ed POC diagnosis and conventional diagnosis has been presented in the light of WHO standards in Table 1, which clearly displays the differences and the specific requirements in these two settings. These specific needs impose challenges and require innovative approaches for efficient delivery of healthcare in POC in resource limited settings [3].

Lab-on-a-chip technologies have been emerging for detection and monitoring of infectious diseases at resource-limited settings [3, 5, 13–24]. Healthcare personnel including technicians, nurses and physicians can use these devices with minimum training to diagnose patients for infectious diseases or monitor the progress of a disease [2, 5]. Thus, these technologies will allow the healthcare workforce to deliver medical services more efficiently without the need for expensive equipment or extensive training [1, 13, 24, 25]. Miniaturization and integration of diagnostic devices would allow rapid and reliable high-throughput chemical and biomedical imaging and analysis from a tiny amount of sample such as a fingerprick volume of blood [7, 26–30]. Optofluidics takes advantage of integrating microfluidics and microelectronic optical components onto the same platform [31, 32]. Such a platform, with fluidics for sample delivery/capture and lensless optics for sensing and detection, can be applied to areas such as ultra wide-field cell monitoring array [14, 33, 34], digital in-line holography [35–41], optofluidic microscopy [42–45], and

nents: (i) a light source, (ii) optical modulators, (iii) lenses, and (iv) a detector, which are sequentially positioned on the spatial beam path [49]. Here, we discuss each of these components, their roles and relevance for POC applications.

2.1.1 Light sources

Microscopes use various light sources ranging from incandescent light bulbs to solid-state light-emitting devices (i.e., light-emitting diodes, LEDs) [50]. LEDs are miniaturized light sources that are commonly used in compact optical devices without high-power demands. However, LEDs emit non-collimated light, whereas high-resolution imaging applications require collimated light sources that minimize diffraction. On the other hand, laser is an intense coherent light source with a narrow bandwidth, high spatial coherence and insignificant chromatic aberration. Laser can be easily focused and facilitates high-resolution imaging [51]. Therefore, laser diodes that combine the portability, low cost and low-power consumption of LEDs and the coherent emission characteristics of lasers would be ideal for on-chip POC diagnostic platforms [52, 53].

2.1.2 Optical modulators

The properties of light (e.g., intensity, path, and wavelength) change as it travels through a medium (e.g., sample of interest), which acts as an optical modulator. The medium reflects, diffracts, and deflects the incident light. Sample characteristics and incident light wavelength affect the sample-light interaction and the observed outcome. For instance, in high-resolution fluorescence imaging, fluorescent molecules transfer energy from the incident light to the emitted light at a different (longer) wavelength. Due to this phenomenon, fluorescence-based detection requires expensive optical filters to eliminate the background noise and the wavelengths other than the emission that carries the relevant information. Therefore, it would be challenging to adapt fluorescence imaging for on-chip microscopy for POC-oriented applications. However, advances in LED and CCD technologies may overcome these challenges and facilitate feasible utilization of fluorescencent luminescence in POC [54, 55].

High-resolution imaging can also be achieved without lenses or filters by employing surfaces as optical modulators (i.e., surface plasmon resonance) [56–60]. Fabrication of nanoscale structures and features on surfaces has been well established enabling the surface plasmon methods for imaging [61–68]. This imaging method is based on optical energy changes, converting incident light into a surface plasmon resonance through interactions between nanoscale structures and incident waves [56, 58–60, 69]. Metals are commonly used for surface-plasmon optical systems as they support surface electric charge waves. Non-metallic materials can also have similar energy transformation properties when used as nanoscale hole arrays on metallic films [70]. High-resolution imaging can also be achieved through light-phase images that differentiate features according to their geometry using a collimated light source [34, 35, 37]. Since these methods do not require expensive filters and can operate in a lensless setting, they may be considered for applications in POC detection.

2.1.3 Lenses

Lens-based imaging is an optical method in which a lens is situated away from the object. Lenses condense and modulate light resulting from the sample of interest (e.g., cells). A lens can be realized by an aperture or using convex or concave optically clear materials. The term aperture in optics refers to an opening that can determine the diffraction angle of a bundle of rays, focusing them on an image plane. The aperture can also determine how much light reaches the image plane. Although the resolution increases with decreased aperture size, images become darker as apertures become narrow due to the constriction of light. Challenges exist regarding both the diffraction limited resolution and practical use of lens-based optical microscopy because of the narrow field of view at high magnifications [71, 72]. Lens-based methods are not capable of imaging nanofeatures (i.e., less than 100 nm) that are smaller than the imaging wavelength (i.e., diffraction limit) [73]. One solution is to send light through a tiny aperture on an opaque screen (e.g., metallic or non-metallic films) without using conventional lenses (i.e., near optical detection approaches). In this method, the target must remain at a sub-wavelength distance (less than the wavelength of the incident light) to the detector to eliminate diffraction effects caused by incoherent light [71, 72, 74]. However, these approaches present challenges in terms of their applications in POC due to requirements such as: expensive high-energy light sources, sensitive detection systems and complex peripheral equipment. Lensless approaches hold great promise in POC testing due to simpler operation and low cost [13, 25, 41, 42].

2.1.4 Detectors

A detector is an electronic sensor that converts incident light into an electrical current as a function of the light intensity. Photomultiplier tubes (PMTs), avalanche photodiodes (APDs), and PIN (p-type-

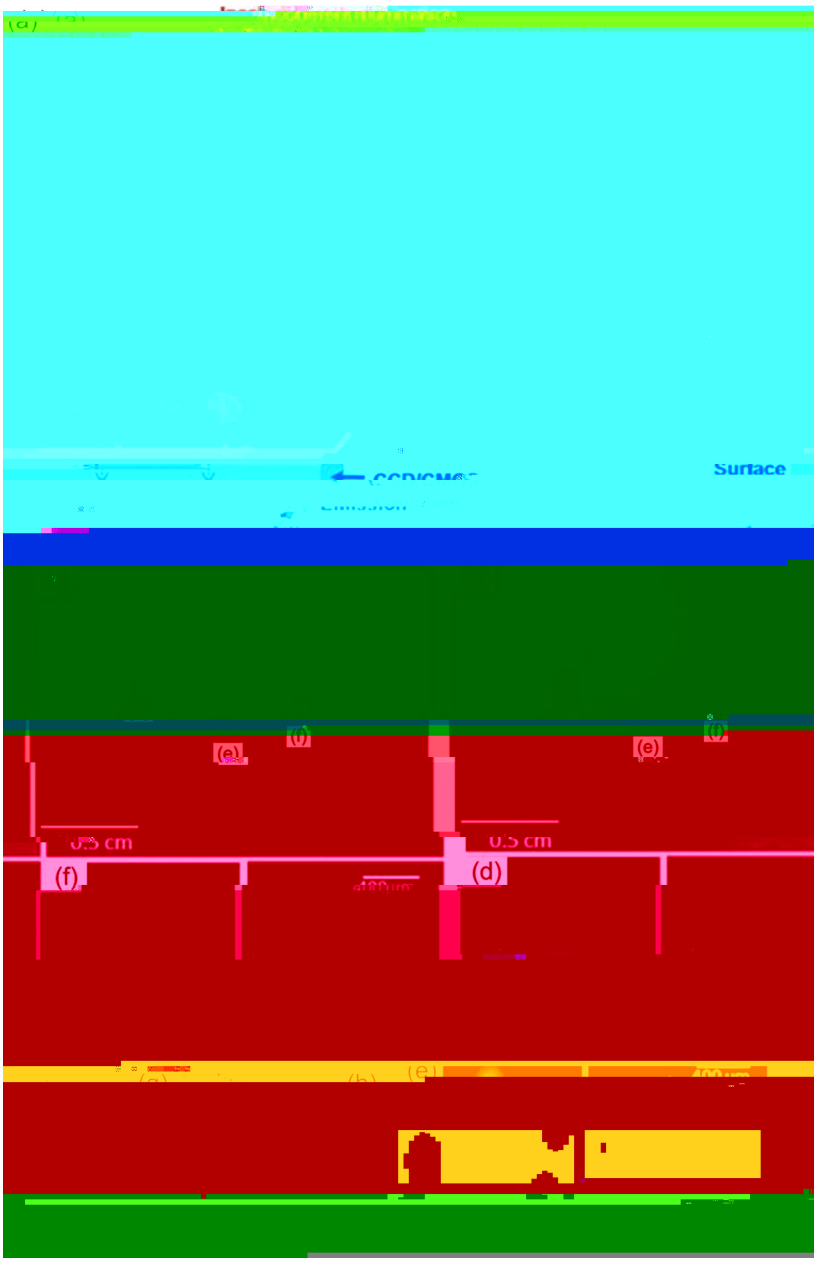

Figure 3.

Digital holography has been integrated with fluorescence imaging to achieve lensless fluorescence detection without any thin-film filters or mechanical scanning with an ultra-wide FOV (2.5 cm × 3.5 cm) [102]. In this approach, the sample was illuminated with an incoherent excitation beam from an LED or a Xenon lamp source located directly above (Fig. 3a). Fluorescence excitation was provided from the side utilizing a rhomboid prism. The incoherent light beam interacted with the sample, undergoing total internal reflection (TIR) at the bottom (Fig. 3a). Detection of the fluorescence emission from the excited cells/particles over the entire FOV of the sensor array (CCD or CMOS) was achieved without using any lenses. Unlike the traditional fluorescence microscopy, the need for expensive interference filters was not a limiting factor for this method. An inexpensive plastic-based absorption filter was used between the sample and detector planes to achieve a better dark-field background. The issue of potential overlapping of diverged fluorescence emission of cells or particles at the sensor plane was addressed by deconvolving the acquired images, which provided a resolution of ~40–50 μm over the entire sensor FOV without the use of a lens. The system was val-

idated by imaging white blood cells as shown in Figs. 3b–h.

The digital holography and lensless fluorescence imaging platforms discussed above are innovative approaches that are transforming microscopy techniques dramatically by simplifying and by reducing the cost of imaging equipment. These methods can provide valuable information about the sample, such as the 3D structure and orientation. Although they are of relatively more com-

ly, individual cells are computationally modeled as uniform circular objects with a reduced field-transmission coefficient. This technology has recently been modularized with microfluidic devices, paving the way for lensless cell counting technologies for POC application. A recent study has also demonstrated the potential of this lensless technology for microfluidic-based HIV monitoring applications [13].

4 Conclusions and perspectives

The needs and challenges in resource-poor POC

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