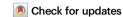


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A roadmap for the widespread adoption of frugal microscopes

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Microscopy drives biological discovery, yet high costs limit its access to resource-limited regions. We highlight examples of successful frugal microscopes that have overcome adoption barriers, offering a roadmap to expand affordable, quantitative imaging tools and foster impactful research in resource-limited settings.

Community access to research-grade frugal microscopy

In contrast to approaches such as bioinformatics, -omics, and clinical research, the reliance on light microscopy as a bedrock for bioscience research has faced uneven uptake between upper-income and low- and middle-income countries (LMICs). This is in part because most commercial research microscopes are costly to purchase, operate, and maintain. This denies many life scientists the power to quantitatively characterize the structural and dynamic underpinnings of a vast range of biological processes. In response, numerous open-access imaging centers were created, offering free global access to advanced imaging technologies. However, this dissemination model alone cannot address the pervasive gaps in access, as it (1) is limited in reach and throughput, and (2) offers primarily cutting-edge technologies that may not yet be suitable for early-stage research. As such, microscopy capacity must be extended in parallel through a more distributed model. This includes more local access to routine research-grade microscopes. These needs were discussed by a global cohort of leading imaging scientists at the "Microscopy Technology Dissemination to Underserved Communities" conference, held at the HHMI Janelia Research Campus1.

Here, we define a "research-grade" microscope as one capable of generating replicable, quantifiable data across a wide range of specimens. Historically, their production has been confined to a few manufacturers with the necessary expertise and infrastructure. However, recent trends have resulted in a bevy of economical, yet high-quality, electro-optical and software technologies. Furthermore, techniques such as 3D printing have enabled automated component fabrication at a fraction of historical costs. Together, these forces have spurred the rapid development of relatively sophisticated "frugal" microscopes^{2–4} – systems that can attain imaging performance comparable to industry-standard systems, but at substantially lower costs.

Consequently, recent literature features numerous microscope designs costing *ca*. USD \$100–10,000, as summarized in a recent review⁴. Within this landscape, several broad applications are apparent. For example, some designs target point-of-care diagnostics and field use. LoaScope^{5,6}. and Planktoscope⁷ are exemplary in this regard. Others excel at education and outreach such as the FoldScope⁸ and OpenFlexure^{9,10} systems.

However, when we consider frugal microscopes aimed at research applications, uptake has lagged in resource-constrained regions. The primary root cause is the high cost of microscopy, which has forced many resource-limited scientific communities to dismiss microscopy as a viable tool. Overtime, this problem has spiraled into a lack of awareness (1) of the analytical power of modern microscopy, and (2) that frugal solutions are increasingly available. This is exacerbated by a common perception that these solutions are too technically demanding to build, operate, and maintain. Simultaneously addressing these issues is thus paramount to interrupt this vicious cycle.

Wenzel et al. have provided an overview of the open hardware landscape across a range of technologies, centering on barriers to accessibility and fabrication¹¹. Here, we critically examine how design, dissemination strategies, user engagement, and long-term support ecosystems determine whether frugal microscopes can transition from functional prototypes to reliable tools for discovery-driven science. Through three case studies, we aim to shift the discussion from "Can it be built?" to "Can it advance science?" – a distinction essential to chart a roadmap toward adoption in under-resourced settings.

Research-grade frugal microscopes

To fulfill our definition of "research-grade", a microscope should incorporate a linear-response digital detector, be nominally diffraction-limited, be robust against image-degrading vibration and environmental fluctuations. Furthermore, it should not be limited to a single-purpose quantitative readout. Commonly, such systems feature multiple magnifications/resolutions and fluorescent channels, a motorized specimen stage, and multiple contrast methods. In some cases, they may be equipped to support live cell imaging for dynamic studies. Customizability is essential to cater to local needs and to fit within often-constrained budgets. In short, a research-grade frugal microscope should enable researchers to conduct reproducible, quantitative studies relevant to their region and generate data that meet international scientific standards. Critically, these demands may differ from those for point-of-care, fieldwork, and educational systems, underscoring the need for purpose-driven design. Using these criteria, we draw upon three examples of frugal microscopes that have shown success not only in their design and performance, but in the unique routes they have taken toward adoption in LMICs.

Study #1: Squid—**bridging design, training, and access.** The "Squid" system (Simplifying Quantitative Imaging Platform and Development) by Prakash and colleagues stands out as an important example¹². From a design perspective, it integrates cost-effectiveness, flexibility, high performance, and ease of operation. Its modular assembly and operation are based on an easily obtainable, robust metal construction, and open-source software. Thus, it is applicable to a wide range of uses from relatively routine histopathology to more complex live-cell

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investigations. Furthermore, it is complemented by freely available machine-learning modules that help researchers maximize the information obtainable from image data.

Squid developers have been particularly successful in promoting the dissemination and adoption of this platform for several reasons. Firstly, a multidisciplinary team of life scientists, engineers, and software experts bridges the gap between user needs and system design¹³. Secondly, this diverse team has undertaken numerous efforts to directly deploy this platform in many resourceconstrained communities and other harsh environments14, identifying local needs to inform further design refinements¹³. This deployment strategy is paired with extensive one-on-one training, emphasizing a "train-the-trainer" approach to propagate operation and maintenance knowledge, thereby magnifying adoption. However, to provide support at the global level, and to leverage the rapidly growing user base, Squid developers have also created an online forum where users can exchange techniques, troubleshooting tips, and experiences. Together, these strategies have created an "ecosystem" of deployment, training, and support necessary for successful adoption. This success has been such that the Squid platform is now commercially available as a pre-built yet fully customizable microscopy solution (Cephla)¹⁵. This further lowers the adoption barrier for many life scientists who may not have the expertise or resources to build this system themselves.

Study #2: openFrame — a scalable imaging platform. Similar to Squid, the openFrame platform, developed by French and colleagues^{16,17} has experienced considerable adoption in resource-constrained regions. Two key design strengths underpin its success: extensibility and compatibility with advanced imaging techniques, including fluorescence lifetime imaging (FLIM) and single-molecule localization microscopy (such as PALM/STORM), among others. Its layered, modular architecture allows users to upgrade it progressively as resources permit, rather than being confined to the set of capabilities decided at the time of purchase. Its robust and flexible construction is compatible with user-fabricated add-on components (available via free CAD files) or fully supported commercial upgrades from Cairn Research Ltd¹⁸. This flexibility/adaptability allows microscopy capabilities to grow from simple to advanced applications in an economically viable way.

The success of openFrame stems from its dissemination model often paired with local multidisciplinary support teams. This approach ensures that the scientific community is fully supported from installation, training, to long-term system maintenance. More importantly, a multi-disciplinary team offers significantly more than just technical support. The local user community will receive stepby-step guidance on quantitative experimental design, from fluorophore selection, sample preparation, image acquisition, to image analysis. The openFrame developer team also fosters a collaborative environment through the openFrame GitHub repository¹⁹, where resources and expertise are freely shared, ensuring self-sustainable support and user-based feedback. Additionally, the platform is available through Cairns Research, Ltd^{18,20}. This partnership enables production on a commercial scale and leverages a larger support network, thus lowering the technical bar for the users who do not have the capability to build their own systems. This model of support and engagement extends beyond initial installation and training, as openFrame also employs a distributed dissemination strategy, partnering with funding bodies to support universitybased deployments, broadening its impact across diverse research settings²¹.

Study #3: Flamingo— a traveling light sheet for global access. Advanced technologies, while transformative, often demand substantial financial investment. Unlike routine conventional microscopy, the need for advanced techniques can be more variable. The lack of opportunity to try them in lab settings not only discourages many resource-limited scientists from purchasing them, but further limits the scope of experiments that can be performed in LMICs.

To address this challenge, the Flamingo light-sheet microscope developed by the Huisken lab^{22,23} has fundamentally transformed the concept of microscopy dissemination. Designed to be light, robust, and portable for easy shipping and on-site configuration, Flamingo is an ideal "traveling microscope". It can be easily packaged and shipped to wherever it is needed and returned when the experiment is over for recalibration prior to the next shipment.

Furthermore, the Flamingo system is designed with multiple possible configurations. This, combined with state-of-the-art optical and detection hardware, makes it suitable for a wide range of uses, including imaging whole live embryos, 3D biopsies, and others. This adaptability and robustness make Flamingo a versatile tool, capable of responding to myriad local needs.

The portability of the Flamingo platform opens innovative and powerful possibilities for its global dissemination. Under this distribution framework, Flamingo microscopes are provided at no cost to researchers worldwide for 1-3-month terms. A trained imaging scientist travels between laboratories to assist with setup, training, and experimental troubleshooting. For users seeking a dedicated instrument, the development team also hosts researchers to build their own system with full in-person guidance before shipping the system back to their home institution. To complement these unique strategies, Flamingo developers are creating software that enables remote access to the microscope for both troubleshooting and operation, as well as for real-time remote image data sharing. This capability supports seamless feedback between developers and users, as well as collaboration amongst users themselves, regardless of physical location. Additionally, the developers support open sharing of Flamingo image data to better foster reproducibility and transparency amongst its users.

Commonalities to success. The preceding examples, while diverse in their designs, applications, and dissemination strategies, share unifying principles that underlie their adoption success (Fig. 1). Their design philosophy prioritizes flexibility and adaptability. For example, the Squid and Flamingo systems are available in multiple pre-designed configurations to address a wide range of applications. Further, the openFrame platform is explicitly engineered to accommodate easily installed, extensible upgrades without having to reconfigure its core components. In each case, this design flexibility does not sacrifice overall robustness against the often-challenging conditions encountered in resource-limited settings. This combined adaptability and robustness is particularly vital in areas where a single microscope must often serve multiple purposes for a wide range of users and is relied upon to generate quantifiable and reproducible data.

However, the transformative power of each of these technologies is derived from innovative and dedicated dissemination strategies. Beyond merely sharing parts lists, software, and other components, these systems have been propagated by direct user engagement through in-person installation, training, and feedback that have

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Keys to Frugal Microscopy Adoption

Design

- Flexible and Modular
- Robust materials and construction
- Portable

Support

- · Dedicated staff
- In-person user training
- Long-term maintenance

Dissemination

- Direct user engagement
- Active user communities
- Commercial partnerships

Fig. 1 | **Key factors contributing to successful microscopy technology adoption.** The framework is represented by three main pillars: Microscope Design, emphasizing flexibility, modularity, robustness, and portability; Support, focusing on dedicated staff, in-person training, and long-term maintenance; and

Dissemination, highlighting direct engagement between developers, disseminators, and users, as well as fostering user communities, and formation of commercial partnerships. These pillars together form a strong foundation for the effective adoption of microscopy technologies in underserved communities.

overcome wide-spread adoption barriers. The Squid and openFrame platforms, for example, can be disseminated either through less-expensive self-built systems or via fully supported commercial products, pre-configured to user requirements. The Flamingo system offers equally innovative dissemination routes – either through the freely-available, limited term "traveling microscope" model, or construction of a dedicated system with expert guidance from the developers themselves. In any case, a highly engaged development team is available to guide users through building, operation, training, and maintenance. This not only helps to ensure successful adoption, but also propagates broader microscopy knowledge throughout a region, further seeding future microscopy uptake.

Innovative frugal design and dedicated dissemination strategies including training - are crucial to introducing microscopy technology to areas where microscopy utilization is lacking. However, to ensure that such uptake is sustainable, a final component must be considered - long term support. In the case of Squid and openFrame, commercial partnerships can leverage already existing instrument support infrastructure that may be difficult to build in a developer lab. Furthermore, these light, portable designs enable users to return systems to a developer lab for more in-depth maintenance and troubleshooting. The remote-support software featured in the Flamingo system is particularly innovative in helping users in difficult to access regions solve commonly encountered operational difficulties. Finally, online user communities are invaluable resources for knowledge and experience sharing, and create an ongoing dialogue between users and developers that fosters a virtuous feedback loop. This ultimately informs future design refinements based on real-world needs, ensuring that these tools remain relevant and effective.

Discussion

More than ever, access to microscopy determines biologists' ability to make fundamental discoveries, and therefore what pressing needs gain priority on the global scientific stage. Historically, microscopy stood as a tool reserved for affluent researchers due to its high cost and its necessary expertise and support. The advent of frugal

microscopy, however, stands at the cusp of overcoming access barriers to this information-rich toolkit.

Despite this opportunity, it is critical to balance cost savings with the necessity of providing researchers with robust tools that will advance scientific output. To that end, "frugal" should not imply a compromise in capability, but rather an innovative use of technology to provide a powerful cost-effective tool. The examples discussed here are exemplary in their ability to deliver advanced functionality at a fraction of the cost of a commercial equivalent. In addition, these systems are notable because they are responsive to the scientific challenges and priorities of their intended users.

For frugal microscope developers to understand users' needs and priorities, however, they must be articulated. It is critical that leaders within underserved institutions engage with developer communities to define local scientific priorities. Commensurately, engaged microscopy user communities are a powerful means for developers to foster a mutual dialogue that guides responsive technology development.

Most importantly, simply placing a robust, cost-effective technology into users' hands – even if it stands to be transformative – will encounter a myriad of barriers to long-term adoption. Free microscopes are not free. There are significant barriers beyond cost, with expertise and support standing out as critical challenges. Pairing innovative technologies with effective training programs is essential to empower users and enable proper utilization. Ongoing support to ensure that tools remain functional and effective in the long term is equally critical. Ultimately, a continuous feedback loop between developers, funders, and users is key to addressing the inevitable challenges that arise in post-deployment. Without these steps, the impact of even the most thoughtfully designed instruments will be limited.

In conclusion, for frugal microscopy to fulfill its promise, both developers and local research communities must work hand in hand, guided by a shared vision of what science can achieve when barriers to access are minimized. This goes beyond cost-saving measures to create robust, adaptable tools that truly address the scientific challenges of the regions they serve.

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Author contributions

M.A.R., C.M.H., T.-L.C., and J.S.A. contributed to the conceptualization, writing, and editing of the manuscript. J.S.A. and T.-L.C. contributed to the supervision of the manuscript preparation and editing.

Competing interests

The authors declare no competing interests.

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