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(54) **MOLDED MICROFLUIDIC FLUID CELL FOR ATOMIC FORCE MICROSCOPY**

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G01Q 30/20 (2010.01)
B28B 11/00 (2006.01)

(52) **U.S. Cl.** **850/18**; 850/40; 850/48; 850/52; 250/310

(58) **Field of Classification Search** 850/1–3, 850/18, 33, 40, 45, 48, 52, 53, 60; 250/306, 250/307, 310, 526
See application file for complete search history.

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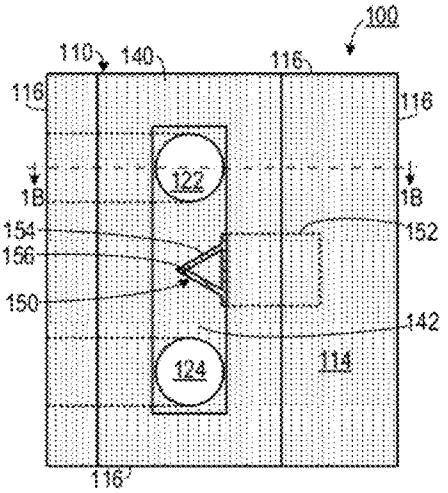
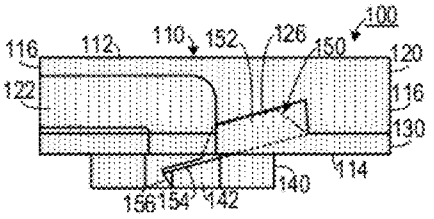
(57) **ABSTRACT**

A microfluidic cell includes a compressible block and a cantilever. The compressible block includes a first horizontal surface, an opposite second horizontal surface and a plurality of vertical surfaces therebetween. A gasket structure depends downwardly from the second horizontal surface. The gasket structure defines an open cavity therein. The compressible block defines a fluid inlet passage and a fluid outlet passage each in fluid communication with the cavity and opening to a selected one of the first horizontal surface and one of the plurality of vertical surfaces. The cantilever includes body portion and a beam extending laterally therefrom. The body portion is embedded in the compressible block and a portion of the beam extends into the cavity defined by the gasket structure.

23 Claims, 5 Drawing Sheets





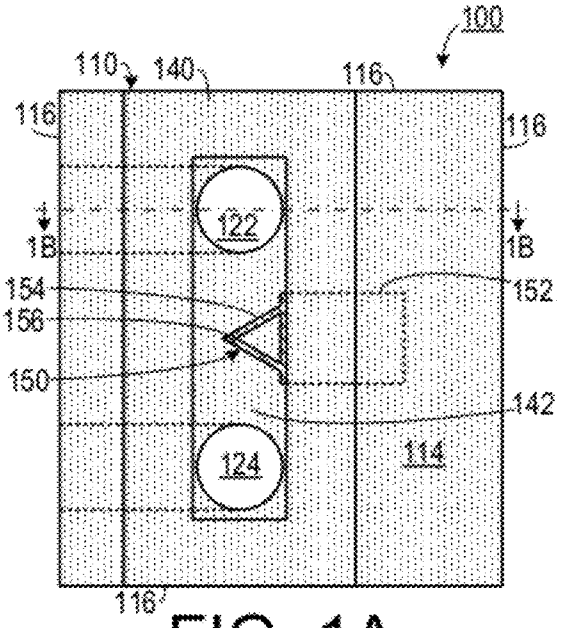


FIG. 1A

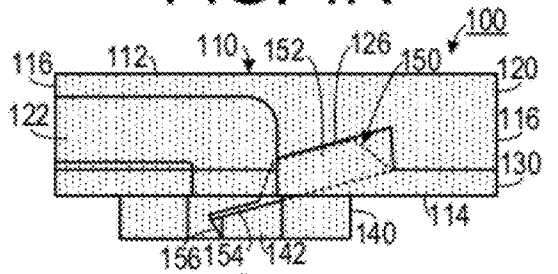


FIG. 1B

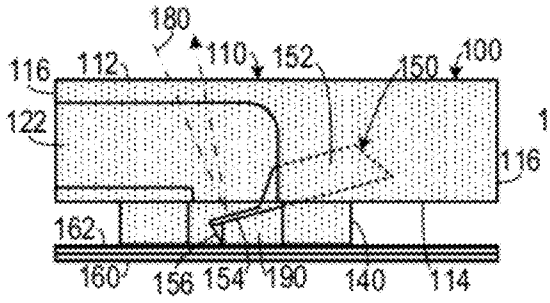


FIG. 2A

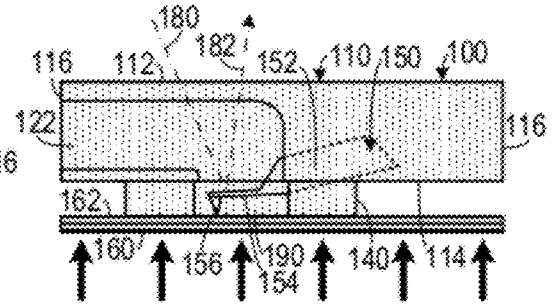


FIG. 2B

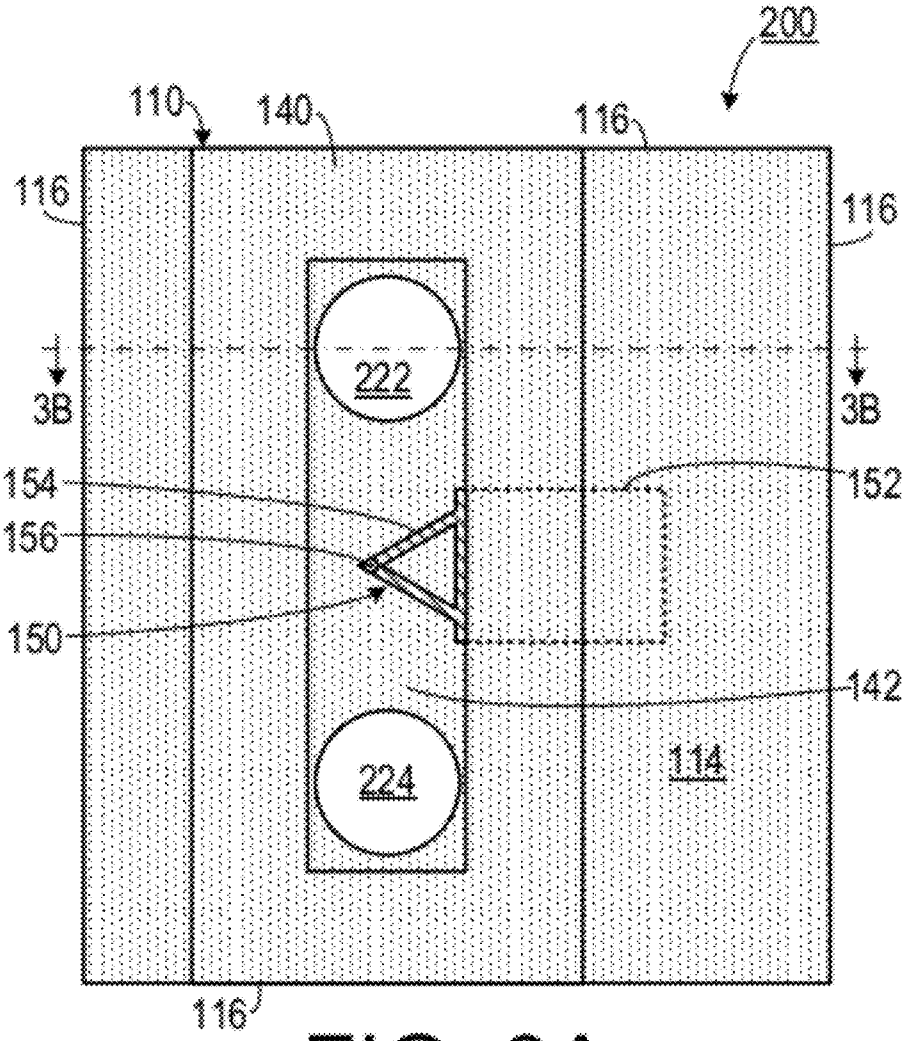

200
110
140
116
116
116
222
3B
3B
154
152
156
150
142
224
114
116

FIG. 3A

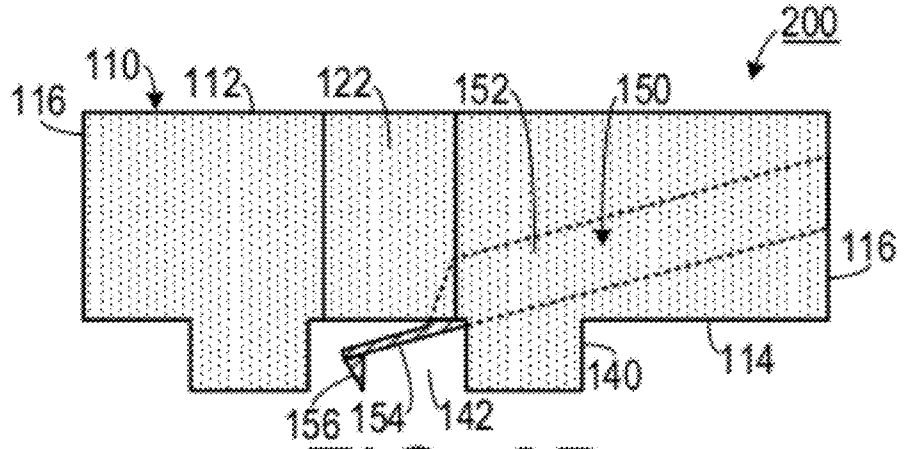

200
110
112
122
152
150
116
116
114
140
156
154
142

FIG. 3B

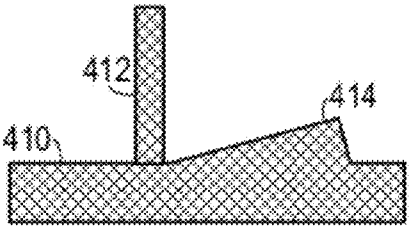


FIG. 4A

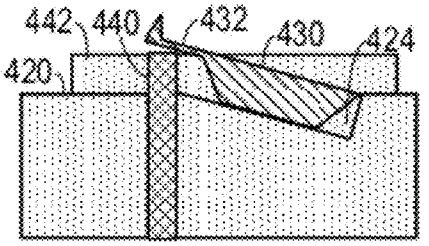


FIG. 4E

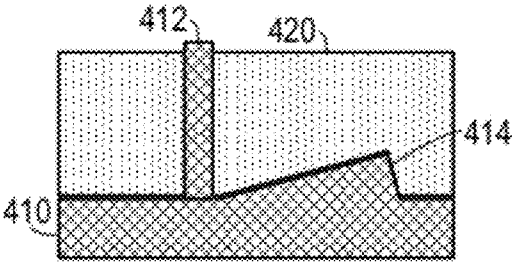


FIG. 4B

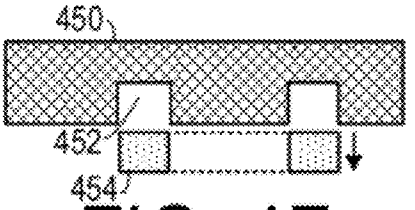


FIG. 4F

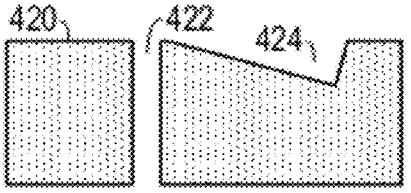


FIG. 4C

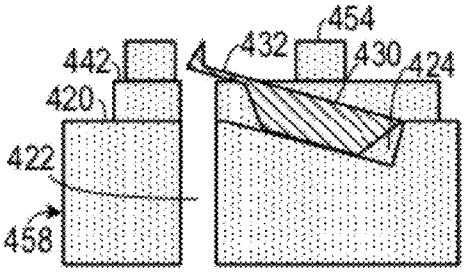


FIG. 4G

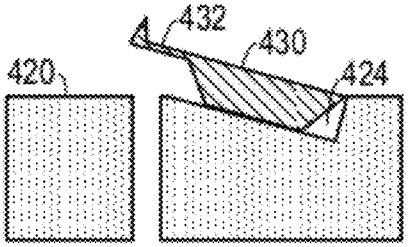


FIG. 4D

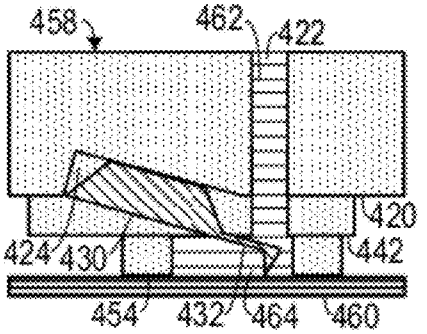


FIG. 4H

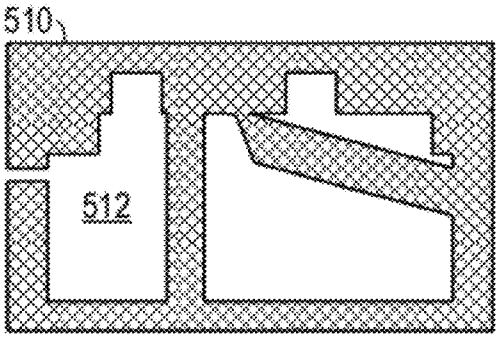


FIG. 5A

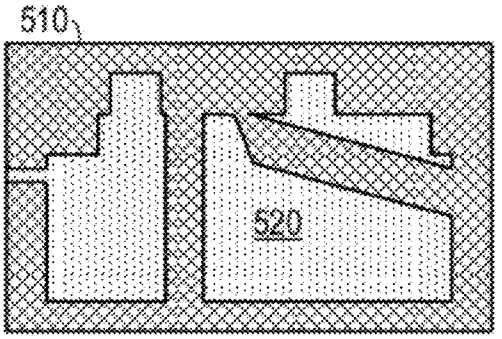


FIG. 5B

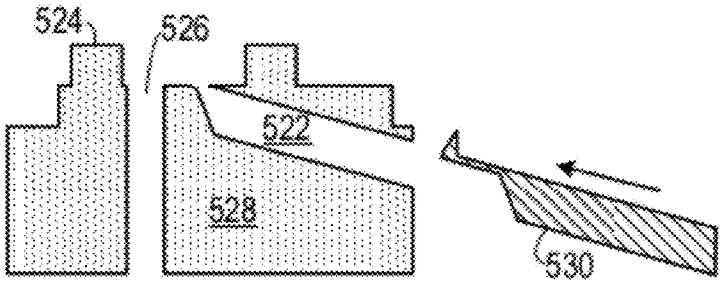


FIG. 5C

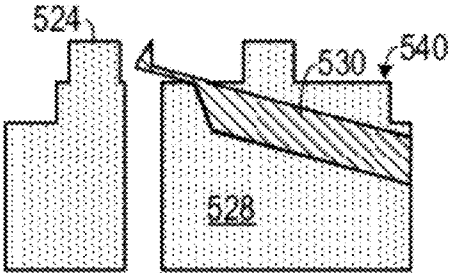


FIG. 5D

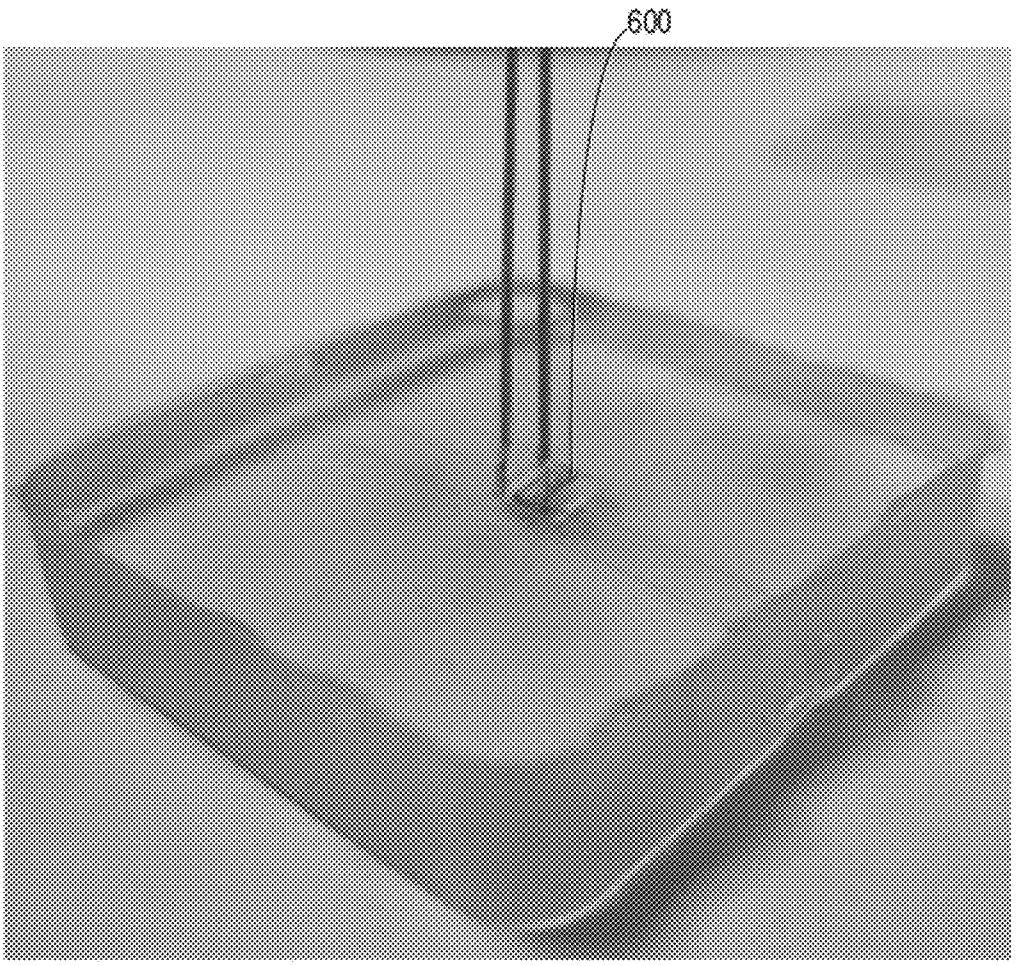


FIG. 6

MOLDED MICROFLUIDIC FLUID CELL FOR ATOMIC FORCE MICROSCOPY

CROSS-REFERENCE TO RELATED APPLICATION(S)

This application claims the benefit of U.S. Provisional Patent Application Ser. No. 61/182,165, filed May 29, 2009, the entirety of which is hereby incorporated herein by reference.

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates to microfluidic systems and, more specifically, to a microfluidic system used in atomic force microscopy.

2. Description of the Related Art

Atomic force microscope (AFM) is used by researchers to image surfaces with nanometer lateral resolution and sub-nanometer height resolution. In addition, high resolution imaging can be performed in physiological environments, which include liquids and physiological buffers. Imaging in an enclosed physiological environment is typically accomplished with a "liquid cell," which can be built in house or obtained commercially. A liquid cell secures the probe of an atomic force microscope and positions the microcantilever tip at the surface to be imaged while maintaining an enclosed and sealed environment containing a small volume of liquid, which can typically be pumped or heated.

However, current systems place the liquids to be imaged in relatively large volumes, thereby making specific molecules difficult to find with the probe. Commercially available liquid cells enclose a volume of liquid using an O-ring gasket that measures approximately one centimeter in diameter or larger and typically enclose a volume of 50 microliters to several milliliters.

For many applications of the AFM, this relatively large volume of liquid is a major drawback. This is because many proteins and other biomaterials are difficult to obtain in large quantities and prolonged imaging assays can only be conducted at very low concentrations of material. As a result, the study of the dynamics of crystal growth by proteins during biomineralization processes is limited by the capability of today's AFM liquid cells. Also current liquid cell designs contain significant "dead volume" in which a reagent pumped to the sample does not distribute uniformly as a consequence of expanding flow lines from the inlet via through the flow cell. A more well-defined flow field would allow a clear interpretation of real-time in situ AFM measurements of kinetic processes.

Typical cells used in AFM imaging include transparent materials to allow the monitoring of cantilever deflection optically and are able to hold the cantilever probe die firmly in place. They also enclose the cantilever in a liquid-tight seal and allow the cantilever tip access to the surface of a sample during imaging or force spectroscopy. Many liquid cells are machined from quartz or plastic with a metal spring that holds the cantilever die in place. A recessed O-ring seals against the sample surface and defines the liquid microenvironment.

Shrinking the flow channel is stymied by the need to enclose both the cantilever, which is microscopic, and the substrate die, which is macroscopic having lengths in millimeters on two dimensions. Many existing liquid cell designs have a macroscopic gasket, which surrounds the entire probe including the cantilever and substrate die.

Therefore, there is a need for a microfluidic cell for use in AFM that maintains a micro-scale volume of liquid near the sensing probe.

SUMMARY OF THE INVENTION

The disadvantages of the prior art are overcome by the present invention which, in one aspect, is a microfluidic cell that includes a compressible block and a cantilever. The compressible block includes a first horizontal surface, an opposite second horizontal surface and a plurality of vertical surfaces therebetween. A gasket structure depends downwardly from the second horizontal surface. The gasket structure defines an open cavity therein. The compressible block defines a fluid inlet passage and a fluid outlet passage each in fluid communication with the cavity and opening to a selected one of the first horizontal surface and one of the plurality of vertical surfaces. The cantilever includes body portion and a beam extending laterally therefrom. The body portion is embedded in the compressible block and a portion of the beam extends into the cavity defined by the gasket structure.

In another aspect, the invention is a microfluidic cell that includes a compressible block and a cantilever. The compressible block includes a gas permeable polymer and includes a first horizontal surface and an opposite second horizontal surface and a plurality of vertical surfaces therebetween. A gasket structure depends downwardly from the second horizontal surface. The gasket structure defines an open cavity therein. The compressible block defines a fluid inlet passage and a fluid outlet passage each in fluid communication with the cavity and opening to a selected one of the first horizontal surface and one of the plurality of vertical surfaces. The gas permeable polymer includes a material that is transparent to a preselected wavelength of electromagnetic energy selected to illuminate a surface of the cantilever by an atomic force microscopy apparatus. The cantilever includes a body portion and a beam extending laterally therefrom. The body portion is embedded in the compressible block and a portion of the beam extends into the cavity defined by the gasket structure.

In yet another aspect, the invention is a method of making a microfluidic cell in which a gas permeable polymer is placed into a mold that defines a void that is complimentary in shape to a compressible block so that the compressible block includes a first horizontal surface and an opposite second horizontal surface and a plurality of vertical surfaces therebetween, a gasket structure depending downwardly from the second horizontal surface so that the gasket structure defines an open cavity therein. Also so that the compressible block defines a fluid inlet passage and a fluid outlet passage each in fluid communication with the cavity and opening to a selected one of the first horizontal surface and one of the plurality of vertical surfaces. The flexible polymer is removed from the mold so as to define the compressible block. A cantilever is inserted into the compressible block. The cantilever includes a body portion and a beam extending laterally therefrom. The cantilever is inserted so that the body portion is embedded in the compressible block and a portion of the beam extends into the cavity defined by the gasket structure.

These and other aspects of the invention will become apparent from the following description of the preferred embodiments taken in conjunction with the following drawings. As would be obvious to one skilled in the art, many variations and modifications of the invention may be effected without departing from the spirit and scope of the novel concepts of the disclosure.

BRIEF DESCRIPTION OF THE FIGURES OF THE DRAWINGS

FIG. **1**A is a bottom plan view of a first representative embodiment of a microfluidic cell.

FIG. **1**B is a cross-sectional view of the microfluidic cell shown in FIG. **1**A taken along line **1**B-**1**B.

FIG. **2**A is a cross sectional view of a microfluidic cell applied to an imaging surface in an uncompressed mode.

FIG. **2**B is a cross sectional view of the microfluidic cell shown in FIG. **2**A applied to an imaging surface in a compressed mode.

FIG. **3**A is a bottom plan view of a second representative embodiment of a microfluidic cell.

FIG. **3**B is a cross-sectional view of the microfluidic cell shown in FIG. **3**A taken along line **3**B-**3**B.

FIGS. **4**A-**4**H are a series of schematic drawings demonstrating a first method of making a microfluidic cell.

FIGS. **5**A-**5**D are a series of schematic drawings demonstrating a second method of making a microfluidic cell.

FIG. **6** is a photograph of one experimental embodiment of a microfluidic cell.

DETAILED DESCRIPTION OF THE INVENTION

A preferred embodiment of the invention is now described in detail. Referring to the drawings, like numbers indicate like parts throughout the views. Unless otherwise specifically indicated in the disclosure that follows, the drawings are not necessarily drawn to scale. As used in the description herein and throughout the claims, the following terms take the meanings explicitly associated herein, unless the context clearly dictates otherwise: the meaning of "a," "an," and "the" includes plural reference, the meaning of "in" includes "in" and "on."

As shown in FIGS. **1**A-**1**B, one embodiment is a microfluidic cell **100** for use in atomic force microscopy that includes a compressible block **110**. The compressible block includes a first horizontal surface **112** and an opposite second horizontal surface **114**. A plurality of vertical surfaces **116** are disposed therebetween. A gasket structure **140** extends downwardly from the second horizontal surface **114** and defines a cavity **142** therein. The compressible block **110** also defines a fluid inlet passage **122** and a fluid outlet passage **124** that are each in fluid communication with the cavity **142** and that open to a selected one of the first horizontal surface **112** and one of the plurality of vertical surfaces **116**. A cantilever **150** includes a body portion **152** and a beam **154** extending laterally therefrom. The body portion **152** is embedded in the compressible block **110** and a portion of the beam **154** extends into the cavity **142**. In certain embodiments, a probe tip **156** extends downwardly from the distal end of the beam **154**. Other embodiments do not employ a probe tip.

In certain embodiments, the compressible block **110** is made from a gas permeable polymer, such as poly(dimethylsiloxane) ("PDMS"). PDMS works well in AFM applications, as it is transparent to the wavelengths of electromagnetic energy used with existing AFM systems to illuminate the beam **154** of the cantilever **150**.

The embodiment shown in FIGS. **1**A-**1**B includes three layers of PDMS. The first layer **120** has a first side that defines an indentation **126** that is configured to receive a first portion of the cantilever **150** therein. A second layer **130** is disposed on the first side of the first layer **120** and embeds a second portion of the cantilever **150**. A third layer (a gasket layer) is disposed on a second side of the second layer and defines the gasket structure **140**.

As shown in FIG. **2**A, the microfluidic cell **100** can be used to image an imaging surface **162** by placing the gasket structure **140** against the imaging surface **162**, which may be supported by a rigid substrate **160**, and injecting a fluid through the fluid inlet passage **122**. Thus, the cavity **142** and the imaging surface **162** form a sample chamber **190** for holding the fluid of interest.

The imaging surface **162** can include a material to be imaged. For example, organic cells of interest can be applied to the imaging surface **162** and the cantilever **150** can be used to image the cells as they interact with the fluid. In another example, the imaging surface **162** can be functionalized with a compound of interest and the fluid can interact with the compound during the imaging process.

In one embodiment, a beam of electromagnetic radiation **180** is reflected off of the cantilever **150** while the compressible block **110** is compressed, causing the probe **156** to engage the imaging surface **162**. Properties of the reflected beam **182** (such as its displacement) can be used to provide imaging or other information about the imaging surface. In the example shown in FIG. **2**B, the block **110** is compressed by driving the imaging surface **162** upwardly against the block **110** in the direction of the arrows. Lateral displacement of the cantilever **150** can be accomplished by compressing the block **110** is a lateral direction.

An embodiment on a microfluidic cell **200**, in which the compressible block **110** comprises a unitary piece of a material, is shown in FIGS. **3**A and **3**B. Also, in this embodiment, the fluid inlet passage **222** and the fluid outlet passage **224** extend upwardly from the cavity **142** to open to the top horizontal surface **112** of the block **110**.

One method of making a microfluidic cell is shown in FIGS. **4**A-**4**H, in which a mold **410** is formed on a rigid material (e.g., a silicon crystal) using, e.g., existing photolithographic techniques. The mold **410** includes a feature **414** that is complementary in shape to an indentation **424** for holding a cantilever **430** therein. The mold **410** also includes two posts (a first post **412** and a second post, the view of which is obscured by the first post **412** in this figure) that correspond to the fluid inlet **422** and the fluid outlet.

A polymer (such as PDMS) is applied to the mold, thereby rendering a cast of the first layer of the block **420**. The polymer is cured and the removed, thereby rendering a cast of the first layer of the block **420**.

A cantilever **430** is placed into the indentation **424** and rods **440** corresponding to the fluid inlet passage **422** and the fluid outlet passage are placed in the block **420**. A second layer **442** of polymer is applied to the first layer of the block **420** to embed the cantilever **430**, but not cover at least a portion of the beam **432** of the cantilever **430**.

Separately, a second mold **450** defines an void **452** in the shape of the gasket structure **454**. Polymer is placed into the void **452**, cured and the gasket structure **454** is removed from the mold **450**. The gasket structure **454** is then applied to the second layer **442**, thereby forming the microfluidic cell **458**. The microfluidic cell **458** may then be placed against the imaging surface **460** and the fluid of interest **462** can be injected through the fluid inlet **422** into the sample chamber **464**.

In another embodiment, as shown in FIGS. **5**A-**5**D, the block **528** can be made as a single unitary structure. In this embodiment, a mold **510** is made so as to be complimentary in shape to the block **528**. A polymer **520** is injected into the mold **510**, cured and the resulting block **528** is removed from the mold **510**. The mold **510** is shaped so as to include a slit **522** into which a cantilever **530** can be slid. The mold **510** also has a void complimentary to the gasket structure **524**. Once

the block **528** is removed from the mold **510**, the cantilever **530** is slid into place and the resulting microfluidic cell **540** is ready for use.

A photograph of a microfluidic cell **600** of the type disclosed herein is shown in FIG. **6**.

The microfluidic liquid cells disclosed herein are capable of high-resolution atomic force microscope (AFM) imaging and force spectroscopy. In one experimental embodiment, a microfluidic liquid cell was assembled from three molded poly(dimethylsiloxane) (PDMS) pieces and integrated with commercially purchased probes. The AFM probe was embedded within the assembly such that the cantilever and tip protrude into the microfluidic channel. This channel is defined by the PDMS assembly on the top, a PDMS gasket on all four sides, and the sample substrate on the bottom, forming a liquid-tight seal. This design features a low volume fluidic channel on the order of 50 nL, which is a reduction of over 3-5 orders of magnitude compared to several existing liquid cells. This device facilitates testing at high shear rates and laminar flow conditions coupled with full AFM functionality in microfluidic aqueous environments, including execution of both force displacement curves and high resolution imaging.

The AFM probe was embedded into the flow cell so that the cantilever and tip protruded into the microfluidic channel. This channel was defined by the PDMS assembly on the top, a PDMS gasket on all four sides, and the sample substrate on the bottom, forming a liquid-tight seal. This design allows for much smaller enclosed liquid volumes than conventional cells. By precisely aligning the cantilever within the microchannel, the volume surrounding the cantilever is reduced by three orders of magnitude or more. In addition, using PDMS, a material permeable to gas, eliminated air bubble formation that is commonly found with commercially available liquid cells. Such bubbles can form quite readily especially for experiments run at physiological temperature and can quickly clog microfluidic flow and impede imaging

In the experimental embodiment, the microfluidic liquid cell was formed from three molded poly(dimethylsiloxane) (PDMS) parts, each assembled was aided by a long working-distance microscope (available Nikon). The cell was designed for use in the Multimode AFM (such as an AFM available from Veeco Metrology). The parts of the cell were formed by pouring uncured PDMS (Sylgard® 184 Silicone elastomer kit, available from Dow Corning) into a custom designed polycarbonate mold. A 13 degree ramp was milled into the polycarbonate mold. This produced a die shaped recess in the cured PDMS with a precise fit and angle for the AFM probe. The polycarbonate mold also provided a method to define inlet and outlet vias to either side of the cantilever. These vias were defined by 100 micron diameter Teflon tubing (available from Upchurch). The tubing was inserted into two holes drilled into the polycarbonate mold on each side of the ramp.

Uncured PDMS was mixed thoroughly with a ratio of 10:1 elastomer to curing agent and degassed under vacuum for 30 minutes to remove air bubbles. The PDMS was injected via a syringe into the mold and then cured in an oven at 60° C. for one hour. The thickness of the first part (Part 1) was determined by a three dimensional Plexiglas box surrounding the polycarbonate mold to contain the injected PDMS. Four identical parts were made from each mold. The parts were then cut apart with a razor blade. Each assembled liquid cell had outer dimensions of 3 cm×4 cm×1 cm. To interface pumped liquid seamlessly into the liquid cell vias, metal inserts were created. The metal inserts molded voids matching the outer diameter of the 234 um outer diameter glass tubing (available from Upchurch).

The cured first part was then removed from the mold and the interior tubing was removed to leave vias. A cantilever chip (e.g., NTESP, available from Veeco Probes) was secured into the recess with a drop of PDMS. The chip included four v-shaped Si_3N_4 cantilevers ranging in length from 85 μm to 320 μm.

A second molded PDMS component (Part 2) was added next. Part 2 surrounded the cantilever die on four sides and provided a uniform platform upon to which the gasket was secured. The thickness of Part 2 was designed to be slightly smaller than the distance from the top of Part 1 to the base of the cantilever, as measured using optical microscopy. Part 2 was adhered to Part 1 with uncured PDMS which seeped into the air gap between the two PDMS pieces and was cured to secure into place.

The third molded PDMS piece was the gasket, which formed the microfluidic channel. The gasket mold was microfabricated using SU-8 (SU-8 2025, available from DuPont) photolithography which created highly accurate definition of PDMS sidewalls and channel height. SU-8 was spun onto a silicon wafer and prebaked. Recommended procedures were used to for spinning and development of SU-8, according to the respective layer thickness. Several gasket molds were created with thicknesses spanning 50 to 80 μm.

To form the gasket, a small amount of uncured PDMS was added by applicator into the mold, squeegeed using a sharply-cut thin rubber square, and baked at 60° C. for 60 minutes. The PDMS gasket formed an interior rectangular channel which was 2700 μm×300 μm and approximately 65 μm thick. The longest cantilever (320 μm) was removed because it was slightly longer than the width of the channel (300 μm). The length of the channel formed by the gasket was chosen to span the width of the cantilever die as well as the inlet and outlet ports. The thickness of the gasket was designed so that the bottom of the gasket, which contacts the sample surface, is closely aligned to the freestanding cantilever tip. This ensured that minimal gasket compression is required before the tip contacted the sample surface during operation.

A suite of gaskets were made with varying thicknesses which achieving the precise offset between the probe tip and the gasket. The offset was measured using optical microscopy for each liquid cell. PDMS gaskets were formed with thicknesses ranging from 50 μm to 80 μm in increments of 10 μm and were selected for each liquid cell to be within +/−5 μm of the probe tip and aligned to the cantilever under a microscope. The gasket was then bonded with a small amount of PDMS for a tight seal. The assembled liquid cell could now be inverted and pressed against a flat surface so that the gasket enclosed the cantilevers. For well controlled flow, a syringe pump (available from Harvard Apparatus) was used.

AFM operation was characterized with the microfluidic liquid cell by completing force-distance curves, which are also used to determine cantilever displacement sensitivity. In a force-distance curve measurement, the cantilever deflection is recorded as the sample surface is raised and lowered slightly such that the tip briefly makes contact with the surface, deflects up, and then is drawn out of contact. Data from this measurement were collected on a Veeco MultiMode AFM with NanoScope Ma controller. The trace during retraction was recorded. In the experiment, the liquid cell was sealed against a flat glass surface and deionized (DI) water was applied with a syringe. The gasket was compressed by the glass sample with a computer controlled stepper motor until deflection was recorded. The amount of compression of the gasket necessary for the tip to make contact varied from device to device, but in general occurred within 5 microns. A z-axis piezotube actuator was used for accurate and linear

motion. A vertical range of 4 microns was used during the force curves. The cantilever was indented 2 microns and then retracted until the cantilever was no longer touching the surface.

A second demonstration of AFM operation with the microfluidic liquid cell was imaging in an aqueous environment. For this measurement, a silicon calibration grating with a one dimensional array of triangular steps having a precise linear and angular dimensions defined by the Silicon <111> crystal planes (TGG01 Grating, available from MikroMasch) was used. Images were taken in contact mode and scanned 10 μm by 3 um. For these measurements, the rough surface of the sample prohibited a water-tight seal, and therefore no flow-through measurements were made.

Another characterization of AFM operation with the microfluidic liquid cell was an analysis of the liquid cell's low Reynolds number laminar flow. This was done through a series of time lapse still frames taken from a video recorded with a 20× objective magnification. The video was acquired with a Nikon Ti-E inverted microscope with brightfield transmission illumination. In this example, the liquid cell was engaged against a flat PDMS sample surface under a slightly compressive force. Although AFM imaging was not performed simultaneously with flow in this example, the applied pressure could be modulated and the cantilever deflection recorded by visual inspection. Pressure driven flow from a syringe was created and small 4 um microbeads (available from Bangs Labs) were suspended in the DI water to aid in flow visualization. In the time lapse images at 15 frames per second, beads travel at a speed of 0 to 500 um/s. The upper value corresponds to a volume flow rate of ~10 nL/s.

There are several areas where this device may prove useful and potentially transformative. Atomic force microscopy has become a vital tool in the study of molecular dynamics of biomineralization. However, quantification of kinetics and thermodynamics of protein adsorption to crystal surfaces requires a constant flow of protein to replenish the depletion layer and overcome mass transport limitations. Modification to commercial fluid cell designs can provide a simpler geometry that allows calculation of flow conditions. Videos taken of liquid flow reveal a laminar flow that is not obstructed by the probe die, as occurs in typical existing designs.

The Reynolds number calculation is estimated from the following equation:

$$Re = \frac{\rho v D_C}{\mu}$$

with the following values for water density ρ~1 g/cm^3, velocity ν~500 μm/s, viscosity μ~1 mPa·s, and

$$D_C = \frac{2wh}{w+h} \sim 107\ \mu m,$$

resulting in a Re~0.05. Computational fluid dynamics simulations of a Veeco fluid cell with a similar flow velocity calculate a Re~**15**. A conservative shear rate of 10 Hz was demonstrated; however, higher shear rates are certainly possible. Importantly for applications requiring high shear rates, the microfluidic cell disclosed herein can also operate at flow velocities 300 times greater and still achieve similar laminar flow of traditional liquid cells.

The calculated volume enclosed by the channel is ~50 nL. The reduced volume of the flow cell may allow AFM visualization of very precious samples at high concentration, for example in experiments of in situ or ex vivo binding of soluble proteins to surfaces. Therefore, experiments involving the constant flow of protein can be recorded for 3 orders of magnitude longer imaging times, or alternatively at much higher protein concentrations, than the same experiment conducted on a traditional liquid cell. The real time visualization of crystal growth can also substantially benefit from a microfluidic liquid cell as the efficiency of crystal growth is enhanced by confined liquid environments due to the suppression of natural convection resulting from the drastic decreases of the Grashof number.

This design has been used to record force-distance curves as well as to obtain high resolution contact mode images—both critical demonstrations of AFM capability. The volume encapsulated by the fluid cell is below 50 nL and further reduction in liquid volume may be achieved. This design succinctly combines batch-fabricated micro-cantilevers with batch-fabricated microfluidic channels.

The above described embodiments, while including the preferred embodiment and the best mode of the invention known to the inventor at the time of filing, are given as illustrative examples only. It will be readily appreciated that many deviations may be made from the specific embodiments disclosed in this specification without departing from the spirit and scope of the invention. Accordingly, the scope of the invention is to be determined by the claims below rather than being limited to the specifically described embodiments above.

What is claimed is:

1. A microfluidic cell, comprising:

a. a compressible block, including a first horizontal surface, an opposite second horizontal surface and a plurality of vertical surfaces therebetween, a gasket structure depending downwardly from the second horizontal surface, the gasket structure defining an open cavity therein, the compressible block defining a fluid inlet passage and a fluid outlet passage each in fluid communication with the cavity and opening to a selected one of the first horizontal surface and one of the plurality of vertical surfaces; and

b. a cantilever including a body portion and a beam extending laterally therefrom, the body portion embedded in the compressible block and a portion of the beam extending into the cavity defined by the gasket structure.

2. The microfluidic cell of claim **1**, wherein the compressible block comprises a polymer.

3. The microfluidic cell of claim **2**, wherein the polymer comprises a gas permeable polymer.

4. The microfluidic cell of claim **3**, wherein the gas permeable polymer comprises poly(dimethylsiloxane).

5. The microfluidic cell of claim **1**, wherein the compressible block comprises a material that is transparent to a preselected wavelength of electromagnetic energy.

6. The microfluidic cell of claim **1**, wherein the cantilever further comprises a probe extending downwardly from a distal end of the beam.

7. The microfluidic cell of claim **1**, wherein the preselected wavelength comprises a wavelength selected to illuminate a surface of the cantilever by an atomic force microscopy apparatus.

8. The microfluidic cell of claim **1**, wherein the compressible block comprises a unitary piece of a material.

9. The microfluidic cell of claim **1**, wherein the compressible block comprises:

a. a first layer having a first side that defines an indentation configured to receive a first portion of the cantilever therein;

b. a second layer disposed on the first side of the first layer and embedding a second portion of the cantilever, the second portion of the cantilever; and

c. a gasket layer disposed on a second side of the second layer, the gasket layer defining the gasket structure.

10. The microfluidic cell of claim **9**, wherein each of the first layer, the second layer and the gasket layer comprise a polymer.

11. The microfluidic cell of claim **10**, wherein the polymer comprises a gas permeable polymer.

12. The microfluidic cell of claim **11**, wherein the gas permeable polymer comprises poly(dimethylsiloxane).

13. The microfluidic cell of claim **1**, further comprising an imaging surface against which the gasket structure is disposed so that the cavity forms a sample chamber.

14. The microfluidic cell of claim **13**, wherein the imaging surface comprises a material to be imaged.

15. A microfluidic cell, comprising:

a. a compressible block comprising a gas permeable polymer and including a first horizontal surface and an opposite second horizontal surface and a plurality of vertical surfaces therebetween, a gasket structure depending downwardly from the second horizontal surface, the gasket structure defining an open cavity therein, the compressible block defining a fluid inlet passage and a fluid outlet passage each in fluid communication with the cavity and opening to a selected one of the first horizontal surface and one of the plurality of vertical surfaces, the gas permeable polymer comprising a material that is transparent to a preselected wavelength of electromagnetic energy selected to illuminate a surface of the cantilever by an atomic force microscopy apparatus; and

b. a cantilever including a body portion and a beam extending laterally therefrom, the body portion embedded in the compressible block and a portion of the beam extending into the cavity defined by the gasket structure.

16. The microfluidic cell of claim **15**, wherein the cantilever further comprises a probe extending downwardly from a distal end of the beam.

17. The microfluidic cell of claim **15**, wherein the gas permeable polymer comprises poly(dimethylsiloxane).

18. The microfluidic cell of claim **15**, wherein the compressible block comprises a unitary piece of a material.

19. The microfluidic cell of claim **15**, wherein the compressible block comprises:

a. a first layer having a first side that defines an indentation configured to receive a first portion of the cantilever therein;

b. a second layer disposed on the first side of the first layer and embedding a second portion of the cantilever, the second portion of the cantilever; and

c. a gasket layer disposed on a second side of the second layer, the gasket layer defining the gasket structure.

20. The microfluidic cell of claim **15**, further comprising an imaging surface, that includes a material to be imaged, against which the gasket structure is disposed so that the cavity forms a sample chamber.

21. A method of making a microfluidic cell, comprising the steps of:

a. placing a gas permeable polymer into a mold that defines a void that is complimentary in shape to a compressible block including a first horizontal surface and an opposite second horizontal surface and a plurality of vertical surfaces therebetween, a gasket structure depending downwardly from the second horizontal surface, the gasket structure defining an open cavity therein, the compressible block defining a fluid inlet passage and a fluid outlet passage each in fluid communication with the cavity and opening to a selected one of the first horizontal surface and one of the plurality of vertical surfaces;

b. removing the flexible polymer from the mold so as to define the compressible block; and

c. inserting a cantilever into the compressible block, including a body portion and a beam extending laterally therefrom, so that the body portion is embedded in the compressible block and a portion of the beam extends into the cavity defined by the gasket structure.

22. The method of claim **21**, wherein the polymer comprises poly(dimethylsiloxane).

23. The method of claim **21**, further comprising the step of placing the gasket structure against an imaging surface so as to seal the gasket structure to the imaging surface.

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