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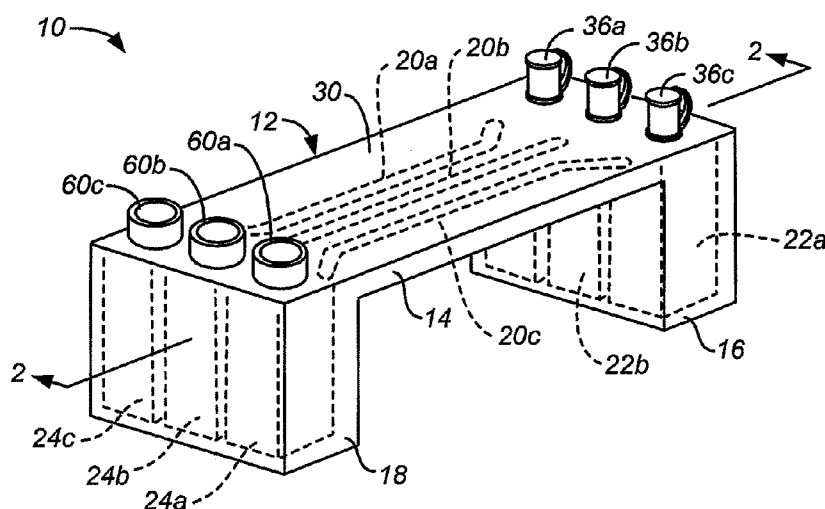


FIG. 1

(57) Abstract: A test cartridge for performing controlled flow or other assays on blood or other biological samples comprises a body having at least one sealable inlet well and at least one sealable collection well. A test channel extends between the sealable inlet well and the sealable collection well, and either or both of the wells is adapted to couple to a pressure source to transfer a test fluid from the inlet well to the collection well. The test cartridge can be used in systems for monitoring biological reactions such as blood clotting or thrombosis formation which occur within the test channel as the biological fluid flows therethrough.

TEST CARTRIDGES FOR FLOW ASSAYS AND METHODS FOR THEIR USE

BACKGROUND OF THE INVENTION

5 1. Field of the Invention

[0001] The present invention relates generally to devices and methods for performing flow-based biological assays. In particular, the present invention relates to a device and method for performing assays on blood or other biological materials flowing through a test cartridge from a source well, through a test channel, and into a collection well.

10 [0002] Published PCT Patent Application WO 2006/065739 describes devices and methods for imaging and analyzing thrombosis formation in a test cartridge over time. In particular, Figs. 3I-3M describe the use of test cartridges having multiple cylindrical test channels in an optically clear test block or body. In use, the test cartridge is connected to a source of blood, and the blood is drawn through the test cartridge into individual syringes temporarily coupled
15 to each channel. While an excellent design in most respects, the test cartridges described in this commonly owned PCT application are not adapted to safely contain a blood or other biological sample for disposal. Also, the coupling of the test cartridge to the source of test sample and the syringes can in rare instances increase the risk of introducing bubbles or other contaminants into the sample as it passes through the test channels.

20 [0003] Another test system for monitoring blood clotting and other biological processes under flow conditions is the BioFlux™ 200 microfluidic flow system for live cell assays, commercially available from Fluxion, South San Francisco, California 94080 (www.fluxionbio.com). The BioFlux™ 200 system uses a microwell plate of generally conventional construction, where a serpentine flow path is micromolded in
25 polydimethylsiloxane (PDMS) onto the plate bottom, connecting pairs of adjacent wells and forming a test channel. A microscope coverslip is then secured over the molded flowpath, and blood or other fluids to be tested can be introduced into one well using a pipette or liquid handling workstation and drawn into the other connecting well using an electropneumatic pump. A light source is placed above the plate and a microscope objective is positioned
30 below the plate to view flow through the flowpath. While functional, the design of the micro well test plate has certain disadvantages. For example, as the wells are filled from their top

and joined by the test channels at the bottom, it can be difficult to control the initiation of flow from the well into the test channel. Additionally, the structure of the test plate presents different thicknesses and shapes for the illumination path necessary to illuminate the sample for quantitative microscopy. Moreover, the product descriptions illustrate open sample and waste wells which make sample containment and disposal more difficult.

[0004] For these reasons, it would be desirable to provide improved test cartridges, test systems, and methods for testing biological fluids by flowing said fluids through test channels. In particular, it would be desirable to provide test cartridges which allow for convenient initial introduction of blood or other test fluid into the cartridge with minimum risk of initiating flow until desired. It would be further desirable to provide test cartridges which permit the convenient and secure containment of the test sample within the cartridge at all times after initial introduction of the test fluid, including both during the test and after the test is complete. It would be still further desirable to provide test cartridges which are designed to minimize the risk of bubble and artifact creation within the test fluid as the test is performed. At least some of these objectives will be met by the inventions described hereinbelow.

2. Description of the Background Art

[0005] WO 2006/065739 has been described above. The BioFlux™ 200 and its use are described in a Product Data Sheet © 2008 Fluxion Biosciences, Inc.; a white paper entitled “BioFlux System for Cellular Interactions: Microfluidic Flow System for Live Cell Assays” © 2008 Fluxion Biosciences, Inc.; and an Application Note entitled Platelet Adhesion: Platelet Aggregation Assays Under Controlled Shear Flow, © 2008 Fluxion Biosciences, Inc. A platelet thrombosis adhesion assay is described in an Application Note C100 published by Cellix Ltd., Dublin, Ireland © 2007 Cellix Ltd., which cites Williams et al. (2002), *J. Assoc. Lab. Automation* 7:135-141. The Cellix VenaFlux™ system (commercially available from Cellix Ltd.) measures cell adhesion to antibody-coated or endothelial-cell cultured microcapillaries under shear stress conditions mimicking physiological flow. The system requires manual assembly of the plastic fluidic device, and blood and buffer samples are delivered to the device from external reservoirs via connecting tubing. Kantak, et al. (2002, 2003); Martin, et al. (2007); Kastrup, et al. (2007); Shen, et al. (2008a); Shen, et al. (2008b); Runyon, et al. (2008); Gutierrez, et al. (2008) describe microfluidic devices designed for the

study of platelet adhesion under shear flow. In general, the devices described in these papers are designed for research purposes, and are not suitable for clinical use in that they typically require either (i) manual assembly, (ii) manual connection of tubing for delivery of blood samples to the device, (iii) cumbersome surface coating techniques, (iv) storage of platelet-enriched plasma or blood samples either in separate containers or in open wells on the device itself, and/or (v) post-experiment data processing and analysis steps. Additional publications of interest include Gutierrez E., Petrich B., Shattil S., Ginsberg M., Groisman A., and Kasirer-Friede A. (2008), Microfluidic devices for studies of shear-dependent platelet adhesion. *Lab Chip* 8(9):1486-95; Kantak A., Gale B., Lvov Y., and Jones S. (2002) Microfluidic platelet function analyzer for shear-induced platelet activation studies. 2nd International IEEE-EMBS Special Topic Conference on Microtechnologies in Medicine and Biology, Poster 192; Kantak A., Gale B., Lvov Y., and Jones S. (2003) Platelet function analyzer: shear activation of platelets in microchannels. *Biomedical Microdevices* 5(3):207-215; Kastrup C., Shen F., Runyon M., and Ismagilov R. (2007), Characterization of the threshold response of initiation of blood clotting to stimulus patch size. *Biophys J.* 93(8):2969-77; Martin Y., Lépine M., Bannari A., and Vermette P. (2007), Instrument and technique for the in vitro screening of platelet activation from whole blood samples. *Rev Sci Instrum.* 78(5):054302; Runyon M., Kastrup C., Johnson-Kerner B., Ha T., and Ismagilov R. (2008), Effects of shear rate on propagation of blood clotting determined using microfluidics and numerical simulations. *J Am Chem Soc.* 130(11):3458-64; Shen F., Kastrup C., and Ismagilov R. (2008a), Using microfluidics to understand the effect of spatial distribution of tissue factor on blood coagulation. *Thromb Res.* 122 Suppl 1:S27-30; Shen F., Kastrup C., Liu Y., and Ismagilov R. (2008b), Threshold Response of Initiation of Blood Coagulation by Tissue Factor in Patterned Microfluidic Capillaries Is Controlled by Shear Rate. *Arterioscler Thromb Vasc Biol.* 28:000-000 (November 2008 issue).

BRIEF SUMMARY OF THE INVENTION

[0006] The present invention provides improved test cartridges, systems, methods, and protocols for performing flow-based assays on blood and other biological fluids. While the cartridges and methods are particularly suitable for performing analysis of the kinetics of thrombosis and coagulation, including platelet adhesion, thrombus growth, stability, reversal, and the like, they are also suitable for testing the behavior of constituents of other biological samples, including blood constituents, such as leukocytes, fibrin, and the like, as well as circulating tumor cells. The test cartridges and methods will also be useful for obtaining

clinically relevant information for characterizing, analyzing, and predicting the utility of response modifiers as affected by genetic, experimental, and/or pharmacological modulation and/or variation.

[0007] In a first aspect of the present invention, a test cartridge comprises a body having at least one inlet well and at least one collection well. A test channel is present in the body and extends from the inlet well to the collection well, thus providing a flow path or a channel suitable for testing and observing the flow of fluids from the inlet well to the collection well, where the flow is typically initiated by a pressure difference initiated between said wells. Usually, at least one of the wells will be adapted to couple to a pressure source to induce transfer or flow of the test fluid from the inlet well, through the test channel, to the collection well. The pressure source may be negative, i.e. a vacuum or partial vacuum, where it is applied to the collection well to draw the test fluid through the test channel. Alternatively, the pressure source may be a positive pressure source where it is applied to the inlet well to cause the test fluid to flow from the inlet well toward the collection well. Usually, use of the negative pressure will be preferred since it reduces the risk of inadvertent loss of test fluid from the test cartridge during the testing procedure.

[0008] In a particular aspect of the present invention, the test cartridge is provided with sealable inlet and collection wells. That is, a cover, cap, seal, valve, or other structure is provided which can cover the well to prevent loss of fluid. Usually, the cover or other structure will be removable during a portion of the testing procedure. For example, the cover over the inlet wells may be removed while the test fluid(s) are transferred into the inlet wells, typically using pipettes, syringes, tubes, pumps, liquid-handling robotics, or other conventional laboratory fluid transfer devices and techniques. The inlet wells may also be open or opened during the fluid transfer phase of the test or protocol to allow connection to a positive pressure source, as discussed above. Alternatively or additionally, the fluid collection wells may be open during the fluid transfer portion of a test protocol, typically to allow connection to a negative pressure source, such as a pump, syringe, or the like. In most or all cases, however, it will be desirable that after the procedure is complete, both the test inlet wells and the collection wells will be covered, sealed, or otherwise closed to prevent loss of blood or other test fluid from the test cartridge. In this way, after its initial collection, the blood or other test fluid will be maintained at all times within the test cartridge, greatly reducing any risk of loss of blood or other test materials and resulting contamination. The

sealed test cartridge may then be disposed of in a conventional manner for the contained biological materials.

[0009] The test cartridges of the present invention may include only a single sealable inlet well, a single sealable collection well, and a single test channel there between. In other
5 embodiments, however, two, three, four, five, or more test channels may be provided in the test cartridge body. Such multiple test channels may be connected to a single, common inlet well and/or common outlet well, but will more usually be connected to individual inlet wells and/or individual outlet wells, where each test channel is connected to one and only one inlet well and/or to one and only one collection well. The cartridge body will be composed at least
10 partially of an optically transparent polymer or other material so that fluid flow through the test channels may be observed using a microscope or other optical equipment. Suitable polymeric materials include polycarbonates, polystyrenes, polyacrylates, and the like. Suitable non-polymeric materials include siliconized glass, and the like. Conveniently, the bodies may be formed from a base and a cover, each having surfaces where the test channels
15 are formed in either or both of the surfaces by machining, etching, laser etching, embossing, molding, or the like. The cover seals against the base thus forming the test channels between the opposed surfaces. Optionally, seals may be provided around the test channels in order to further prevent leakage. The test channels have surfaces which may be coated, treated, or otherwise formed to interact with the test fluid in some desired manner. For example, for
20 thrombosis testing, the surfaces of the test channels may have an immobilized thrombotic or other substance thereon to initiate thrombosis as blood flows there through.

[0010] The test channels may have any cross-sectional geometry or size, but will typically have a rectangular cross-section with a width in the range from 0.25 mm to 1.5 mm and a depth in the range from 25 μ m to 500 μ m. The cross-sectional geometry of the test channels
25 will depend on a number of factors including the materials and fabrication techniques. For example, the isotropic etching of glass will typically produce a U-shaped channel, while the anisotropic etching of a negative mold, such as a silicon mold, can provide rectangular channels. Wide, rectangular channels are generally desirable to improve optics as curved surfaces can introduce optical distortion. The wide, shallow channel dimensions above are
30 desirable as they provide a relatively flat velocity profile across the width of the channel when the test fluid flows as a result of a pressure differential.

[0011] The test channels are preferably linear between their inlet end and their outlet end. Further, the width of the test channel is typically much greater than the depth. Linear channels that are aligned in parallel are preferable since they facilitate optical imaging, and linear, rectangular channels which are wide and shallow in the region of the viewing window are particularly desirable as the resulting fluidics help assure that the volumetric flow rates through the channels are the same and that the flow velocity profile is flat across the width of each channel.

[0012] In another specific aspect of the present invention, the test channels will be formed in an upper surface of the body of the test cartridge where the inlet and outlet wells extend downwardly from the upper surface. The wells, in turn, are connected to the inlet and outlet ends of the test channels by vertical "chimneys" which connect to the lower end of the inlet well and allow fluid to flow upward to the inlet end of the test channel under a pressure gradient. Similarly, the outlet end of the test well is connected to the lower end of the collection well by another vertical chimney, allowing the test fluid to flow downwardly through the chimney into the bottom of the collection well. This design is particularly advantageous because any bubbles which may be introduced during the filling of the cartridge are inhibited from entering the test channel. Also, depending on the particular dimensions of the chimney and test channel, and the wettability (surface characteristics) of the materials of the chimney and test channel, spontaneous filling of the test channel from the chimney can be prevented, i.e. capillary flow is inhibited. Thus, the flow and testing can begin when the differential pressure is applied to the test cartridge above some threshold level as described in more detail below.

[0013] Test systems according to the present invention comprise test cartridges, generally as described above, in combination with a pressure source having connector(s) capable of being coupled to each of the collection wells and/or inlet wells, preferably where the pressure sources can independently apply a pressure differential across each of the test channels. In the exemplary embodiments, the pressure source will comprise a plurality of syringes, where the syringes may be connectable to the collection wells in order to draw fluid through the test channels and/or to the inlet wells in order to push fluid through the test channels. The detection system will further include optical or other systems for observing and monitoring the blood or other biological fluids which flow through the test channels. In an exemplary embodiment, the detection systems will include one or more cameras for viewing each test channel. In some instances, each test channel will have an individual or dedicated camera

arranged to observe flow in that channel. In other instances, the detection system will employ a single camera with optics which allow for observing each of the test channels, usually by sequentially viewing each test channel. Exemplary embodiments usually further include fluorescent emission detection means for observing the accumulation of fluorescent markers within the assay system.

[0014] In another specific aspect of the present invention, methods for analyzing a biological fluid sample comprise introducing at least one sample into an inlet well in a test cartridge. A pressure differential is applied to a first test channel in the test cartridge, where the pressure differential induces flow of the biological fluid sample from the inlet well through the test channel into a collection well in the test channel. The biological fluid sample is analyzed as it flows through and is contained within the test channel, and the test cartridge is disposed of while the biological fluid remains contained and sealed within the test cartridge. The differential pressure may be applied to draw a plurality of fluid samples through a plurality of test channels and into a plurality of collection wells. In such cases, the differential pressure may be applied at different levels to at least some of said plurality of test channels in order to draw the fluid biological sample at different rates and/or in different amounts through at least some of the test channels. The sample may be initially contained in a single inlet well, but will more usually be provided in different inlet wells, more usually in inlet wells dedicated to particular test channels. In that way, different samples and/or different sample preparations may be provided for each of the test channels. The biological fluid sample may comprise any biological specimen which is a fluid or which may be turned into a fluid or a solution, but will most usually comprise blood or a blood product. The most common analytical test performed will be for thrombus formation, blood coagulation, inflammatory response detection, circulating tumor cell recruitment, and the like. Thrombus formation and blood coagulation may be detected by monitoring platelet accumulation on the thrombogenic surface of the test channel. The analysis will be performed before, during, or after the biological material is caused to flow through the test channel, but will usually be analyzed at least partially while the sample is flowing through the test channel.

BRIEF DESCRIPTION OF THE DRAWINGS

[0015] Fig. 1 is a perspective view of a cartridge for testing biological fluid samples constructed in accordance with the principles of the present invention.

[0016] Fig. 2 is a cross-sectional view of the test cartridge of Fig. 1, taken along line 2-2 of Fig. 1, shown with the inlet and collection well seals removed.

[0017] Fig. 3 is a top view of the test cartridge of Fig. 2, shown with the inlet and collection well seals removed.

5 [0018] Fig. 4 is a cross-sectional view taken along line 4A-4A of Figs. 2 and 3, illustrating the cross-sections of the test channels.

[0019] Fig. 4A is a detailed view of a single test channel taken along line 4A-4A of Fig. 4.

[0020] Fig. 5 is a schematic view illustrating the optics of a test system of the present invention.

10 DETAILED DESCRIPTION OF THE INVENTION

[0021] Referring to Figs. 1-3, a test cartridge 10 constructed in accordance with the principles of the present invention comprises a body 12 having a central bridge section 14, an inlet well section 16, and a collection well section 18. The test cartridge 10 includes three generally axial test channels 20a, 20b, and 20c, respectively. Each of the test channels 20 is connected to a single inlet well 22 formed in the inlet well section 16, with a cross-section of inlet well 22b illustrated in Fig. 2. Similarly, each of the test channels 20 will be connected to a single collection well 24, with collection well 24b connected to test channel 20b illustrated in the cross-sectional view of Fig. 2.

20 [0022] Conveniently, the test cartridge body 12 may have an inverted-U profile with the central bridge section 14 defining an upper surface 30 with the test channels 20 being exposed through an optically transparent portion thereof. The inlet wells 22 depend from one side of the central bridge section 14 in the vertical inlet well section 16. Similarly, the collection wells 24 depend from the central bridge section 14 in the vertical collection well section 18.

25 [0023] The top surface 30 of the central bridge section 14 is best illustrated in Fig. 3 where the test channels 20 are observable through the optically transparent window. Also can be seen are openings 32a, 32b, and 32c to the inlet wells 22a, 22b, 22c, as well as openings 34a, 34b, and 34c to the collection wells 24a, 24b, and 24c, respectively. The inlet openings 32 provide an open passage, as best seen in Fig. 2, for allowing the blood or other biological test fluid to be introduced into the well, typically using a syringe, pipette, or other common analytical fluid transfer tool. Some structure for sealing the openings 32 will also be

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provided, such as flip-open caps 36a, 36b, and 36c, as seen in Fig. 1. A variety of other openable/sealable covers, such as screw tops, snap-open tops, and the like, could also be used. Sealable tops allow the openings 32 to be sealed to prevent loss to the biological fluid after the fluid has been introduced. Typically, the tops will be vented to allow air to enter the inlet wells 22 as the fluid is being drawn through the test channels using a vacuum applied to the collection wells, as described below. In other embodiments, of course, the sealable cap will be open to allow a syringe or other positive pressure source to be connected to the inlet openings 32 in order to drive or push the test fluid through the system.

[0024] The outlet openings 34 will typically be configured to facilitate coupling to a bank of three syringes or other vacuum source. As best illustrated in Fig. 2, the openings 34 may comprise a conical passage through the top surface 30 as well as a raised flange portion 38 surrounding the conical opening.

[0025] Fluid from the inlet wells 22 passes through the test channels 20 through a vertical “chimney” 40, as best seen in Fig. 2 where chimney 40b is connected to inlet well 22b by a short horizontal passage 42b. Thus, by applying a vacuum to the collection well 24b or applying positive pressure to the inlet well 22b, fluid within the inlet well 22b will be caused to flow into the bottom of the chimney 40b and upward to the inlet end 44b of the test channel 20b. Similar chimneys 40 will be provided for each of the inlet wells (although for ease of illustration, they are not shown in the drawings). The collection wells 24 are similarly connected to the test channels 20 by vertical chimneys 50, as best shown in Fig. 2. In Fig. 2, vertical chimney 50b is connected to the bottom of collection well 24b by the short horizontal connector passage 52b and into the bottom of the collection well 24b.

[0026] In the preferred embodiments, the fluids will be drawn through the system by applying a vacuum to the openings 34 of the test cartridge body 12. The use of the vertical chimneys allows the fluid initially held in the inlet wells 32 to be transferred from the bottom of the wells to the test channels which are generally aligned with the tops of the wells. Taking the fluids from the bottoms of the wells reduced the risk of bubbles entering the test channel and maximizes the amount of the fluid which may actually be accessed and drawn into the test wells.

[0027] Coupling elements 60a, 60b, and 60c may be provided on the outlet openings 34 of the collection wells 24. The couplings may take a variety of configurations, and in some instances may be included in a single pad or foot structure, in order to facilitate interface of

the collection wells with a syringe or other vacuum structure for drawing blood or other test fluids into the test channels. The syringes may be independently controlled, in which case different volumes and/or flow rates may be drawn through the test channels. In other instances, the syringes may be ganged together so that the flow volumes and flow rates are identical in each test channel. In still other instances, it may be possible to employ a single syringe or pump for drawing vacuum simultaneously on all three collection wells 24.

[0028] Referring now to Figs. 4 and 4A, the test channels 20 may be formed by etching, machining, molding or otherwise shaping into a surface of the test body cartridge 12. For example, the central bridge section 14 may comprise a lower component 66 and an upper plate 68. Test channels may be formed in an upper surface of the lower portion 66, where the test channels are then closed by placement of the upper plate 68. The test channels are preferably shallow with a width w in the range from 0.25 mm to 1.5 mm and a depth d in the range from 25 μm to 500 μm . The use of wide, shallow test channels is advantageous in a number of respects, as discussed above. The inlet wells will typically have a maximum volume in the range from 2 ml to 5 ml, and the collection wells will typically have a volume in the range from 2 ml to 5 ml. The actual volumes of the inlet wells and outlet wells will be determined by the particular assay protocol. For example, a specific volumetric flow rate may be needed to achieve a desired shear rate, so that the volume requirements are dependent on the duration of the assay and the dimensions of the test channels as well as the flow rates, which in turn are dependent on the magnitude of the applied pressure differential.

[0029] As illustrated, the test channels are disposed in an axial direction and are visible from the upper surface of the central bridge section 14. Often, reinforcing structure will be provided on the lower surface of the central bridge section 14, although no reinforcement is illustrated for the sake of simplicity in the drawings.

[0030] Referring now to Fig. 5, an optical system 70 for observing a fluorescent tag being accumulated within a test channel 20 in the test cartridge 10 of the present invention will be described. The test cartridge 10, a portion of which is shown in Fig. 5, is held in a movable relationship with the remainder of the optical test system 70. Typically, the test cartridge 10 will be held on a movable X-Y platform so that it can be positioned relative to an objective lens 72 of the system 70. A light source, such as a light-emitting diode (LED) 74 (or laser source) is arranged to deliver light through the objective lens 72, for example by focusing the light through a plano-convex lens 76, then through an excitation filter 78 and then onto a

dichroic mirror, which reflects the light downward through the objective lens 72 and illuminates the fluorescent label which has accumulated in the test channel 20, typically as a result of a biological action such as incorporation of fluorescently labeled materials flowing through the test channel into a thrombus as it forms on the surface of the test channel. The
5 light excites the fluorescent label, causing the fluorescent label to fluoresce and emit longer wavelength photons which are collected by the objective lens 72 and passed through the dichroic mirror 80. The fluorescent light may be detected by a camera 82 after it passes through an emission filter 84. Suitable systems and chemistries employing these general principles are described in commonly-owned PCT application WO 2006/065739, which has
10 been previously incorporated herein by reference.

[0031] While the above is a complete description of the preferred embodiments of the invention, various alternatives, modifications, and equivalents may be used. Therefore, the above description should not be taken as limiting the scope of the invention which is defined by the appended claims.

WHAT IS CLAIMED IS:

1. A test cartridge comprising:
a body having at least one sealable inlet well and at least one sealable collection well; and
at least one test channel in the body extending from the sealable inlet well to the sealable collection well,
wherein at least one of the wells is adapted to couple to a pressure source to transfer a test fluid from the sealable inlet well, through the test channel, and into the collection well.
2. A test cartridge as in claim 1, wherein the sealable collection well is adapted to couple to a vacuum pressure source.
3. A test cartridge as in claim 1, wherein the sealable inlet well is adapted to connect to a positive pressure source.
4. A test cartridge as in claim 1, wherein the body includes a plurality of test channels extending between the at least one sealable inlet well and the at least one sealable collection well.
5. A test cartridge as in claim 4, wherein the body includes a plurality of sealable collection wells, with each collection well connected to receive test fluid from one and only one test channel.
6. A test cartridge as in claim 4, wherein the body includes a plurality of sealable inlet wells, with each inlet well connected to supply test fluid to one and only one test channel.
7. A test cartridge as in claim 4, wherein the body includes a plurality of inlet wells and a plurality of collection wells, with each inlet well and each collection well connected to supply and receive test sample from and to one and only one test channel.
8. A test cartridge as in claim 1, wherein the body is composed at least partially of an optically transparent polymer.

9. A test cartridge as in claim 8, wherein the polymer is selected from the group consisting of polycarbonates, polystyrenes, and polyacrylates.
10. A test cartridge as in claim 1, wherein the body is composed at least partially of siliconized glass.
11. A test cartridge as in claim 1, wherein the body comprises a base having a surface and a cover having a surface, wherein the surfaces seal against each other and define the test channels therebetween.
12. A test cartridge as in claim 1, wherein the test channels comprise a thrombotic substance.
13. A test cartridge as in claim 1, wherein the test channel has a rectangular cross-section.
14. A cartridge as in claim 8, wherein the test channel has a width in the range from 0.25 mm to 1.5 mm and a depth in the range from 25 μm to 500 μm .
15. A test cartridge as in claim 1, wherein the inlet well has a volume in the range from 2 ml to 5 ml and the collection well has a volume in the range from 2 ml to 5 ml.
16. A test cartridge as in claim 1, wherein the test channel is disposed in an axial direction along a top surface of the body.
17. A test cartridge as in claim 16, wherein the inlet and collection wells are disposed at inlet and outlet ends of the test channel, respectively, and are disposed in a vertical direction so that each well has a bottom spaced-apart from the inlet and to which it is connected.
18. A test cartridge as in claim 17, wherein the bottoms of each inlet and collection well is connected to the test channel by a vertical chimney to permit flow between the bottom of the well and the test channel.
19. A test system comprising:
a blood test cartridge according to any one of claims 2 to 4;

a pressure source having a plurality of connectors, with one connector coupled to each of the collection and/or inlet wells to independently apply a pressure differential across each test channel.

20. A test system as in claim 19, wherein the pressure source comprises a plurality of syringes.

21. A test system as in claim 19, further comprising a detection system which views each of the plurality of test channels.

22. A test system as in claim 21, wherein the detection system has separate optics with a plurality of cameras for viewing each test channel.

23. A test system as in claim 21, wherein the detection system has a single optical system with one camera for viewing all test channels.

24. A test system as in claim 21, wherein the detection system detects fluorescent emissions.

25. A method for analyzing a fluid biological sample, said method comprising:

introducing at least one sample into an inlet well in a test cartridge;

applying a pressure differential to a first test channel in the test cartridge, wherein the pressure differential induces the fluid biological sample to flow from the inlet well through the test channel and into a collection well in the test cartridge;

analyzing the fluid biological sample as it flows through and is contained within the test channel; and

disposing of the test cartridge while the biological fluid remains contained and sealed within the test cartridge.

26. A method as in claim 25, wherein the pressure differential is applied to a plurality of test channels to draw the fluid biological sample through said test channels and into a plurality of collection wells.

27. A method as in claim 26, wherein the differential pressure is applied at different levels to at least some of said plurality of test channels, wherein the fluid biological

sample is drawn at different rates and/or in different amounts through said at least some test channels.

28. A method as in claim 27, wherein at least some of said plurality of test channels are connected to receive fluid biological sample from different inlet wells.

29. A method as in claim 25, wherein the fluid biological sample comprises blood or a blood product and analyzing comprises quantifying thrombus formation, blood coagulation, an inflammatory response, or circulating tumor cell recruitment.

30. A method as in claim 29, wherein analyzing comprises monitoring platelet accumulation on a thrombogenic surface of the test channel.

31. A method as in claim 25, wherein analyzing is performed at least partially while the sample flows through the test channel.

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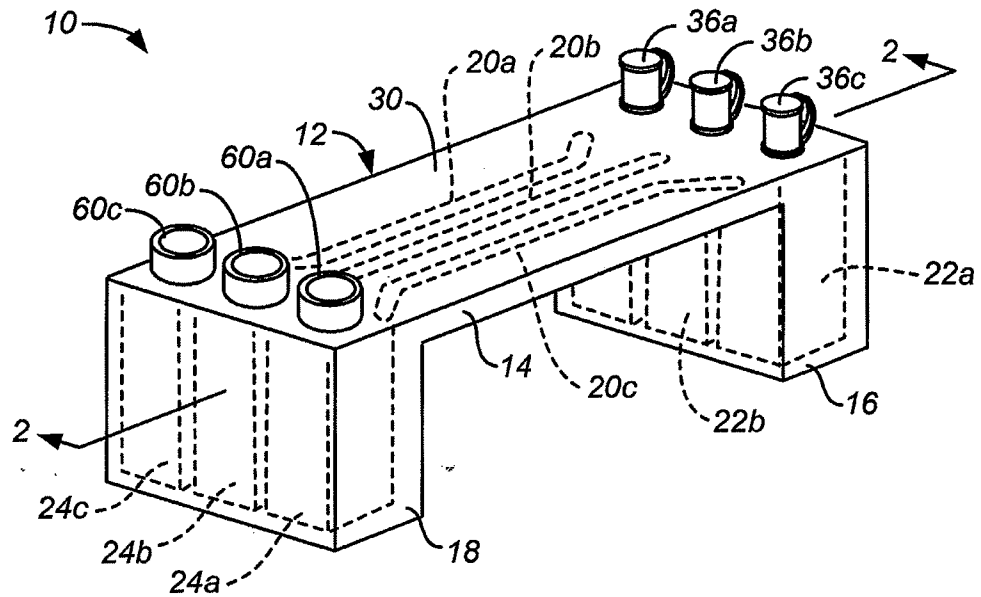


FIG. 1

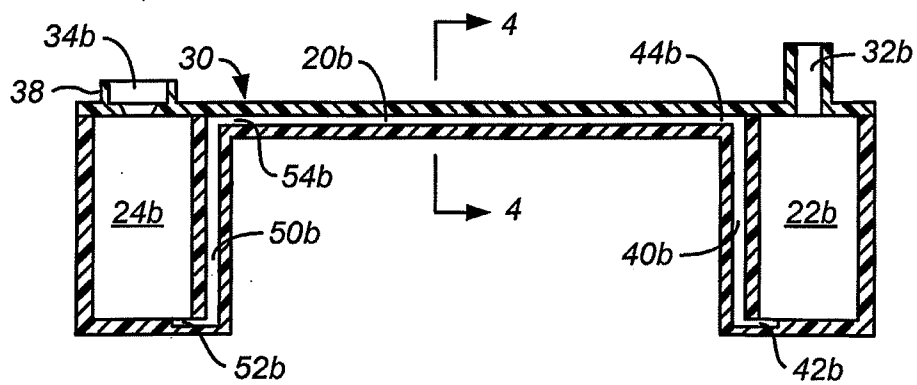


FIG. 2

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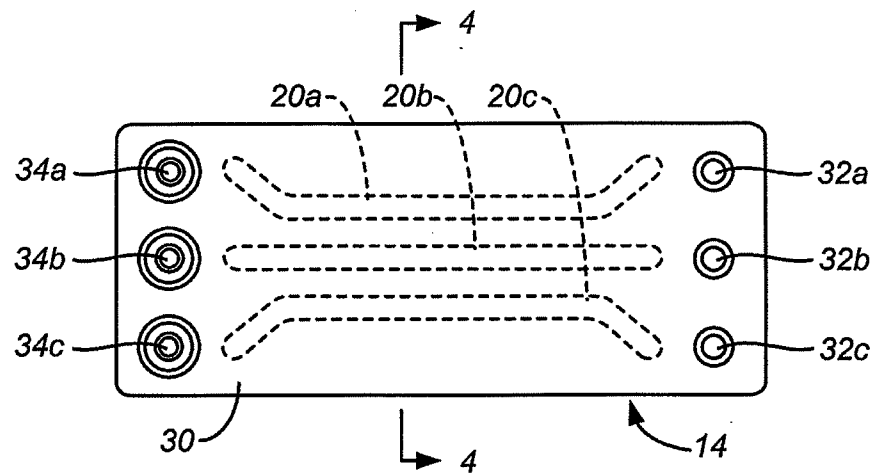


FIG. 3

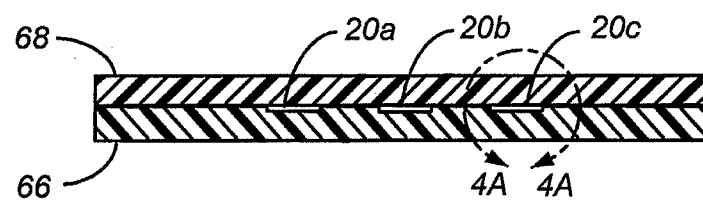


FIG. 4

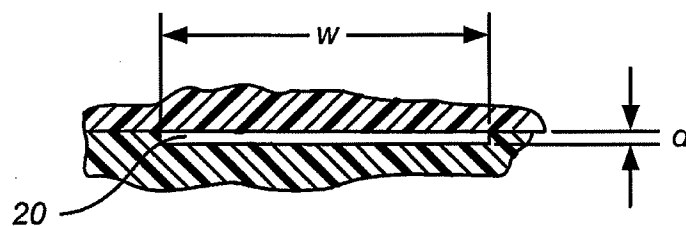


FIG. 4A

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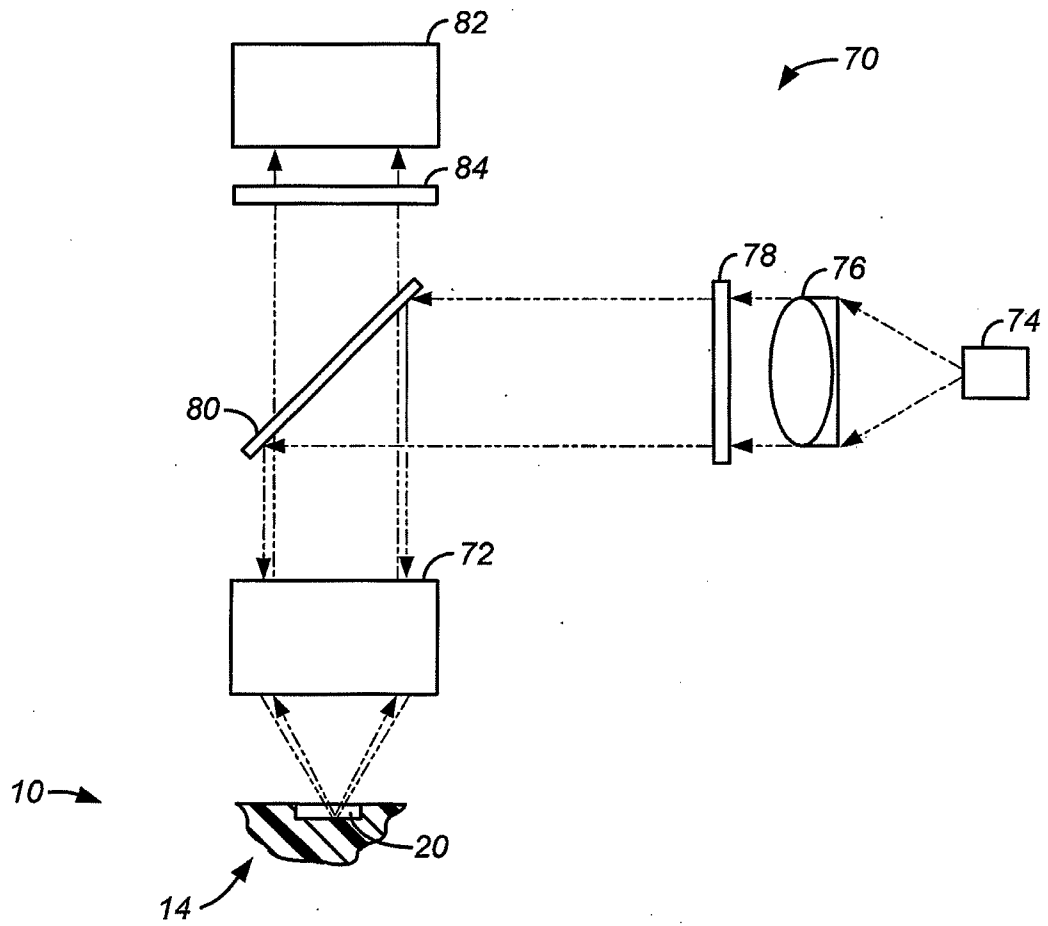


FIG. 5

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2009/067742

A. CLASSIFICATION OF SUBJECT MATTER
INV. B01L3/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
B01L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DE 101 48 210 A1 (IBIDI GMBH [DE]) 24 April 2003 (2003-04-24) paragraphs [0014], [0015], [0016], [0018], [0019], [0021], [0032], [0034]; figures 1,4,5 -----	1-15
X	US 2006/215155 A1 (THINXXS GMBH [DE]; WEBER LUTZ [DE]) 28 September 2006 (2006-09-28) paragraphs [0007], [0020], [0021], [0023], [0024], [0026], [0042], [0047], [0051], [0053]; figures 2,4,5 -----	1-15, 19-24
X	WO 01/68238 A2 (MICRONICS INC [US]) 20 September 2001 (2001-09-20) figure 1 page 7, line 19 - page 8, line 21 ----- -/--	25-29,31

☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

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Date of the actual completion of the international search

26 February 2010

Date of mailing of the international search report

11/03/2010

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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2009/067742

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

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