IMAGING 2024 THE FUTURE

CZI Imaging Program
Austin, TX ▪ Nov 12–15
#ImagingTheFuture

Chan Zuckerberg Initiative

IMAGING THE FUTURE 2024 MEETING PROCEEDINGS

Imaging the Future 2024

Meeting Proceedings

Meeting Organizers:
CZI Imaging Program,
Events and Engagement

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Executive Summary

The CZI Imaging Program convened the first Imaging the Future meeting on November 12-15, 2024, in Austin, Texas. The meeting included attendees from across the CZI Imaging grantee community, alongside individuals across the imaging ecosystem representing global imaging organizations, funding entities, research publishers, scientific thought leaders, and industry representatives.

Focused on a central theme of *Life Illuminated*, the meeting had three main objectives:

1. Celebrate the work of the diverse members of the Imaging ecosystem, including imaging scientists, innovators, data analysts, software developers, educators, and global imaging advocates.

2. Focus attention on key biological knowledge gaps and the potential that imaging technologies have to accelerate breakthroughs in those areas.

3. Provide a platform for networking across scientific silos, exchanging ideas, sharing information and sparking collaboration opportunities among attendees.

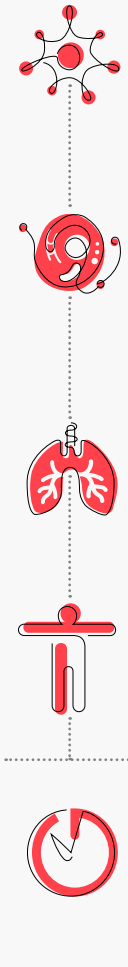
The meeting provided a mix of sessions to allow for a balance of information distribution, group discussions and interactive idea generation. Session takeaways, as well as poster and technology demo abstracts can be found within these Proceedings.

CZI Imaging: State of the Field

Stephani Otte, Ph.D.
Senior Science Program Officer, Imaging

Dr. Otte highlighted the progress of the CZI Imaging ecosystem in tackling the bold mission of illuminating life itself. She detailed CZI Imaging's three Grand Challenges — Visual Proteomics, Dynamic Imaging, and Deep Tissue Imaging. She also outlined the "innovation engine," CZI Imaging's multi-faceted approach to accelerating scientific progress, encompassing grant funding, technology incubation at the Imaging Institute, support for a vibrant, evolving global imaging community, and development of robust new platforms. The presentation showcased advancements made by the CZI Imaging community in imaging technologies and open source imaging software, emphasized the transformative potential of AI, as well as underscored the importance of interdisciplinary collaboration in achieving real-time, comprehensive biological observation to support the breakthroughs of the future.

Grand Challenges



Visual Protemonics
Image proteins and their interactions in cells at atomic resolution

Deep Tissue Imaging
Image through skin and bone at cellular resolution

Dynamic Imaging
Image molecular and cellular dynamics

Chan Zuckerberg Institute for Advanced Biological Imaging

Bridget Carragher, Ph.D.
Founding Technical Director, Chan Zuckerberg Institute for Advanced Biological Imaging

Dr. Carragher provided an overview of the Chan Zuckerberg Imaging Institute (CZ Imaging Institute). With the mission of enabling deep insights into complex biological systems through the incubation of novel imaging technologies, the CZ Imaging Institute is currently tackling its first Grand Challenge: imaging the molecular architecture of the cell to near-atomic resolution using cryo-electron tomography (cryoET). Notable achievements this year include the development of a robust dual laser phase plate to enhance image contrast, significant improvements to the cryoET processing pipeline, and the launch of a Kaggle competition.

Keynote Summaries

Building Community Data Resources for Structural Biology

Helen Berman, Ph.D.
Board of Governors Professor of Chemistry and Chemical Biology, Director Emerita, RCSB Protein Data Bank, Rutgers University, University of Southern California

Dr. Berman's keynote traced the history of the development and evolution of the Protein Data Bank (PDB), emphasizing the crucial role of community activism to help create vital shared data resources and data standards to define and advance new fields. Her presentation emphasized the principles of community building, including bottom-up and top-down approaches, and the importance of perseverance and multi-stakeholder alignment for advancing common interests.

Optical Tools to Map Brain Function Across Scales

Karel Svoboda, Ph.D.
Vice President and Executive Director, Allen Institute for Neural Dynamics

Dr. Svoboda discussed the significance of technology development in scientific progress, particularly in the context of brain function mapping. He highlighted the challenges and importance of creating and disseminating new technologies, referencing the impact of specific innovations in the field's understanding of brain dynamics and activity at different scales. He highlighted the need for data sharing and standardized processing pipelines to facilitate collaborative research in neuroscience.

From Nano to Macro: Unlocking the Brain with AI-Driven Imaging Insights

Nina Miolane, Ph.D.
Assistant Professor, University of California, Santa Barbara

Dr. Miolane discussed the potential of AI to revolutionize our understanding of the brain — and in particular, women's brain health, which has been vastly understudied. Her talk bridged physical scales — from nano to macro, and bridged AI applications from CryoET to MRI. The presentation emphasized the underrepresentation of women in brain imaging studies and introduced the concept of AI-powered digital twins to personalize brain healthcare for women, particularly in areas like pregnancy and menopause. Nina outlined key challenges such as the need for reliable and interpretable AI models, the importance of collaboration, and the necessity of sharing AI tools with the international community to accelerate imaging-guided discoveries.

Talk Highlights

Biological Problems in Need of Imaging Solutions

This session highlighted key biological challenges that hold the potential to significantly advance our understanding of health and disease, and explored opportunities for imaging technologies to make significant impacts.

Rebecca Alvania, Ph.D.
CEO, American Society for Cell Biology

Dr. Alvania provided an overview of the American Society for Cell Biology, and highlighted two biological knowledge gaps that could benefit from imaging solutions:

- Measuring force in vivo during development, and
- Visualizing membrane contact dynamics.

She discussed how non-invasive imaging tools are needed for better in vivo measurements of biological force, and shared how the discovery of the interconnectedness of organelles (membrane contact sites) is revolutionizing the field's understanding of cellular biology. High-throughput imaging and "big data" approaches could provide insights into the general rules of system activity and regulation across cell states, potentially offering predictive value in determining cell state transitions.

Nonia Pariente, Ph.D.
Editor-in-Chief, PLOS Biology

Dr. Pariente provided an overview of the open source journal PLOS Biology, and highlighted the following biological knowledge gaps that could benefit from imaging solutions:

- The geography of infection across time, which could reveal previously unknown pathogen reservoirs, help us understand pathogen movement in the body, as well as improve drug treatment efficacy.
- The challenge of observing microbial community structure, which could accelerate the understanding of microbial functioning and aid in designing stable microbial communities for diverse applications.
- The ability to study protein structures within their native physiological context.
- The need to understand tissue-level function in real time, which would enable following the immune response from antigen detection to amplification and following cancer cells as they move through the niche and metastasize.

Anne Claiborne, J.D.
Director, Strategic Operations and Policy, CZI Science in Society

Dr. Claiborne provided an overview of the CZI Science in Society Rare as One Program (RAO), and discussed the importance of imaging in research for rare diseases. The presentation highlighted the burden of rare diseases and the power of patient communities in driving research. A key focus of her talk was introducing a survey of RAO Network grantees, whose results indicated that over 90 percent of respondents felt imaging was important to their work. The presentation highlighted specific imaging modalities, including optical imaging (emphasizing challenges in specificity and access to advanced techniques), electron microscopy (highlighting limitations in throughput and 3D reconstruction), spatial imaging (discussing challenges in multiplexing and data integration), live-cell imaging (noting the need for higher throughput and advanced models), and clinical imaging (mentioning lack of standardization and radiation concerns). The talk concluded by emphasizing the need for improved access to imaging technologies and standardized protocols to advance research, enable earlier disease detection, and empower subcellular and *in vivo* imaging techniques, imaging biomarkers, and cross-disease imaging studies.

Adam Lewandowski, Ph.D.
Deputy Chief Scientist, UK Biobank,
Associate Professor, University of Oxford

Dr. Lewandowski introduced the UK Biobank: a large-scale biomedical database and research resource containing in-depth genetic and health information from half a million UK participants. The database is unique in its scale, depth, length, and accessibility, and is being used by researchers worldwide to study a wide range of health conditions.

- The project began in 2006 with the recruitment of 500,000 participants aged 40-69, and has since collected a vast amount of data on their health, lifestyle, and genetics. Key milestones in the project's timeline include the launch of a major imaging study in 2014, the release of genotyping data in 2017, and the availability of whole genome sequencing data on all 500,000 participants in 2023.
- The imaging study is the largest of its kind ever conducted, and is providing valuable insights into the brain, heart, and other organs.
- The UK Biobank is a powerful resource for researchers seeking to understand the causes of disease and develop new treatments.

Imaging Tools & Their Applications

This session focused on how innovative imaging technologies have been successfully applied to address key biological problems.

Landscape Expansion Microscopy (land-ExM) Uncovered Nuclear Tunnel's New Function in Upregulating Ribosome Biogenesis

Xiaoyu Shi, Ph.D.
Assistant Professor, Departments of Developmental and Cell Biology, Chemistry, and BME, University of California, Irvine

Dr. Shi discussed work on the development of a new technique, Landscape Expansion Microscopy (Land-ExM) to visualize protein and lipid context simultaneously, enabling the study of organelle interactions and membrane contact sites in breast cancer cells. She provided data to show how Land-ExM is a powerful tool for studying organelle-organelle interactions, membrane contact sites, and cell-material interactions. This technology has uncovered a new structure-function relationship in the nuclear envelope, with implications for understanding cancer and aging.

Scalable Mapping of Cell Dynamics

Shalin Mehta, Ph.D.
Platform Leader, Computational Microscopy, Chan Zuckerberg Biohub San Francisco

Dr. Mehta discussed the need for better understanding the complexities of cellular dynamics, and shared data from the Mantis microscope, capable of high-throughput 4D imaging and analysis of the molecular and physical architecture of cells. He highlighted a self-supervised framework, DynaCLR, to model cell dynamics via contrastive learning of representations of time-lapse datasets, and emphasized how the combination of imaging data, reconstruction algorithms and deep learning is accelerating the pace of dynamic cell system mapping in health and disease.

Using Label-Free Imaging and AI to Improve Brain Tumor Surgery

Todd Hollon, M.D.
Assistant Professor of Neurosurgery, Program Director, Artificial Intelligence in Neurosurgery, University of Michigan

Brain tumor surgery is challenging due to the difficulty in differentiating between tumor and normal brain tissue, and the risk of causing neurological deficits. Dr. Hollon discussed how FastGlioma, an AI-powered tool, utilizes bed-side Stimulated Raman Histology (SRH) images to provide rapid, label-free imaging of brain tumor margins during surgery. The technology has been tested on a large dataset across multiple medical centers, and is illustrative of the promise of medical foundation models in improving the care of patients with cancer.

Vascular Mapping With HiP-CT

Claire Walsh, Ph.D.
Senior Research Fellow, University College London

Dr. Walsh described HiP-CT, a multi-scale X-ray imaging technique which is capable of scanning intact human organs ex vivo at single-cell resolution. She highlighted its application in creating detailed structural information of ex vivo vasculature, particularly of the kidney, and demonstrated how this structural data can be combined with functional analysis to understand the impact of disease or physiological changes like hypertension on organ function. The presentation also introduced the Human Organ Atlas HUB (HOAHub), a public database housing HiP-CT imaged organs in both healthy and diseased states.

Panels & Participants

Panel: Extramural Perspectives

Rebecca Alvania, Ph.D.
American Society for Cell Biology

Ileana Hancu, Ph.D.
ARPA-H

Nonia Pariente, Ph.D.
PLOS Biology

Jason Swedlow, Ph.D.
University of Dundee

Fireside Chat: The Impact of Computational Tools and AI in Imaging

Maryellen Giger, Ph.D.
University of Chicago/MIDRC

Nina Miolane, Ph.D.
University of California, Santa Barbara

Loic Royer, Ph.D.
Chan Zuckerberg Biohub San Francisco

Behrouz Shabestari, Ph.D.
National Institute of Biomedical Imaging and Bioengineering

Roundtable Discussion Summaries

BIOLOGICAL PROBLEM ROUNDTABLE DISCUSSIONS: BREAKOUT ROOM SUMMARIES

These meeting summaries were generated by AI and reviewed by a member of the Imaging Program Team.

Biological Applications — Across Physical Scales

Attendees joined roundtable discussions to explore compelling challenges within various biological domains, and brainstorm solutions for imaging to make an impact within them.

The following summary includes AI generated content, and was reviewed by a member of the Imaging Program Team.

Advanced imaging technologies are revolutionizing biological research across molecular, cellular, and organismal scales. Discussions highlighted key opportunities for breakthroughs, such as mapping protein structure and dynamics within native cellular contexts, studying host-pathogen interactions, and linking molecular mechanisms to tissue and organismal processes. Emerging applications like adaptive optics for small organisms, label-free imaging for metabolic activities, and standardized organoid systems are driving innovations in drug screening, developmental biology, and immune system research.

Exciting discoveries discussed included observing exocytosis, vesicle trafficking, and body plan development through light-sheet microscopy; real-time protein interactions with cryoEM tomography; and cellular heterogeneity using Cell Painting and MINFLUX. Techniques like expansion microscopy (ExM) and fluorescence multiplexing are enabling unprecedented resolution and dynamic insights.

Innovations have unlocked significant potential: AI-driven tools improve data analysis and prediction, correlative imaging integrates modalities for comprehensive insights, and time-resolved cryoEM captures dynamic processes. High-speed, low-noise cameras, iterative fluorescence techniques, and spatial omics bridge scales, enabling holistic understanding of cellular and molecular systems.

Despite these advances, barriers remain. Accessibility and cost of equipment, data management challenges, and interdisciplinary gaps hinder progress. Proposed solutions include establishing shared facilities, fostering team science, and leveraging AI for data interpretation. Standardization efforts and better career pathways for imaging specialists were emphasized as critical for sustaining innovation.

In summary, imaging technologies are transforming biology by enabling dynamic, multi-scale studies. Addressing technical, cultural, and logistical challenges will be essential to realize the full potential of these advancements across disciplines and scales.

IMAGING TOOLS ROUNDTABLE DISCUSSIONS: BREAKOUT ROOM SUMMARIES

These meeting summaries were generated by AI and reviewed by a member of the Imaging Program Team.

Imaging Tools

Attendees joined roundtable discussions to discuss various cutting edge technologies on the frontiers of imaging, and identify opportunities for biological impact.

The following summary includes AI generated content, and was reviewed by a member of the Imaging Program Team.

Discussions explored advancements across key topics, including CryoET and volume EM, AI/ML in imaging, imaging probes, large data management, and label-free optical imaging. Common themes highlighted the transformative potential of emerging technologies and the importance of collaborative, interdisciplinary approaches.

Key Advances

- **CryoET and vEM:** Innovations like plasma FIB for sample preparation, machine learning for segmentation, and multimodal labels are expanding applications in structural biology and disease research.
- **AI/ML:** Tools such as pre-trained segmentation models, virtual staining, and generative models enable data-driven insights, particularly for high-resolution imaging and predictive modeling.
- **Imaging Probes:** Advances in CLICK-chemistry, metabolic probes, and nanobodies have enhanced targeted labeling, live-cell imaging, and multimodal capabilities.
- **Label-Free Optical Imaging:** Techniques like stimulated Raman spectroscopy, 3-photon excitation, and quantitative phase microscopy provide non-invasive, high-resolution insights into tissue and cellular dynamics.
- **Data Management:** Unified standards, metadata integration, and FAIR principles are essential to managing the growing volume and complexity of imaging data.

Biological Applications

These tools are advancing our understanding of cellular processes, tissue structures, and disease mechanisms. Applications range from cancer detection and immune system studies to developmental biology and neuroscience. Label-free and multimodal imaging methods minimize perturbation and maximize functional readouts, supporting personalized medicine and high-throughput research.

Challenges and Solutions

Key challenges include data heterogeneity, lack of incentives for sharing, and technical barriers to adoption. Proposed solutions emphasize education, streamlined tools, open-access repositories, and community-driven standards to foster widespread adoption and collaboration.

Across these topics, the integration of advanced imaging technologies with AI, multimodal methods, and robust data practices is driving innovation in biomedical research and translational applications.

Deep Dive Session Abstracts

List of Deep Dive Session Abstracts

Deep Dive sessions were led by meeting participants, and included a variety of topics and formats that enabled attendees to engage on shared interests, challenges, and innovative solutions in the field of advanced bioimaging.

Cryogenic Electron Imaging of Tissues, Cells and Macromolecules

Wah Chiu

Cryogenic electron imaging, specifically through cryo-electron microscopy (cryoEM), cryo-electron tomography (cryoET), and cryo-focused ion beam and scanning electron microscopy (cryoFIB-SEM), enables scientists to directly visualize biological structures including tissues, cells, and macromolecules at different scales. By capturing 3D images of cellular and molecular structures, these methods allow the study of biological processes in their native state, without the need for traditional staining or fixing techniques. Many technical challenges remain from sample vitrification to data collection and image processing. Integrating 3D image data from these various scales (tissues to molecular assemblies) is critical for advancing biomedical research, from studying normal cell function to identifying the molecular underpinnings of diseases and possible therapeutic intervention strategies.

Coherent Raman Microscopy

Hervé Rigneault, Ji-Xin Cheng, Randy Bartels

Today, it is possible to purchase or build a microscope that performs chemical imaging without the need for labeling or staining. These microscopes use coherent Raman imaging contrasts, known as CARS (Coherent Anti-Stokes Raman Scattering) and SRS (Stimulated Raman Scattering). Recent advances have enabled these microscopes to address key challenges in biological and medical sciences, including virtual histology.

This session will cover the following points:

1. Basics of coherent Raman microscopy
2. Examples of coherent Raman applications in biology, material science, environmental sciences, and medical sciences
3. Technical implementation and commercial solutions
4. Open questions

Disseminating Open Instrumentation

Paul French, Teng-Leong Chew, Jason Swedlow, Mark Tsuchida, Caron Jacobs

Why can't/don't we give capabilities to people who (we think) need them? Many labs are developing open-source tools (hardware and software), with potential to widen access to capabilities for research, training and for biomedical applications — often with an aspiration to benefit hard-pressed research and healthcare systems, including in LMIC. However, with no IP barriers, it is difficult to disseminate such technology and to obtain regulatory approval, e.g., for medical applications. This potentially impedes benefits to lower resourced communities — and limits potential cost reductions in healthcare systems generally. How should developers of open-source tools share their capabilities and who might fund the process? This Deep Dive discussion aims to identify key challenges and brainstorm potential solutions — or at least priorities.

LLMs for Imaging: Revolutionizing Bioimage Analysis

Loic A. Royer

This deep-dive session will explore how Large Language Models (LLMs), including multimodal models, are set to transform the field of bioimage analysis. With recent advances, LLMs can now assist in complex image processing tasks such as segmentation, object tracking, and data quantification — tasks that previously required extensive manual effort and coding expertise.

We will discuss how these models, trained on vast datasets, are capable of understanding and interpreting both images and text-based queries. This enables a new, interactive approach to bioimaging workflows, where users can leverage natural language instructions to perform advanced analyses, reducing the barriers of technical proficiency.

Topics will include the application of LLMs in automating bioimage analysis, their potential to overcome the challenges of manual annotation, and their ability to generalize across diverse imaging modalities. The session will also highlight future directions in combining LLMs with specialized image-centric models to further enhance accuracy and efficiency in bioimage research.

Attendees will gain insights into how these cutting-edge AI models can be integrated into their own research to streamline and elevate bioimaging analysis.

Roadmap to Innovation: Technology Development and Implementation

Kevin W. Eliceiri, Claire M. Brown

Bring together stakeholders from diverse backgrounds to develop a Roadmap to Innovation by identifying and finding solutions to the road-blocks hindering broad dissemination and implementation of new technologies to answer fundamental biomedical questions. The session will engage community members who are instrument builders, software and tool developers, and biomedical researchers. This will ensure an understanding of shared challenges and potential solutions due to contributions from diverse perspectives.

A Deep Dive in New Opportunities for Deep-Tissue Imaging

Xiang Wu, Tianyu Wang

Light scattering in biological tissues significantly limits the penetration depth of optical imaging techniques in vivo. To address this challenge, many new exciting techniques have been demonstrated, including in vivo tissue clearing techniques, multi-photon microscopy, near-infrared emitters, adaptive optics, computational and AI-based methods. In this session, we will bring together experts from different sub-fields and brainstorm potential synergies between these newly developed approaches. Specifically, the session will start with a brief introduction about recent advances and challenges for each method by 1~2 speakers (per approach). We will then have in-depth group discussions led by the speakers, and participants can freely join or switch discussion groups. By the end, we will invite volunteers to share any interesting thoughts or questions with all participants.

Challenges and Opportunities in Translational AI: Focusing on Existing Data and Tools

Maryellen Giger, Joe Jacob, Heather Whitney

Focus: Barriers to developing clinical and translational AI, as well as the potential opportunities that can be realized using existing data.

Expanding Scanning Dimensions in Label-Free Imaging: Spectroscopic Imaging in Frequency and Time Domains

Leonel Malacrida, Dmitry Fishman, Rajesh Menon

This session aims to bring together a diverse imaging community to explore advancements in label-free imaging that harness intrinsic molecular, and thus chemical, signatures in both frequency and time domains. Featuring concise expert presentations followed by interactive discussions, this session will seek to identify key challenges and propose actionable solutions for broadening the implementation of these imaging modalities — specifically, their clinical application and democratization.

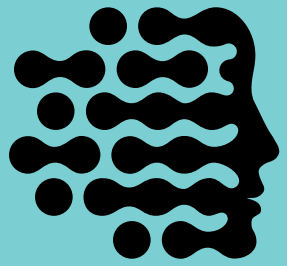
Unlocking Innovation: The Impact of Imaging Networks on Technology Development and Collaborative Research

Yara Reis, Johanna Bischof

This session will explore the transformative role that global imaging networks, like Global BioImaging and its constituent networks, play in driving innovation and collaboration in life sciences research. These networks connect imaging scientists, facility managers, technology developers and researchers across borders, accelerating the dissemination and adoption of cutting-edge technologies and fostering international partnerships. Key topics will include the role of core facilities and imaging networks in technology dissemination and uptake, cross-border collaboration, and building sustainable imaging communities. Since 2015, Global BioImaging has established a global network spanning 60+ countries, promoting equitable access to advanced imaging infrastructure and expertise and supporting research and imaging innovation worldwide. This interconnected network facilitates the exchange of expertise, best practices, and resources. It also tackles critical global challenges by democratizing access to advanced imaging technologies, promoting the FAIR principles for data management, and enhancing reproducibility in scientific research.

Poster & Tech Demo

List of Poster and Demo Abstracts



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