Erik Meijering, Vince D. Calhoun, Gloria Menegaz,
David J. Miller, and Jong Chul Ye

Deep Learning in Biological Image and Signal Processing

Biological research on the fundamental structural and functional properties of life—from molecules to cells, tissues, organs, and complete organisms, including human life—relies heavily on advanced imaging systems and measurement devices generating data of ever-increasing quantity and complexity. Automated processing and analysis of these data through increasingly sophisticated computational methods have become indispensable in exploiting relevant information and enabling researchers to detect patterns that may be unnoticeable to human senses.

For a long time, the primary modus operandi in developing such methods has been to hand-design mathematical models of underlying phenomena and translate them into computational algorithms. In the past decades, many models have been successfully developed for typical biological data analysis tasks, such as image/signal reconstruction, restoration, enhancement, detection, segmentation, tracking, classification, and quantification. However, the manual engineering of dedicated solutions does not scale well with the growing number of application domains and increasing data volumes.

Recently, a major paradigm shift has taken place with the widespread adoption and application of deep learning technologies, which are now rapidly replacing traditional data analysis approaches in virtually all fields of science, including biological image and signal processing. With sufficient training data and computing power, deep artificial neural networks can learn the right data-driven models for virtually any analysis task. Deep learning has become a popular approach for solving a wide range of biological data analysis problems where multimodal, multidimensional, multiparametric data sets need to be jointly processed, posing a clear challenge to traditional methods. Yet many scientific and engineering difficulties remain to further improve the performance of deep learning methods and make them reliable enough for critical tasks in biological research applications.

This special issue of *IEEE Signal Processing Magazine* surveys recent advances in deep learning for applications in biological image and signal processing. Focusing on fundamental biological research, it fills a gap left by special issues of other journals, which covered deep learning for clinical medical imaging applications (*IEEE Transactions on Medical Imaging*, May 2016, June 2018, and October 2021; *IEEE Journal of Biomedical and Health Informatics*, July 2019 and April 2020; and *IEEE Journal of Selected Topics in Signal Processing*, October 2020) and more general computer vision and image/signal processing applications (*IEEE Journal of Selected Topics in Signal Processing*, February 2021; *IEEE Signal Processing Magazine*, November 2017; and *International Journal of Computer Vision*, May 2015 and April 2020). The seven articles selected from three dozen submissions cover a range of topics in terms of data modalities, processing tasks, and applications, as outlined in the following.

In This Issue

Image fidelity and quality are fundamental factors determining the likelihood of success in biological image analysis. Thus, the first three articles are concerned with image formation, reconstruction, and enhancement. In "Unsupervised Deep Learning Methods for Biological Image Reconstruction and Enhancement: An Overview From a Signal Processing Perspective," Akçakaya et al. observe that while deep learning has become popular for solving inverse problems, the reference data required for supervised learning methods are often unavailable, which calls for unsupervised approaches. The authors review two such techniques, namely, self-supervised learning and the use of generative adversarial networks.

Another observation, made by Ben Sahel et al. in "Deep Unrolled Recovery in Sparse Biological Imaging: Achieving Fast, Accurate Results," is that objects of interest in biological imaging are typically smaller than the diffraction limit of the imaging system, which presents a challenge for subsequent analysis. At the same time, the images are often

Digital Object Identifier 10.1109/MSP.2021.3134525
Date of current version: 24 February 2022

sparse, which enables leveraging specialized approaches. The article surveys how algorithm unfolding—a strategy for designing deep neural networks based on domain knowledge—enables ultrahigh-speed superresolution imaging in single-molecule localization microscopy, ultrasound localization microscopy, and other potential applications.

High-speed imaging is also often needed in neuroscience studies of cellular activity and neural circuits in living brain tissue. One of the best ways to capture the fast dynamics of large populations of neurons in three dimensions is by using scanless imaging techniques, such as light field microscopy. However, unlike with scanning microscopes, faithful volumetric reconstruction from light field data is challenging due to the reduced spatial resolution, light scattering in deep tissues, and spatial and temporal sparsity of the fluorescent signals. In "Light-Field Microscopy for the Optical Imaging of Neuronal Activity: When Model-Based Methods Meet Data-Driven Approaches," Song et al. review how incorporating model-based priors in deep learning-based methods can improve image reconstruction.

Once image acquisition is complete, various processing operations need to be performed to obtain the desired quantitative measurements for downstream analyses, depending on the goals of the study at hand. The article "A Practical Guide to Supervised Deep Learning for Bioimage Analysis: Challenges and Good Practices," by Uhlmann et al., reviews key challenges faced by practitioners in using supervised deep learning models for this purpose. It outlines best practices to answer questions about choosing a pretrained model, dealing with discrepancies between the training data and a user's data, assessing the reliability of results, and avoiding the misuse and overuse of deep learning.

The final three articles focus on deep learning for neuroimage and neurosignal processing. Neuroimaging data are often high dimensional, multimodal, heterogeneous, and lacking solid ground truth, and the sample size may be quite limited, which hampers the use of deep learning. In their article "Deep Learning in Neuroimaging: Promises and Challenges," Yan et al. survey the state of the art in using deep learning for diverse categories of neuroimage analysis tasks, including classification for biomarker detection; regression for brain age prediction; leveraging functional dynamic, multimodal, and multisite information; and visualizing and interpreting results.

As in many other fields, the interpretability and explainability of deep learning models and results are receiving increasing attention in biological image and signal processing, as they help us gain a better understanding of and confidence in the predictions made by the models. "Explainable Artificial Intelligence for Magnetic Resonance Imaging Aging Brainprints: Grounds and Challenges," by Boscolo Galazzo et al., explores this topic, with a focus on neuroimaging research into brain aging. Specifically, the authors discuss the use of machine and deep learning in modeling the complex interplay between endogenous and exogenous factors of different types and their impact on brain aging in health and disease.

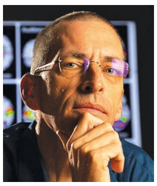
Another important noninvasive tool in neuroscience is electroencephalography (EEG), which measures the electrical activity of the brain and is used in many applications, such as brain–computer interfacing, clinical diagnostics, and cognitive monitoring. "Toward Open-World Electroencephalogram Decoding via Deep Learning: A Comprehensive Survey," by Chen et al., discusses how deep learning methods may improve the decoding of EEG signals in real-world scenarios, where unseen and unexpected situations can easily emerge, which is a problem for traditional methods designed in more static, well-controlled lab environments. This touches on the topics of robustness and generalizability, which, in addition to others mentioned in the preceding, are key issues in designing deep learning solutions for biological image and signal processing across the board. Altogether, the articles in this special issue highlight many research directions for solving these matters.

Acknowledgments

This special issue would not have been possible without contributions from many people. We are grateful to Robert Heath, past editor-in-chief (EiC) of *IEEE Signal Processing Magazine*, for his encouragement with developing the concept and to Christian Jutten, the present EiC, for his guidance toward completion as well as to Area Editors Ervin Sejdic and Xiaoxiang Zhu and IEEE Signal Processing Society Publications Administrator Rebecca Wollman for continual support and assistance throughout the process. We thank all the authors whose submissions shaped the topics we envisioned in the call for articles. Regrettably, we could accept only a limited number of manuscripts. Special thanks go to the reviewers for their generous efforts in providing constructive and timely feedback. We trust that the readers will enjoy the fruit of your labor as much as we have.

Guest Editors

Erik Meijering (erik.meijering@unsw.edu.au) received his Ph.D. degree from Utrecht University, Utrecht, The Netherlands. He is a professor of biomedical image computing in the School of Computer Science and Engineering, University of New South Wales, Sydney, NSW 2052, Australia. He is an associate editor of *IEEE Transactions on Medical Imaging*, a former associate editor and guest editor of *IEEE Transactions on Image Processing*, and a guest editor of *IEEE Signal Processing Magazine*. He was chair of the IEEE Signal Processing Society (SPS) Technical Committee on Bio Imaging and Signal Processing (2018–2019) and technical program chair of the IEEE International Symposium on Biomedical Imaging (2006, 2010, and 2018). He also served/serves on a variety of other international conference, advisory, and review boards. He is a Fellow of IEEE and an SPS Distinguished Lecturer (2022–2023).



Vince D. Calhoun (vcalhoun@gatech.edu) received his Ph.D. degree from the University of Maryland Baltimore County. He is the founding director of the tri-institutional Center for Translational Research in Neuroimaging and Data Science, Atlanta, Georgia, 30303, USA, and holds appointments at Georgia State University, Georgia Institute of Technology, and Emory University. He was a guest editor for *Journal of Signal Processing Systems*, *IEEE Transactions on Multimedia*, *NeuroImage*, and *NeuroImage: Clinical*. He served as chair of Human Brain Mapping (2018–2019) and the IEEE Signal Processing Society (SPS) Technical Committee on Machine Learning for Signal Processing (2015–2016), and he currently serves on the SPS Technical Committee on Bio Imaging and Signal Processing. He is a Fellow of IEEE, the American Association for the Advancement of Science, and the International Society of Magnetic Resonance in Medicine, among others.

Gloria Menegaz (gloria.menegaz@univr.it) received her Ph.D. degree from the Swiss Federal Institute of Technology, Lausanne, Switzerland. She is a professor of bioengineering in the Department of Computer Science, University of Verona, 37134, Italy. She serves as an associate editor of *IEEE Signal Processing Letters* and *EURASIP Journal on Image and Video Processing*, and she was a guest editor of *Journal of Display Technology*. She was chair of three editions of the IEEE Signal Processing Society (SPS) Winter School on Brain Connectomics (2016, 2017, and 2019) and SPS Winter School on Imaging Genetics (2019), and a member of the Organizing Committee of the IEEE International Symposium on Biomedical Imaging (2019 and 2022). She is a Senior Member of IEEE, a member of the SPS Technical Committee on Bio Imaging and Signal Processing, SPS Representative to the IEEE Transactions on Medical Imaging Steering Committee (2021–2023), and a member of IEEE Woman in Engineering.

David J. Miller (djm25@psu.edu) received his Ph.D. degree from the University of California Santa Barbara. He is a professor in the School of Electrical Engineering and Computer Science, Pennsylvania State University, State College, Pennsylvania, 16802, USA. He was an associate editor of *Journal of VLSI Signal Processing Systems for Signal, Image, and Video Technology* and *IEEE Transactions on Signal Processing*. He was chair of the IEEE Signal Processing Society (SPS) Technical Committee on Machine Learning for Signal Processing (2007–2009), general chair of the IEEE Workshop on Neural Networks for Signal Processing (2001), and program chair of the IEEE Workshop on Machine Learning for Signal Processing (2005), and he serves on the IEEE SPS Conference Board. He received the National Science Foundation CAREER Award in 1996. He is a Senior Member of IEEE.

Jong Chul Ye (jong.ye@kaist.ac.kr) received his Ph.D. degree from Purdue University. He is a professor in the Department of Bio/Brain Engineering and an adjunct professor in the Department of Mathematical Sciences and Graduate School of Artificial Intelligence, Korea Advanced Institute of Science and Technology, Daejeon, 34141, South Korea. He was an associate editor of *IEEE Transactions on Image Processing* and *IEEE Transactions on Computational Imaging*, an editorial board member of *Magnetic Resonance in Medicine*, and a guest editor of *IEEE Transactions on Medical Imaging* and *IEEE Journal of Selected Topics in Signal Processing*. He is an associate editor of *IEEE Transactions on Medical Imaging* and a senior editor of *IEEE Signal Processing Magazine*. He was the chair of the IEEE Signal Processing Society Technical Committee on Computational Imaging (2020–2021) and general cochair of the IEEE Symposium on Biomedical Imaging (2020). He is a Fellow of IEEE and an IEEE Engineering in Medicine and Biology Society Distinguished Lecturer (2020–2021).

SP