light and to direct the refracted source light through a well containing a fluid. This refracted source light interacts with particles suspended in the fluid to produce scattered light, which is then directed to an imager. The illumination system is configured in such a manner that the refracted source light is also diverted away from the imager. In other words, a substantial amount of light received by the imager, which is used for particle image analysis, is the scattered light. This illumination system prevents the source light from washing out the scattered light, providing a large depth of field and allowing accurate imaging of the entire volume of fluid at the same time.

[0005] The plate-reading system described herein also agitates momentarily to facilitate image analysis. In particular, the imager may capture an image before and after the plate is agitated. In doing so, the image analysis discriminates between particles suspended in the fluid (which move when the plate is agitated) and other static artifacts (which do not move after plate agitation). As a result of this image analysis, the size and number of particles suspended in the fluid may be directly measured.

[0005a] According to a first aspect of the present invention, there is provided a well plate inspection system, comprising:

a stage configured to receive a plate including a vessel containing a fluid;

a light source configured to generate incoherent source light;

an axicon disposed between the light source and the stage, the axicon being configured to direct the incoherent source light through the fluid contained in the vessel to produce scattered light as a result of an interaction between the incoherent source light and particles suspended in the fluid;

an imager configured to acquire images using the scattered light, wherein the axicon is further configured to divert the incoherent source light away from the imager;

one or more beam expanders disposed between the light source and the axicon, and configured to vary a diameter of the incoherent source light entering the axicon; and

a controller configured to determine, from the images, a size and a number of particles in the fluid,

wherein the stage and/or the axicon are movably mounted to adjust a distance between the axicon and the vessel.

[0005b] According to a second aspect of the present invention, there is provided a well plate inspection system, comprising:

a stage configured to selectively agitate and to receive a plate including a vessel containing a fluid;

a light-emitting diode (LED) light source configured to generate incoherent source light;

an axicon disposed between the LED light source and the stage, the axicon being configured to refract the incoherent source light to produce refracted source light,

wherein the refracted source light interacts with particles suspended in the fluid contained in the vessel to produce scattered light that is directed to a mirror while the axicon diverts the refracted source light away from the mirror;

one or more beam expanders disposed between the LED light source and the axicon, and configured to vary a diameter of the incoherent source light entering the axicon;

an imager configured to acquire sequential images using the scattered light that is reflected off the mirror; and

a controller configured to determine, from the sequential images, a size and a number of particles in the fluid,

wherein the stage and/or the axicon are movably mounted to adjust a distance between the axicon and the vessel.

[0005c] According to a third aspect of the present invention, there is provided a method for calculating a size and a number of particles in a fluid contained in a vessel included in a plate placed on a stage, comprising:

generating, via a light source, incoherent source light;

varying, via one or more beam expanders disposed between the light source and an axicon, a diameter of the incoherent source light entering the axicon;

adjusting a distance between the axicon and the vessel;

refracting, via the axicon, the incoherent source light to produce refracted source light;

supplying, via an optical system, scattered light to an imager as a result of an interaction between the refracted source light and particles suspended in the fluid;

diverting, via the axicon, the refracted source light away from the imager;

acquiring, via the imager, sequential images using the supplied scattered light; and

determining, via a controller, a size and a number of particles in the fluid using the sequential images.

BRIEF DESCRIPTION OF THE DRAWINGS

[0006] The skilled artisan will understand that the figures, described herein, are included for purposes of illustration and are not limiting on the present disclosure. The drawings are not necessarily to scale, emphasis instead being placed upon illustrating the principles of the present disclosure. It is to be understood that, in some instances, various aspects of the described implementations may be shown exaggerated or enlarged to facilitate an understanding of the described implementations. In the drawings, like reference characters throughout the various drawings generally refer to functionally similar and/or structurally similar components.

What is claimed is:

1. A well plate inspection system, comprising:

a stage configured to receive a plate including a vessel containing a fluid;

a light source configured to generate incoherent source light;

an axicon disposed between the light source and the stage, the axicon being configured to direct the incoherent source light through the fluid contained in the vessel to produce scattered light as a result of an interaction between the incoherent source light and particles suspended in the fluid;

an imager configured to acquire images using the scattered light, wherein the axicon is further configured to divert the incoherent source light away from the imager;

one or more beam expanders disposed between the light source and the axicon, and configured to vary a diameter of the incoherent source light entering the axicon; and

a controller configured to determine, from the images, a size and a number of particles in the fluid,

wherein the stage and/or the axicon are movably mounted to adjust a distance between the axicon and the vessel.

2. The system of claim 1, wherein the light source is a light emitting diode (LED).

3. The system of claim 1 or claim 2, wherein the stage is configured to selectively agitate, and

wherein the imager is configured to acquire a first image prior to the stage being agitated and a second image after the stage is agitated.

4. The system of claim 1 or claim 2, wherein:

the stage is configured to selectively agitate, and

the imager is configured to acquire a plurality of images after the stage is agitated; and

the controller is further configured to generate a minimum intensity projection (MinIP) from the plurality of images, to subtract the MinIP from each of the plurality of images to generate an image stack, and to determine the size and the number of particles in the fluid from

the image stack.

5. The system of claim 1 or claim 2, wherein:

the vessel is from among a plurality of vessels included in the plate,

the controller is further configured to determine the size and the number of particles in each of the plurality of vessels included in the plate, and

the stage further includes a plate holder configured to selectively receive and release the plate, the plate holder being further configured to hold the plate in the stage and to maintain each vessel from among the plurality of vessels in the same field of view with respect to one another while the controller determines the size and the number of particles in each of the plurality of vessels included in the plate.

6. The system of claim 1 or claim 2, wherein the vessel is configured to hold a volume of fluid up to 200 microliters.

7. The system of claim 1 or claim 2, further comprising:

an optical system configured to direct the scattered light to the imager.

8. A well plate inspection system, comprising:

a stage configured to selectively agitate and to receive a plate including a vessel containing a fluid;

a light-emitting diode (LED) light source configured to generate incoherent source light;

an axicon disposed between the LED light source and the stage, the axicon being configured to refract the incoherent source light to produce refracted source light,

wherein the refracted source light interacts with particles suspended in the fluid contained in the vessel to produce scattered light that is directed to a mirror while the axicon diverts the refracted source light away from the mirror;

one or more beam expanders disposed between the LED light source and the axicon, and configured to vary a diameter of the incoherent source light entering the axicon;

an imager configured to acquire sequential images using the scattered light that is reflected off the mirror; and

a controller configured to determine, from the sequential images, a size and a number of particles in the fluid,

wherein the stage and/or the axicon are movably mounted to adjust a distance between the axicon and the vessel.

9. The system of claim 8, wherein the sequential images include a background image and an analysis image, the background image being acquired prior to the stage being agitated, and the analysis image being acquired after the stage is agitated.

10. The system of claim 9, wherein the background image and the analysis image are associated with the fluid being viewed from an underside of the vessel.

11. The system of claim 8, wherein the imager is configured to acquire the sequential images after the stage is agitated, and

wherein the controller is further configured to generate a minimum intensity projection (MinIP) from the sequential images, to subtract the MinIP from each of the sequential images to generate an image stack, and to determine the size and the number of particles in the fluid from the image stack.

12. The system of any one of claims 8-11, wherein the plate has a 96-well standard format including 96 vessels.

13. The system of any one of claims 8-11, wherein:

the vessel is from among a plurality of vessels included in the plate,

the controller is further configured to determine the size and the number of particles in each of the plurality of vessels included in the plate, and

the stage further includes a plate holder configured to selectively receive and release the plate, the plate holder being further configured to hold the plate in the stage and to maintain each vessel from among the plurality of vessels in the same field of view with respect to one another while the controller determines the size and the number of particles in each of the plurality of vessels included in the plate.

14. The system of any one of claims 8-10, wherein the vessel is configured to hold a volume of fluid up to 200 microliters.

15. The system of any one of claims 8-10, wherein the axicon is configured such that the sequential images acquired by the imager using the scattered light reflected off the mirror have a depth of field corresponding to the entire volume of fluid contained in the vessel.

16. A method for calculating a size and a number of particles in a fluid contained in a vessel included in a plate placed on a stage, comprising:

generating, via a light source, incoherent source light;

varying, via one or more beam expanders disposed between the light source and an axicon, a diameter of the incoherent source light entering the axicon;

adjusting a distance between the axicon and the vessel;

refracting, via the axicon, the incoherent source light to produce refracted source light;

supplying, via an optical system, scattered light to an imager as a result of an interaction between the refracted source light and particles suspended in the fluid;

diverting, via the axicon, the refracted source light away from the imager;

acquiring, via the imager, sequential images using the supplied scattered light; and

determining, via a controller, a size and a number of particles in the fluid using the sequential images.

17. The method of claim 16, further comprising:

agitating the plate, and

wherein the act of acquiring the sequential images using the scattered light comprises:

acquiring a first image prior to the plate being agitated; and

acquiring a second image after the plate is agitated.

18. The method of claim 16, wherein the act of determining the size and the number of particles in the fluid using the sequential images includes subtracting, via a controller, the first image from the second image to provide a difference image, and determining the size and the number of particles in the fluid by analyzing the difference image.

19. The method of claim 16, wherein the act of acquiring the sequential images includes acquiring the sequential images after the plate is agitated, and

wherein the act of determining the size and the number of particles in the fluid using the sequential images includes generating a minimum intensity projection (MinIP) from the sequential images, subtracting the MinIP from each of the sequential images to generate an image stack, and determining the size and the number of particles in the fluid from the image stack.