Transforming the development and dissemination of cutting-edge microscopy and computation

We propose a network of national imaging centers that provide collaborative, interdisciplinary spaces needed for the development, application, and teaching of advanced biological imaging techniques. Our proposal is based on recommendations from a National Science Foundation (NSF)-sponsored workshop on realizing the promise of innovations in imaging and computation for biological discovery.

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Recent improvements in light microscopy have transformed researchers' ability to probe the structure and function of cells, tissues, and whole organisms. These advances were made possible by a combination of insights from different disciplines, including physics, chemistry, engineering, computation, and, of course, biology. This interdisciplinary foundation for biological imaging has created three critical needs in the scientific community: (1) further promotion of team-based approaches to the development of new technologies that incorporate methods from multiple disciplines, (2) more rapid dissemination of technological innovations to maximize benefits to the community, and (3) the development of training opportunities at the interface of biology, physics, and engineering. In the United States in particular, these unmet needs have limited the impact of innovations in microscopy and computational imaging on the biological sciences.

To find effective approaches to address these needs, the NSF sponsored a workshop, "Enabling Biological Discovery through Innovations in Imaging and Computation," at the Marine Biological Laboratory (MBL) in Woods Hole, Massachusetts, in November 2018 (Supplementary Information). The workshop convened 79 interdisciplinary experts and trainees to identify approaches that would transform the way technologies are developed and deployed. We highlight a consensus for the creation of national centers for innovation, dissemination, and training in biological imaging.

The role of national centers in developing imaging technologies

The past 20 years have seen explosive growth in bioimaging technologies, including the development of super-resolution[1] and light-sheet microscopy[2], the invention of new probes for imaging[3] and manipulating neuronal activity in live organisms[4], and the emergence of machine learning as a potent tool for image analyses[5]. Some developments have emerged from individual labs, and others from larger institutions that prioritize collaborative imaging-technology development (such as the European Molecular Biology Laboratory (EMBL) in Heidelberg, Germany, and the Howard Hughes Medical Institute's Janelia Research Campus (JRC); see, for example, refs. [6,7]).

Although optical imaging and computation have undergone transformative changes, these tools have been slow to make an impact on biology. One limiting barrier is that training, collaboration, and dissemination are largely left to local core facilities, which primarily serve the needs of specific academic and research institutions[8–10]. Successful, but rare, alternatives that promote dissemination include the access programs at EMBL and JRC, which host outside investigators and support them in using newly developed instruments, as well as training courses and workshops at the abovementioned institutions and at places such as the MBL and Cold Spring Harbor Laboratory (CSHL).

Other challenges also hamper the development and dissemination of biological imaging technologies. For example, it is increasingly difficult for individual labs to maintain sufficient expertise across all parts of the imaging chain, from specimen preparation to quantitative image analysis, and to keep current with advances in biological imaging. Existing courses are oversubscribed (for example, related courses at MBL are typically oversubscribed by 50% to 300% of capacity), and new courses are developed too slowly to keep pace with the latest developments, especially in computational image analysis. Because of the lack of collaborative spaces, technologies fail to fully benefit from the input of biologists and computational scientists in the design phase. Even in the best-case scenarios in which a technology is successfully developed and validated by proof-of-principle biology, its impact is limited unless there are avenues to educate and train the broader biological community in its use. Promising technologies linger in developers' laboratories for years before commercialization and deployment to the community. Staff scientist positions that can fully translate the new technologies for use by biologists are lacking, and where they exist, their funding is often unstable. These barriers create unmet needs that are particularly pressing within the research ecosystem of the United States, where the transformative role of staff scientists and the concept of national collaborative centers for biological imaging are underdeveloped.

Therefore, we propose the creation of a network of centers for biological imaging and computation as outlined below.

Collaborative infrastructures. To capture the promise of recent advances in microscopy, probe development, and computation for biological discovery, we propose newly configured centers that will serve as convening places for multidisciplinary teams from different institutions, as well as training spaces for the next generation of imaging collaborators. Our vision for the proposed centers is informed by institutions that are currently catalyzing the development of imaging innovations, such as EMBL and JRC, and by the success of the colocation of technologies and expertise into a hub like a national lab, albeit in a more distributed manner. It is also informed by recent efforts in Europe under the umbrella of Euro-BioImaging, through which European governments support the creation of centers of excellence in biological imaging at 29 affiliated institutions across 12 countries (web-based resources are listed in the Supplementary Information).

Interdisciplinary centers of innovation. The proposed centers would break away from the traditional (vertical) structure of academic institutions and instead use a horizontal structure that facilitates engagement across disciplines and institutions to catalyze new interactions. This interdisciplinary support is usually not available at local core facilities, which typically supply commercialized instrumentation under a tight user schedule that does not incentivize de novo instrument building or the modification of existing equipment. Furthermore, core facilities often provide a diverse array of techniques such as imaging, sequencing, and high-throughput screening. Therefore, their innovation potential lies primarily in the creation of 'packages of support' for scientists who need to combine several techniques and methods to arrive at their research goals[11]. Instead, the proposed new imaging centers would focus on the innovation pipeline in biological imaging, which requires its own set of expertise that cuts across traditional disciplines and is best captured through the collaboration of expert staff scientists.

A distributed national network. We believe that rather than a single national center, a network of smaller centers that each serve a group of regional academic and research institutions will provide more effective support for this large and diverse imaging community. Some centers could have specific emphases, such as light microscopy, electron microscopy, computational imaging, or imaging across scales. However, although they will be geographically dispersed, they will represent one community in their aspiration to enhance biological discovery through innovations in microscopy, computation, and probe development. Similar to Euro-BioImaging, the network of imaging centers in the United States should include a unifying web presence that provides user support by implementing access routes to instrumentation and computational tools, and by moderating communication platforms such as BioImaging NorthAmerica.

Training the trainers. The plethora of complex new technologies requires new approaches to training. At present, even when new imaging systems make their way into new settings, their use is often limited, not by the technology, but by user training. To address the need for advanced instrumentation and training, many institutions have created their own core facilities that consider training as one of their key activities[8]. The proposed imaging centers would not replace or compete with these local efforts but would seek instead to 'train the trainers' by introducing core facility staff to new technologies and best practices for their use. The centers also would provide access to cutting-edge technology for institutions that lack certain instruments or core facilities altogether. Therefore, we expect the proposed centers to create powerful synergies with core facilities, extending their spheres of influence and impact in the biological sciences.

We consider the National Center for Microscopy and Imaging Research (NCMIR) at the University of California, San Diego, as a potential template on which to model individual centers in the proposed network. Much of the NCMIR's activity is focused on electron microscopy and is funded through a P41 grant from the US National Institute of General Medical Sciences, part of the National Institutes of Health. Its mission goes beyond that of a core facility and includes innovation, early adoption, and training beyond the host institution. Integration of these three mission goals is not only practical but necessary for the NCMIR and for the proposed network centers, in order to harness the synergies from interdisciplinary collaborations to the maximum benefit of the research community. Integration of these approaches will also help to catalyze the innovation cycle by lowering the entry barrier for early adopters.

Computational imaging needs. Computation has become a critical part of biomedical imaging, not just for analyzing acquired data but also increasingly as an integral part of computational imaging systems[12]. The proposed imaging centers would be natural hubs linking microscope developers to algorithm developers, allowing them to spend time together identifying and integrating, from the beginning, potential collaborative strategies that push both fields forward. Smaller, proof-of-principle collaborations demonstrating the value of this approach have already nucleated at places such as the MBL[13–19]. Exposing new technology to a collaborative environment like those found in the MBL courses and summer research programs has helped to disseminate and refine technologies such as the LC-PolScope, dual-view selective plane illumination microscope, and lattice light-sheet microscope. A larger-scale implementation of these collaborative efforts could be transformative for biology and imaging.

Image-analysis software has proven indispensable for coping with the data flood in biological imaging. Early efforts harnessed individual initiatives to create a number of general, open-source software packages, such as ImageJ[20,21], that are effective in many research projects. However, increasingly complex biological questions benefit from specific task-driven algorithms or machine-learning strategies that require collaboration with computer scientists[17,19]. Development and dissemination of new tools will benefit from convening centers, as demonstrated by a recent National Center for Brain Mapping workshop (http://brain-doe.org/deep-learning/) at MBL, which introduced students to new computational packages such as the CARE (content-aware image restoration) algorithm[22] and segmentation tools for large-scale electron microscopy data[23].

Organizational principles

Personnel. To fulfill their mission, the centers would require permanent staff who are world-leading experts in various aspects of the imaging chain (hardware, software, probe development) and can drive the techniques forward while supporting the biologists who use them or inspire their development. A natural model is the set of beamline scientists at synchrotron user facilities, who balance their time between improving the techniques available at their beamlines and supporting visiting users in exploiting these techniques to advance their own science. Like at synchrotrons, the proposed imaging centers would need to set aside time when users were not scheduled so that instruments could be maintained, modified, and improved.

Staff scientists will play pivotal roles in creating a feedback loop among the main players of the imaging ecosystem: biologists, microscopists, and computational imaging specialists. The multidisciplinary interactions represent a good teaching opportunity even at the early graduate and undergraduate levels. Collaborations must thus be forged between educators and the centers in order to create courses that give training access to students, who will become 'native' in this new way of interdisciplinary thinking and project development.

It is difficult to fund such high-level staff scientists in traditional university environments in the United States. In Europe, staff scientist positions are better developed, to the benefit of initiatives like the ones described here and the scientific community. To extend the impact of imaging, funders and academic centers must recognize the barriers imposed by the current funding system. In the United States, some foundations, such as the Chan Zuckerberg Initiative, have recognized this challenge and issued a request for applications to support a number of staff imaging scientists for 2–5 years. The proposed imaging centers would require longer-term sources of support. Salaries for permanent staff would need to be competitive with industry, especially for IT personnel.

In addition to permanent staff, the centers would welcome visiting scientists for collaborative projects over periods spanning days to months. We envision that such projects will typically be supported by outside grants and stipends, or by contracts with companies interested in the development and application of cutting-edge microscopy. The centers thus would need convenient and flexible housing options and logistical support, as well as essential laboratory space and equipment for sample preparation prior to imaging. The organization of access to the centers and associated logistics might be modeled on processes established at the MBL and CSHL (Supplementary Information).

Access to new or high-end imaging equipment and software. Centers should lead not only to the dissemination of new technologies developed in-house but also to early applications of instruments and methods developed by other research labs and companies. In the spirit of Open Science[24,25], ideas include 'road-testing' of alpha- and beta-stage instrumentation and software in the centers with input from industry and academic experts. It was suggested that tech industry scientists could use their sabbatical time as 'scientists in residence' at these imaging centers, thereby sharing their skills to advance scientific projects. Such collaborations would be particularly helpful for permanent center staff, who could assist in matching the right biological applications to new technologies. Centers would thus catalyze a 'crossing of the chasm' between early adopters (pioneers) and broad acceptance in the biological community[17,26,27].

Conclusions

The workshop "Enabling Biological Discovery through Innovations in Imaging and Computation" was designed to illuminate the need for improved development, dissemination, and training in imaging technologies for biology. There was strong consensus from participants on the need for new opportunities and new spaces for interdisciplinary bioimaging technology development and dissemination. On the basis of that feedback, we propose a vision for the creation of a network of distributed national imaging centers as a critical component in this effort.

While we do not address the question of how to fund this national effort, US federal agencies such as the National Science Foundation, the National Institutes of Health, and the Department of Energy are well positioned in terms of expertise and resources to coordinate and establish the centers, including through the use of funds from the BRAIN initiative[28].

As a next step toward transforming these ideas into a concrete vision, we are organizing a meeting that will serve as a follow-up to the original workshop. The meeting will bring together some of the key players in the field, including heads of facilities and institutions that we hope to attract as network members, managers of core facilities with an imaging focus, and representatives of funding agencies. The meeting will also include discussions of concrete governance structures that would best benefit the proposed imaging centers and would help catalyze deployment of the first test centers nationally. The meeting is scheduled to occur in the fall of 2019 (look for an announcement at https://www.mbl.edu/nsf-workshop/). We encourage everybody who has helpful comments and ideas to send them to us before the meeting at ImagingNetwork@MBL.edu. ❐

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Competing interests

The authors declare no competing interests

Additional information

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