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Open hardware in microscopy

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ABSTRACT

The field of microscopy has been empowering humankind for many centuries by enabling the observation of objects that are otherwise too small to detect for the naked human eye. Microscopy techniques can be loosely divided into three main branches, namely photon-based optical microscopy, electron microscopy, and scanning probe microscopy with optical microscopy being the most prominent one. On the high-end level, optical microscopy nowadays enables nanometer resolution covering many scientific disciplines ranging from material sciences over the natural sciences and life sciences to the food sciences. On the lower-end level, simplified hardware and openly available description and blueprints have helped to make powerful microscopes widely available to interested scientists and researchers. For this special issue, we invited contributions from the community to share their latest ideas, designs, and research results on open-source hardware in microscopy. With this collection of articles, we hope to inspire the community to further increase the accessibility, interoperability, and reproducibility of microscopy. We further touch on the standardization of methodologies and devices including the use of computerized control of data acquisition and data analysis to achieve high quality and efficiency in research and development.

A. Introduction

In the late 17th century, Antoni van Leeuwenhoek used a self-built, single lens microscope to discover bacteria thereby succeeding in making the previously invisible visible [1,2]. Interestingly, van Leeuwenhoek never disclosed how he achieved the remarkable quality of his lenses and even discouraged teaching his methods to others [1]. As an alternative to single-lens microscopes, compound microscopes consisting of an objective/lens and an eyepiece were already known and had been popularized by Robert Hooke [3–5]. These compound microscopes, however, lacked the optical quality to compete in resolution for another 100+ years. It remains a thought experiment to think about how microscopy would have evolved if Leeuwenhoek would have decided to share his expertise with others. To this day, there is an ongoing tension between the open-science movement that is seeking to improve “reproducibility, transparency, sharing and collaboration” as outlined by the UNESCO [6] and commercial entities or individuals, who keep access to detailed information on techniques limited for commercial gain or personal reasons. For open microscopy, we follow a previous definition describing it as a “movement to make scientific research involving microscopy, any associated data and dissemination thereof accessible to all levels of an inquiring society” with associated data defined as “information on (i) how to build, use and maintain microscopes (hardware), (ii) how to prepare, handle and measure samples (assays) and (iii) how to analyze, distribute and store experimental data and computational models (software)” [7]. With this Hardware X Special Issue our goal is to provide space for detailed descriptions of imaging hardware and control software. The variety of presented modalities covering microscopy, partially already building on each other, is a testament for the unlimited opportunities that open-source hardware in general has to offer [8].

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B. Overview of the work presented in this special issue

Within the field of optical microscopy, single-molecule localization microscopy (SMLM) is a popular technique that relies on the identification of single fluorescent emitters and has recently started breaking the one nanometer resolution barrier [9]. Recently published microscopy frameworks for SMLM closely resemble the layout of conventional upright commercial microscopes but feature a higher degree of modularity and customizability [10–12]. Here, two of the contributions were derived from the miCube framework [12,13] improving it in many aspects. Niederauer and co-authors present the K2 single-molecule TIRF microscope which features a focus lock, the possibility to perform fluorescence recovery after photobleaching (FRAP) experiments and an extended detection path allowing simultaneous multi-color detection in dedicated areas of the camera [14]. Alsamam and co-authors present the miEye framework, which sets a stronger focus on cost effectiveness [15]. The authors replaced, for example, the scientific-grade camera with an industry-grade one, thereby achieving cost saving in the order of 10x on the detector, whilst demonstrating comparable performance. Further, the authors used a simpler sample position system and replaced expensive single-mode lasers with a more cost-effective multi-mode laser engine. Intriguingly, the entire software is controlled by a newly written Python software framework. Python was also used by Casas Morena and co-authors, who present their computational software framework for image acquisition, reconstruction, and analysis [16] building on ImSwitch [17] and Napari [18]. We note that a very recent pre-preprint combined ImSwitch with the real-time SMLM capabilities of miEye [19].

Peters and co-authors present a different platform for focus-locked, high-NA microscopy in either back- scattering or cross-polarization, which is compatible with the widely-used optomechanical components from Thorlabs [20].

One challenge in microscopy is the synchronous control of lasers, detectors, stages, and other electronic driven parts. Whilst ARDUINO boards are often used, the simultaneous triggering of, for example, multiple lasers with sub millisecond resolution has remained challenging. To tackle that issue, Deschamps and co-authors introduce the design of a field programmable gate array (FPGA) for microscopy dupped MicroFPGA enabling fast (sub microsecond) and accurate control over more than 30 channels [21].

Another challenge in microscopy is the precise control of the conditions under which samples are measured. Here, microfluidics plays an essential role, as they allow for example to exchange buffer or analytes during and between measurements. Two publications are presenting new options. Deng and Beliveau present a customisable fluidic system in which up to 16 channels are individually addressable allowing the flow of specific fluorescently labelled DNA probes for fluorescence in-situ hybridisation (FISH) experiments to the sample on the microscope [22]. Similarly, and with a focus on using more commercially available components, Yang and co-authors present a fluidic based solution for precise and automated sample preparation [23]. Tsan and co-authors present a low-cost solution for acoustic trapping of micron-sized particles in the field of view of a simple microfluidic device [24].

Illumination is a major contributing factor to the quality of microscopic images. In fact, proper sample illumination is as essential for imaging as having proper optics in the detection path. Tulijak and co-authors present a solution for the temporal, sub-microsecond resolved illumination control for transmitted-light microscopy [25]. Moustafa and co-authors present the design of a microscope featuring a LED array for illumination that enables brightfield, darkfield and quantitative phase imaging in live cells [26]. A microscopy platform built for the high-speed recording of laser-induced cavitation experiments in microfluidic devices is presented by Nagalingam and co-authors [27]. Buitrago-Duque and co-authors present a lensless holographic microscope that manages to visualise blood samples on a tiny footprint [28]. The small footprint here paves the way for using the device for point-of-care testing. Two more articles fall in the category of imaging systems. Vlasov and co-authors describe the design of an electron detector for scanning electron microscopy with bill of materials of only 100 Euros [29]. Bandila presents a LED-based illumination and smart-phone based detection system for the highly sensitive characterisation of gels cast for characterising electrophoretic mobilities of, for example, DNA and proteins as commonly used in the biological sciences [30].

To obtain reproducible results in microscopy, consistent sample preparation is essential. Pazaitis and Kaiser present a toolkit for the rapid generation of tissue microarrays that are used, for example, in the clinical setting to identify diseases regions of interest [31]. Finally, repurposing consumer-grade commercial hardware for use in scientific instrumentation can be a democratizing and cost-efficient strategy to build high performance devices and disseminate cutting edge research. Two articles from the En-Te Hwu group clearly demonstrate this opportunity. In their first article, they present an open-source controller that can operate an atomic force microscope at high speed [32]. In the second article, they use hardware made for operating quadcopters to make a centrifugal microfluidics device [33]. These innovative solutions emphasize the opportunities that arise from taking an open-source hardware route to knowledge transfer from and between research and engineering disciplines.

C. Final thoughts

We thank all the referees who have helped improving and shaping the submitted manuscripts in this HardwareX Special Issue. We note that reviewing manuscripts containing such detailed information on how to set up and use microscopy equipment is challenging. Ideally, reviewers would have the interest, time, and resources to build and specifically test any hardware. As this is hardly practicable, we encourage anyone who decides to use the detailed plans as intended to contact the authors providing comments and potential suggestions. Most of the projects have dedicated Git-controlled web pages associated, which enable users to provide public feedback in the spirit of open science. Finally, we would like to highlight the issue of costs of open-source hardware and its implementation. We emphasize that open-source hardware does not equate cheap hardware. The bill of materials for some of the instruments published in this special issue can cost above $50,000 and does not include the cost of the labor to assemble the hardware. It is clear, however, that open-source hardware can provide much more affordable and cost-efficient solutions compared to fully commercial solutions. This is especially important for starting principal investigators who need to equip their laboratory with often custom-made equipment and might encounter severe delays because of the tightness of the supplies for the research-grade instruments. In this regard open-source hardware can be instrumental for starting labs to obtain or customise the equipment they need and focus their time and fresh energy on the main research questions and their start-up plans. We therefore encourage especially students and early-career researchers to familiarize themselves with open-source hardware and contribute back to the community.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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