

Blood analysis using a cost-effective microscope for low resource settings

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First aid stations in low resource settings and in war areas operate autonomously and the laboratory equipment must be designed for use in non-air-conditioned environments and under extreme conditions. In addition, it is important that local personnel are able to carry out maintenance and repair work independently in the event of malfunctions. Today's complex medical devices require maintenance by trained service personnel and contain proprietary components and interfaces that make on-site repair impossible.

For manual point-of-care blood analysis, at least a microscope with a resolution of about 500nm and a photometer are the necessary instruments for recording a blood count and specific blood values (e.g. malaria). This is difficult to guarantee in mobile hospitals in war zones or low resource settings.

For the point-of-care testing (POCT) of blood samples a microscope is developed in this work for the combined use of a cell phone to benefit from its image sensor and image software. Some solutions already address this problem. Slides clipped directly onto the mobile phone are cheap, but do not achieve sufficient resolution for a detailed cell differentiation. To overcome resolution problems, holographic microscopy is an adequate approach [1]. In order to image diffraction patterns in a range between near and far field resolving a sufficient number of diffraction maxima for reconstruction, distances must be carefully selected [2,3].

This work presents the development of a robust microscope for blood cell analysis, which is designed for the combination with mobile phones as well as simple CMOS sensors. The catalogue of requirements was developed exemplarily in first aid stations in the Kyrgyz mountains. At the same time the design is based on simple components available worldwide. The investigation of the dimensioning of the pinhole size, the distance between sample and sensor are investigated depending on the sensor resolution. Images are reconstructed by a machine learning approach using a U-net architecture. Here a classifier is trained directly on scattering images for cell type analysis. The classification network has been pretrained on the BCCD database adapted via transfer learning to own data. As ground truth samples were pre-classified by medical personnel. The analysis is tested on stained blood smear samples without further chemical pre-treatment. The classification network can easily be extended to a specific issue in blood cell testing.

[1] L. Repetto, E. Piano, and C. Pontiggia, "Lensless digital holographic microscope with light-emitting diode illumination", *Optics Letters*, **29**, 10, 1132 (2004).

[2] Aydogan Ozcan and Euan McLeod, "Lensless Imaging and Sensing", *Annu. Rev. Biomed. Eng.*, 18:77–102 (2016).

[3] Yichen Wu and Aydogan Ozcan, "Lensless digital holographic microscopy and its applications in biomedicine and environmental monitoring", *Methods*, **136**, 4-16 (2018).