. Except as hereinafter described, upper surface **106** of lower plate **104** is hydrophobic. Upper surface **106** of lower plate **104** includes first recess **110** formed therein. In the depicted embodiment, first recess **110** is defined by concave recessed surface **112** intersecting upper surface **106** at edge **114**. Edge **114** has a generally circular configuration. However, it is noted that first recess **110** may have other configurations without deviating from the scope of the present invention. It is intended for first recess **110** to retain a selected fluid therein, as hereinafter described. As such, it is contemplated for recessed surface **112** to be hydrophilic.

Upper surface **106** of lower plate **104** may further include second and third recesses **116** and **118**, respectively. Second and third recesses **116** and **118**, respectively, are defined by concave recessed surfaces **120** and **122**, respectively, inter-

secting upper surface **106** at edges **124** and **126**, respectively. Edges **124** and **126** have generally circular configurations. However, it is noted that second and third recesses **116** and **118**, respectively, may have other configurations without deviating from the scope of the present invention. It is intended for second and third recesses **116** and **118**, respectively, to retain selected fluids therein, as hereinafter described. As such, it is contemplated for recessed surfaces **120** and **122**, respectively, to be hydrophilic. Further, the portion of upper surface **106** of lower plate **104** outside of first, second and third recesses **110**, **116** and **118**, respectively, defines hydrophobic region **128**.

Device **100** further includes an upper plate **130** having upper and lower surfaces **132** and **134**, respectively. Except as hereinafter described, upper and lower surfaces **132** and **134**, respectively of upper plate **130** are hydrophobic. Upper surface **132** of upper plate **130** includes first recess **136** formed therein. In the depicted embodiment, first recess **136** is defined by concave recessed surface **138** intersecting upper surface **132** at edge **140**. Edge **140** has a generally circular configuration. However, it is noted that first recess **136** may have other configurations without deviating from the scope of the present invention. It is intended for first recess **136** to retain a selected fluid therein, as hereinafter described. As such, it is contemplated for recessed surface **138** to be hydrophilic. Passageway **140** extends between nadir **141** of recessed surface **138** and lower surface **134** of upper plate **130**. It is intended for the diameter of passageway **140** to be of sufficient dimension so as to allow fraction-bound solid phase substrate **66** to pass therethrough, for reasons hereinafter described. It is understood that length of passageway **140** may vary without deviating from the scope of the present invention. By way of example, it is contemplated for passageway **140** to take the form of an opening communicating with both first recess **136** and lower surface **134** of upper plate **130**.

Upper surface **132** of upper plate **130** may further include second and third recesses **142** and **144**, respectively. Second and third recesses **142** and **144**, respectively, are defined by concave recessed surfaces **146** and **148**, respectively, intersecting upper surface **132** at edges **150** and **152**, respectively. Edges **150** and **152** have generally circular configurations. However, it is noted that second and third recesses **142** and **144**, respectively, may have other configurations without deviating from the scope of the present invention. It is intended for second and third recesses **142** and **144**, respectively, to retain selected fluids therein, as hereinafter described. As such, it is contemplated for recessed surfaces **146** and **148**, respectively, to be hydrophilic and for the portion of upper surface **132** of upper plate **130** outside of first, second and third recesses **136**, **142** and **144**, respectively, to define hydrophobic region **154**. Passageways **156** and **158** extend between corresponding nadirs **160** and **162** of recessed surfaces **146** and **148**, respectively, and lower surface **134** of upper plate **130**. It is intended for the diameters of passageways **156** and **158** to be of sufficient dimensions so as to allow fraction-bound solid phase substrate **66** to pass therethrough, for reasons hereinafter described. It is further understood that length of passageways **156** and **158** may vary without deviating from the scope of the present invention. By way of example, it is contemplated for passageways **156** and **158** to take the form of openings communicating with second and third recesses **142** and **144**, respectively, and lower surface **134** of upper plate **130**.

In operation, droplets **170a-170c** of biological sample **62** are deposited in first, second and third recesses **136**, **142** and

144, respectively, in upper surface **132** of upper plate **130** in any conventional matter such that passageways **140**, **156** and **158** are filled with biological sample **62**. It can be appreciated that the hydrophilic nature of first, second and third recesses **136**, **142** and **144**, act to maintain droplets **170a-170c** therein. In addition, the hydrophobic nature of lower surface **134** of upper plate **130** along with the surface tension of the biological sample at the outputs of passageways **140**, **156** and **158** further act to retain the portions of biological sample **62** within passageways **140**, **156** and **158**, respectively.

In addition, droplets **172a-172c** of desired reagents (e.g. wash, secondary antibody, etc.) are deposited in first, second and third recesses **110**, **116** and **118**, respectively, in upper surface **106** of lower plate **104**. It is contemplated for the volumes of droplets **172a-172c** to be generally equal. It can be appreciated that the hydrophilic nature of first, second and third recesses **110**, **116** and **118**, respectively, act to retain droplets **172a-172c** therein. In addition, the hydrophobic nature of upper surface **106** of lower plate **104** further acts to retain droplets **172a-172c** in first, second and third recesses **110**, **116** and **118**, respectively.

After depositing droplets **172a-172c** in first, second and third recesses **110**, **116** and **118**, respectively, of lower plate **104**, upper plate **130** is positioned such that passageways **140**, **156** and **158** of upper plate **130** are in registry with first, second and third recesses **110**, **116** and **118**, respectively, of lower plate **104**. As a result, droplets **170a-170c** are in registry with and spaced from droplets **172a-172c** by air gaps **174a-174c**, respectively. With upper plate **130** positioned, as heretofore described, magnet **60** is positioned adjacent lower surface **108** of lower plate **104** such that magnet **60** magnetically attracts fraction-bound solid phase substrate **66** in droplets **170a-170c** and draws fraction-bound solid phase substrate **66** toward upper surface **106** of lower plate **104**, FIG. 10. More specifically, the magnetic force generated by magnet **60** draws fraction-bound solid phase substrate **66** from droplets **170a-170c**, through passageways **140**, **156** and **158** and air gaps **74a-74c**, respectively, and into droplets **172-172a**, respectively, in first, second and third recesses **110**, **116** and **118**, respectively, of lower plate **104**, FIG. 11. Any undesired (or unbound) material in droplets **170a-170c** is retained therein by surface tension. Magnet **60** may be moved to a location spaced from lower plate **104** such that the magnetic force generated thereby no longer acts on fraction-bound solid phase substrate **66** in droplets **172a-172c**. As such, fraction-bound solid phase substrate **66** in droplets **172a-172c** are available for further processing.

Referring to FIG. 12, a still further embodiment of a device for extracting and purifying a targeted fraction, such as an analyte, from complex biological samples, including cultured cells, tissue samples and other biological materials, in accordance with the present invention is generally designated by the reference numeral **200**. Device **200** includes upper plate **130** and lower plate **104**, as heretofore described. It is contemplated to provided one or more additional upper plates, e.g. upper plate **130a**, between upper plate **130** and lower plate **104**, as hereinafter described. Upper plate **130a** is identical in structure to upper plate **130**. As such, the previous description of upper plate **130** is understood to describe upper plate **130a**, as if fully described herein.

In operation, droplets **170a-170c** of biological sample **62** are deposited in first, second and third recesses **136**, **142** and **144**, respectively, in upper surface **132** of upper plate **130** in any conventional matter such that passageways **140**, **156** and **158** are filled with biological sample **62**. In addition, drop-

lets **202a-202c** of desired reagents (e.g. wash, secondary antibody, etc.) are deposited in first, second and third recesses **136**, **142** and **144**, respectively, in upper surface **132** of upper plate **130a** in any conventional matter such that passageways **140**, **156** and **158** of upper plate **130a** are filled therewith. Similarly, droplets **172a-172c** of desired reagents (e.g. wash, secondary antibody, etc.) are deposited in first, second and third recesses **110**, **116** and **118**, respectively, in upper surface **106** of lower plate **104**. As described, droplets **170a-170c** are in registry with and spaced from droplets **202a-202c** by air gaps **204a-204c**, respectively, and droplets **202a-202c** are in registry with and spaced from droplets **172a-172c** by air gaps **206a-206c**, respectively.

Magnet **60** is positioned adjacent lower surface **108** of lower plate **104** such that magnet **60** magnetically attracts fraction-bound solid phase substrate **66** in droplets **170a-170c** and draws fraction-bound solid phase substrate **66** toward upper surface **106** of lower plate **104**. More specifically, the magnetic force generated by magnet **60** draws fraction-bound solid phase substrate **66** from droplets **170a-170c**, through passageways **140**, **156** and **158** and air gaps **204a-204c**, respectively, and into droplets **202a-202c**, respectively, in first, second and third recesses **136**, **142** and **144**, respectively, in upper surface **132** of upper plate **130a** wherein the reagent(s) therein are free to act on the fraction-bound solid phase substrate **66**. Any undesired (or unbound) material in droplets **170a-170c** is retained therein by surface tension. Thereafter, the magnetic force generated by magnet **60** draws fraction-bound solid phase substrate **66** from droplets **202a-202c**, through passageways **140**, **156** and **158** in upper plate **130a** and air gaps **206a-206c**, respectively, and into droplets **172-172a**, respectively, in first, second and third recesses **110**, **116** and **118**, respectively, of lower plate **104**. Magnet **60** may them be moved to a location spaced from lower plate **104** such that the magnetic force generated thereby no longer acts on fraction-bound solid phase substrate **66** in droplets **172a-172c**. As such, fraction-bound solid phase substrate **66** in droplets **172a-172c** are available for further processing.

It can be appreciated that the above descriptions of devices are merely exemplary of the present invention. Various modes of carrying out the invention are contemplated as being within the scope of the following claims particularly pointing out and distinctly claiming the subject matter, which is regarded as the invention.

We claim:

1. A device for isolating a target from a sample, the sample including the target bound to solid phase substrate to form target bound solid phase substrate, comprising:

a first plate lying in a first plane and having a first surface, the first surface including a first region for receiving at least a portion of the sample;

a second plate lying in a second plane which is generally parallel to and spaced from the first plate along an axis generally perpendicular to the first and second planes by a distance, the second plate having a first surface directed toward the first surface of the first plate and including a first region for receiving a reagent; and

a magnetic force generator positionable adjacent the second plate, the magnetic force generator generating a magnetic force which draws the target bound solid phase substrate away from the first surface of the first plate toward the first surface of the second plate in a direction generally parallel to the axis when the portion of the sample is received on the first region of the first plate;

wherein:

when the portion of the sample is received on the first region of the first plate and when the reagent is received on the first region of the second plate, the distance between the first plate and the second plate being sufficient:

to provide an air gap between the portion of the sample received by first region of the first plate and the reagent received by the first region of the second plate; and

for the target bound solid phase substrate in the portion of the sample to be drawn through the air gap and into the reagent by the magnetic force generated by the magnetic force generator.

2. The device of claim **1** wherein the first region of the first plate is defined by a portion of the first surface of the first plate.

3. The device of claim **2** wherein the first region of the first plate is hydrophilic.

4. The device of claim **2** wherein the first surface of the first plate external of the first region thereof is hydrophobic.

5. The device of claim **1** wherein the first region of the second plate is defined by a portion of the first surface of the second plate.

6. The device of claim **5** wherein the first region of the second plate is hydrophilic.

7. The device of claim **5** wherein the first surface of the second plate external of the first region thereof is hydrophobic.

8. The device of claim **1** wherein the first plate includes a second surface and wherein the first region of the first plate includes a recess in the second surface and a passageway extending between the recess and the first surface of the first plate.

9. The device of claim **1** wherein the first region of the second plate includes a recess in the first surface of the second plate.

10. The device of claim **1** wherein the second plate includes a second surface and wherein the magnetic force generator is a magnet positioned adjacent the second surface of the second plate for generating the magnetic force.

11. A device for isolating a target from a sample, the sample including the target bound to solid phase substrate to form target bound solid phase substrate, comprising:

a first sample receiving region disposed on a first plate for receiving at least a portion of the sample;

a first reagent region disposed on a second plate for receiving a reagent, the first reagent region opposing the first sample receiving region; and

a magnetic force generator adjacent the second plate, the magnetic force generator generating a magnetic force for drawing the target bound solid phase substrate from the at least the portion of the sample, through an air gap and into the reagent when the at least the portion of the sample is received on the first sample receiving region of the first plate and when the reagent is received on the first reagent region of the second plate;

wherein:

the first and second plates are generally parallel to and spaced from each other along an axis generally perpendicular to the first and second planes by a distance such that when the at least the portion of the sample is received on the first sample receiving region of the first plate and when the reagent is received on the first reagent region of the second plate:

the distance between the first plate and the second plate is sufficient to provide the air gap between the at least

the portion of the sample received by first sample receiving region of the first plate and the reagent received by the first reagent region of the second plate; and

the target bound solid phase substrate in the at least the 5
portion of the sample is drawn from the at least the
portion of the sample, through the air gap, and into
the reagent by the magnetic force generated by the
magnetic force generator.

12. The device of claim 11 wherein the first plate includes 10
a first surface, the first sample receiving region being defined
by a portion of the first surface of the first plate.

13. The device of claim 12 wherein the first sample
receiving region of the first plate is hydrophilic and wherein
the first surface of the first plate external of the first sample 15
receiving region thereof is hydrophobic.

14. The device of claim 12 wherein the first plate includes
a second surface and wherein the first sample receiving
region of the first plate includes a recess in the second
surface and a passageway extending between the recess and 20
the first surface of the first plate.

15. The device of claim 12 wherein the first reagent region
of the second plate includes a recess in the first surface of the
second plate.

16. The device of claim 11 wherein the second plate 25
includes a first surface, the first reagent region being defined
by a portion of the first surface of the second plate.

17. The device of claim 16 wherein the first reagent region
of the first plate is hydrophilic and wherein the first surface
of the second plate external of the first reagent region thereof 30
is hydrophobic.

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