Chapter 4
Compact and Field Portable Biophotonic Sensors for Automated Cell Identification (Plenary Address)

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Abstract In this Plenary address paper, we overview recently published work for automated cell identification using 3D optical imaging in compact and field portable biophotonic sensors. Digital holographic microscopy systems and lensless pseudorandom phase encoding systems capture 3D information of biological cells and make highly accurate automated cell identification possible. Overviewed systems include sickle cell disease diagnosis based on spatio-temporal cell dynamics in a field-portable 3D-printed shearing digital holography as well as lensless cell identification of both single and multicell samples using pseudorandom phase encoding.

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4.1 Introduction

Compact and field portable three-dimensional (3D) biophotonic sensors capable of capturing 3D information of biological cells and performing highly accurate automated cell identification continue to be a growing research topic with quickly expanding capabilities [1–14]. Two key technologies in this field include digital holographic microscopy (DHM) and pseudorandom phase encoding as methods for 3D optical imaging. In this Plenary address paper, we overview previously published works and recent applications of compact and field portable biophotonic sensors for automated cell identification. Notable applications include the use of dynamic spatio-temporal features derived from cell membrane fluctuations for sickle cell disease diagnosis and applications of compact lensless single random phase encoding (SRPE), and double random phase encoding (DRPE) systems.

4.2 Field Portable Biophotonics Sensors for Cell Identification

4.2.1 Compact and Field Portable 3D Printed Shearing DHM for Automatic Cell Identification

The shearing microscope offers a simple implementation for common-path interferometric microscopy. It uses a glass plate to reflect two laterally sheared beams from its front and back surfaces which generates an interference pattern at the sensor [1, 4]. A schematic of the shearing microscope is shown in Fig. 4.1a, b shows a 3D-printed prototype for the microscope. After hologram recording, the phase profile can be numerically reconstructed using the angular spectrum method [1, 3].

From the reconstructed profiles, features can be extracted for cell identification and classification [6–12]. In [12], extracted morphological and spatio-temporal features were used for the diagnosis of sickle cell disease. Example reconstructions for RBCs of healthy and sickle-cell diseased patients are shown by Fig. 4.1c, d, respectively. The 3D-printed shearing DHM systems offer high temporal stability

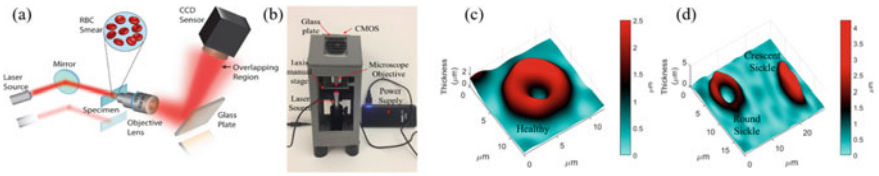

Fig. 4.1 **a** Diagram of the lateral shearing interferometric system, and **b** 3D-printed lateral shearing digital holographic microscope, **c** 3D optical path length profiles from a healthy RBC, and **d** from sickle cell diseased RBCs [2, 12]

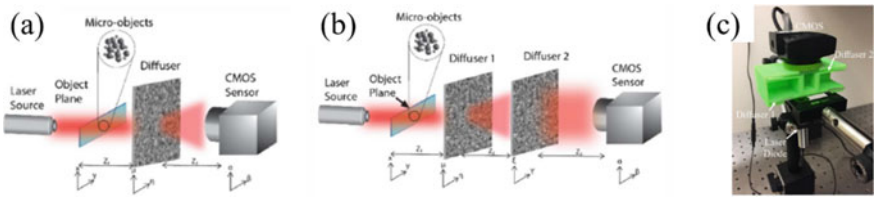

Fig. 4.2 Configuration for **a** single random phase encoding and **b** double random phase encoding, **c** experimental setup for both configurations [2, 14]

over two beam systems [1, 4], highly accurate cell identification capabilities [1, 2, 6–12], and potential low-cost alternative diagnostic systems for the developing world.

4.2.2 Lensless Cell Identification Using Single and Double Random Phase Encoding

Lensless cell identification systems enable rapid classification of micro-objects without 3D reconstruction [13, 14]. Diffusers pseudo-randomly encode a target specimen's complex amplitude, then the samples unique opto-biological signature is recorded at the sensor plane and finally, variations in the recorded opto-biological signatures between samples are used for classification. Classification in pseudo-random phase encoding systems has been performed for both single cell [13], and multicell samples [14]. Schematic diagrams for SRPE and DRPE, and the experimental setup are shown by Fig. 4.2a–c respectively. Lensless systems do not require reconstruction and are not limited by the numerical aperture of a lens.

4.3 Conclusion

In summary, previously published works for compact and field portable biophotonic sensors in 3D optical imaging and automated cell identification have been overviewed. Shearing based DHM systems and lensless pseudorandom phase encoding systems provide low-cost, compact, and field portable systems for automated cell identification. Fourier plane Integral Imaging Microscopy [15] is another subject of our investigation. T. O'Connor acknowledges support from Department of Education under GAANN Fellowship. B. Javidi acknowledges support in part by Office of Naval Research (ONR) (N000141712405).

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