sample stage). The fluid medium is selected for having a higher index of refraction than air, which increases the numerical aperture (NA) of the inverted microscope objective, thereby increasing the resolution of the inverted microscope as compared to imaging in air. Thus, such high NA optical systems depend upon the integrity of physical contact of the fluid medium between the inverted microscope objective and the sample focal plane for high throughput imaging.

[0005] An example of inverted microscopy is provided by U.S. Patent No. 8,199,407 B2, issued on June 12, 2012, entitled "Immersion Object, Apparatus for Forming an Immersion Film and Method," which is hereby incorporated by reference as if fully set forth herein.

SUMMARY

[0005a] In a first aspect, the present disclosure provides a control system for fluid immersion for inverted microscopy, the control system comprising: a sensor ring coupled to a distal portion of a microscope lens used with an inverted microscope, wherein the sensor ring forms an annulus in fluid communication with the microscope lens, wherein the annulus is enabled to convey a fluid that forms an immersion layer at a surface of the microscope lens during imaging using the microscope lens, and wherein the sensor ring further comprises: a plurality of sensor electrodes located circumferentially about the annulus, wherein each of the plurality of sensor electrodes remains in contact with the fluid when the fluid immerses the microscope lens; a common electrode located within the annulus, wherein the common electrode remains in fluid communication with the fluid; and a fluid port to receive additional fluid to replenish the immersion layer; a fluid replenishment system coupled to the fluid port and enabled to provide the additional fluid; an immersion controller coupled to the plurality of sensor electrodes, the common electrode, and the fluid replenishment system, the immersion controller enabled for: when the fluid immerses the microscope lens, measuring a first resistance of the fluid, respectively, between each of the plurality of sensor electrodes and the common electrode, to detect the fluid at each respective sensor electrode of the plurality of sensor electrodes; when the fluid exposes a first sensor electrode included in the plurality of sensor electrodes, measuring a second resistance of an air gap at the first sensor electrode; and responsive to detecting the air gap, controlling the fluid replenishment system to provide the additional fluid.

[0005b] In a second aspect, the present disclosure provides a microscope objective for fluid immersion for inverted microscopy, the microscope objective comprising: a sensor ring

coupled to a distal portion of a microscope objective used with an inverted microscope, wherein the sensor ring forms an annulus in fluid communication with the microscope objective, wherein the annulus is enabled to convey a fluid that forms an immersion layer at a surface of the microscope objective during imaging using the microscope objective, and wherein the sensor ring further comprises: a plurality of sensor electrodes located circumferentially about the annulus, wherein each of the plurality of sensor electrodes remains in contact with the immersion layer when the fluid immerses the microscope objective; a common electrode located within the annulus, wherein the common electrode remains in fluid communication with the fluid; and a fluid port to receive additional fluid to replenish the immersion layer; wherein the microscope objective is enabled to operate with: a fluid replenishment system coupled to the fluid port and enabled to provide the additional fluid; an immersion controller coupled to the plurality of sensor electrodes, the common electrode, and the fluid replenishment system, the immersion controller enabled for: when the fluid immerses the microscope objective, measuring a first resistance of the fluid, respectively, between each of the plurality of sensor electrodes and the common electrode, to detect the fluid at each respective sensor electrode of the plurality of sensor electrodes; when the fluid exposes a first sensor electrode included in the plurality of sensor electrodes, measuring a second resistance of an air gap at the first sensor electrode; and responsive to detecting the air gap, controlling the fluid replenishment system to provide the additional fluid.

[0005c] In a third aspect, the present disclosure provides a method for inverted immersion microscopy, the method comprising: using a microscope objective to view a first sample included in a plurality of samples loaded into an inverted microscope, wherein the microscope objective is immersed in a fluid at a distal portion of the microscope objective, wherein the microscope objective further comprises: a sensor ring coupled to the distal portion and forming an annulus in fluid communication with the microscope objective, wherein the annulus is enabled to convey the fluid, and wherein the sensor ring further comprises: a plurality of sensor electrodes located circumferentially about the annulus, wherein each of the plurality of sensor electrodes remains in contact with the fluid when the fluid immerses the microscope objective; a common electrode located within the annulus, wherein the common electrode remains in fluid communication with the fluid; and a fluid port to receive additional fluid from a fluid replenishment system to replenish the fluid; and using an immersion controller coupled to the plurality of sensor electrodes, the common electrode, and the fluid replenishment system,

maintaining the fluid over an optical axis diameter of the distal portion when at least one of the microscope objective and the first sample are moved with respect to each other.

BRIEF DESCRIPTION OF THE DRAWINGS

[0006] For a more complete understanding of the present invention and its features and advantages, reference is now made to the following description, taken in conjunction with the accompanying drawings, in which:

[0007] FIGURE 1 depicts selected elements of an inverted microscope system;

[0008] FIGURE 2 depicts selected elements of a fluid immersion control system;

[0009] FIGURE 3 depicts selected elements of a measurement circuit;

[0010] FIGURE 4 depicts a prior art inverted microscope objective in motion;

[0011] FIGURE 5 depicts an inverted microscope objective with immersion fluid control in motion;

[0012] FIGURE 6 depicts details of a sensor ring mounted to a microscope objective;

[0013] FIGURE 7 depicts a top view of a sensor ring in detail;

[0014] FIGURE 8 depicts a bottom view of a sensor ring in detail;

[0015] FIGURE 9 depicts further details in a sectional view of a sensor ring;

[0016] FIGURE 10 depicts further details in a sectional view of a sensor ring mounted to a microscope objective;

[0017] FIGURE 11 depicts a working distance in a sectional view of a sensor ring mounted to a microscope objective;

WHAT IS CLAIMED IS:

1. A control system for fluid immersion for inverted microscopy, the control system comprising:

a sensor ring coupled to a distal portion of a microscope lens used with an inverted microscope, wherein the sensor ring forms an annulus in fluid communication with the microscope lens, wherein the annulus is enabled to convey a fluid that forms an immersion layer at a surface of the microscope lens during imaging using the microscope lens, and wherein the sensor ring further comprises:

a plurality of sensor electrodes located circumferentially about the annulus, wherein each of the plurality of sensor electrodes remains in contact with the fluid when the fluid immerses the microscope lens;

a common electrode located within the annulus, wherein the common electrode remains in fluid communication with the fluid; and

a fluid port to receive additional fluid to replenish the immersion layer;

a fluid replenishment system coupled to the fluid port and enabled to provide the additional fluid;

an immersion controller coupled to the plurality of sensor electrodes, the common electrode, and the fluid replenishment system, the immersion controller enabled for:

when the fluid immerses the microscope lens, measuring a first resistance of the fluid, respectively, between each of the plurality of sensor electrodes and the common electrode, to detect the fluid at each respective sensor electrode of the plurality of sensor electrodes;

when the fluid exposes a first sensor electrode included in the plurality of sensor electrodes, measuring a second resistance of an air gap at the first sensor electrode; and

responsive to detecting the air gap, controlling the fluid replenishment system to provide the additional fluid.

2. The control system of claim 1, further comprising:

a sensor interface enabled to couple the immersion controller to the plurality of sensor electrodes and the common electrode, wherein the sensor interface further comprises:

a current source enabled to form a circuit between the common electrode and the plurality of sensor electrodes; and

a signal conditioning unit enabled to generate a plurality of voltage signals respectively from the plurality of sensor electrodes.

3. The control system of claim 2, wherein the immersion controller enabled for measuring the first resistance and the second resistance further comprises the immersion controller enabled for:

receiving the plurality of voltage signals; and

generating a plurality of digital voltage values corresponding to the plurality of voltage signals.

4. The control system of claim 3, wherein the immersion controller further comprises:

a multiplexer enabled to receive the plurality of voltage signals; and

an analog-to-digital converter to generate the digital voltage values from an output of the multiplexer.

5. The control system of claim 4, wherein the multiplexer includes sample-and-hold circuitry.

6. The control system of claim 3, wherein the immersion controller further comprises:

a plurality of analog-to-digital converters respectively receiving the plurality of voltage signals to generate the plurality of digital voltage values.

7. The control system of claim 1, wherein the fluid replenishment system further comprises:

a reservoir enabled to store a volume of the additional fluid; and

a pump in fluid communication with the reservoir and the fluid port.

8. The control system of claim 1, wherein controlling the fluid replenishment system to provide the additional fluid further comprises:

providing the additional fluid until the first resistance is respectively measured from each of the plurality of sensor electrodes.

9. The control system of claim 1, wherein the microscope lens is located in proximity to a transparent sample plate, and wherein the fluid forms a meniscus between the transparent sample plate and the sensor ring surrounded by the distal end of the microscope lens.

10. The control system of claim 9, wherein the inverted microscope is enabled for imaging different samples on the transparent sample plate by moving at least one of the transparent sample plate and the microscope lens with respect to each other.

11. The control system of claim 10, wherein the transparent sample plate and the microscope lens are enabled to move with respect to each other in a plane perpendicular to an optical axis of the microscope lens.

12. The control system of claim 10, wherein the immersion controller is enabled to maintain a first diameter of the meniscus that is greater than a second diameter of the microscope lens, wherein the second diameter corresponds to an optical axis of the microscope lens.

13. The control system of claim 12, wherein the immersion controller is enabled to maintain the first diameter of the meniscus when the transparent sample plate and the microscope lens move with respect to each other.

14. The control system of claim 12, wherein the plurality of sensor electrodes located circumferentially about the annulus defines the first diameter.

15. The control system of claim 1, wherein the sensor ring and the distal portion of the microscope lens form a planar surface, wherein the distal portion of the microscope lens and the plurality of sensor electrodes are at the same height.

16. The control system of claim 1, wherein the plurality of sensor electrodes includes at least three sensor electrodes.

17. A microscope objective for fluid immersion for inverted microscopy, the microscope objective comprising:

a sensor ring coupled to a distal portion of a microscope objective used with an inverted microscope, wherein the sensor ring forms an annulus in fluid communication with the microscope objective, wherein the annulus is enabled to convey a fluid that forms an immersion layer at a surface of the microscope objective during imaging using the microscope objective, and wherein the sensor ring further comprises:

a plurality of sensor electrodes located circumferentially about the annulus, wherein each of the plurality of sensor electrodes remains in contact with the immersion layer when the fluid immerses the microscope objective;

a common electrode located within the annulus, wherein the common electrode remains in fluid communication with the fluid; and

a fluid port to receive additional fluid to replenish the immersion layer;

wherein the microscope objective is enabled to operate with:

a fluid replenishment system coupled to the fluid port and enabled to provide the additional fluid;

an immersion controller coupled to the plurality of sensor electrodes, the common electrode, and the fluid replenishment system, the immersion controller enabled for:

when the fluid immerses the microscope objective, measuring a first resistance of the fluid, respectively, between each of the plurality of sensor electrodes and the common electrode, to detect the fluid at each respective sensor electrode of the plurality of sensor electrodes;

when the fluid exposes a first sensor electrode included in the plurality of sensor electrodes, measuring a second resistance of an air gap at the first sensor electrode; and

responsive to detecting the air gap, controlling the fluid replenishment system to provide the additional fluid.

18. The microscope objective of claim 17, further comprising:

A sensor interface enabled to couple the immersion controller to the plurality of sensor electrodes and the common electrode.

19. The microscope objective of claim 17, wherein the fluid replenishment system further comprises:

a reservoir enabled to store a volume of the additional fluid; and

a pump in fluid communication with the reservoir and the fluid port.

20. The microscope objective of claim 17, wherein controlling the fluid replenishment system to provide the additional fluid further comprises:

providing the additional fluid until the first resistance is respectively measured from each of the plurality of sensor electrodes.

21. The microscope objective of claim 17, wherein the microscope objective is located in proximity to a transparent sample plate, and wherein the fluid forms a meniscus between the transparent sample plate and the sensor ring.

22. The microscope objective of claim 21, wherein the inverted microscope is enabled for imaging different samples on the transparent sample plate by moving at least one of the transparent sample plate and the microscope objective with respect to each other.

23. The microscope objective of claim 22, wherein the transparent sample plate and the microscope objective are enabled to move with respect to each other in a plane perpendicular to an optical axis of the microscope objective.

24. The microscope objective of claim 22, wherein the immersion controller is enabled to maintain a first diameter of the meniscus that is greater than a second diameter of the microscope objective.

25. The microscope objective of claim 24, wherein the immersion controller is enabled to maintain the first diameter of the meniscus when the transparent sample plate and the microscope objective move with respect to each other.

26. The microscope objective of claim 24, wherein the plurality of sensor electrodes located circumferentially about the indentation defines the first diameter.

27. The microscope objective of claim 17, wherein the sensor ring and the distal portion of the microscope objective form a planar surface, wherein the distal portion of the microscope objective and the plurality of sensor electrodes are at the same height.

28. The microscope objective of claim 17, wherein the plurality of sensor electrodes includes at least three sensor electrodes.

29. A method for inverted immersion microscopy, the method comprising:

using a microscope objective to view a first sample included in a plurality of samples loaded into an inverted microscope, wherein the microscope objective is immersed in a fluid at a distal portion of the microscope objective, wherein the microscope objective further comprises:

a sensor ring coupled to the distal portion and forming an annulus in fluid communication with the microscope objective, wherein the annulus is enabled to convey the fluid, and wherein the sensor ring further comprises:

a plurality of sensor electrodes located circumferentially about the annulus, wherein each of the plurality of sensor electrodes remains in contact with the fluid when the fluid immerses the microscope objective;

a common electrode located within the annulus, wherein the common electrode remains in fluid communication with the fluid; and

a fluid port to receive additional fluid from a fluid replenishment system to replenish the fluid; and

using an immersion controller coupled to the plurality of sensor electrodes, the common electrode, and the fluid replenishment system, maintaining the fluid over an optical axis diameter of the distal portion when at least one of the microscope objective and the first sample are moved with respect to each other.

30. The method of claim 29, wherein maintaining the fluid over the optical axis diameter of the distal portion further comprises:

When the fluid immerses the microscope objective, measuring a first resistance of the fluid, respectively, between each of the plurality of sensor electrodes and the common electrode, to detect the fluid at each respective sensor electrode of the plurality of sensor electrodes;

when the fluid exposes a first sensor electrode included in the plurality of sensor electrodes, measuring a second resistance of an air gap at the first sensor electrode; and

responsive to detecting the air gap, controlling the fluid replenishment system to provide the additional fluid.

31. The method of claim 29, further comprising:

causing at least one of the microscope objective and the first sample to be moved with respect to each other in order to view a second sample included with the plurality of samples using the microscope objective; and

wherein maintaining the fluid over the optical axis diameter of the distal portion further comprises maintaining the fluid over the optical axis diameter before the microscope objective is aligned with the second sample.