



Explainable Deep Learning for Label-Free Cell Classification: The LIVECell-CLS Benchmark

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Abstract

Label-free cell classification from microscopy images has emerged as a valuable alternative to traditional staining techniques, enabling high-throughput analysis while preserving cellular integrity. Despite promising advances through deep learning, progress has been hindered by the absence of large, standardized datasets to support model development and evaluation.

In this study, LIVECell-CLS is introduced as the largest benchmark dataset for label-free cell classification to date, comprising over 1.6 million cropped images derived from the LIVECell segmentation dataset and encompassing eight morphologically distinct cell lines. A diverse set of deep learning architectures - including ResNets, Vision Transformers (ViTs), and MLP-Mixers—along with their Tensor Network-based variants, have been systematically evaluated. These models incorporate a *C. elegans* connectome-inspired module designed to enhance latent feature representation prior to classification.

To gain insights into model behavior and feature representations, multiple Explainable AI (XAI) methods have been applied in conjunction with UMAP-based visualizations. The results indicate that improvements in classification accuracy are closely associated with increased feature separability and interpretability, particularly in challenging cases involving closely related cell morphologies. This work provides a comprehensive benchmark for future developments in label-free microscopy and underscores the importance of model explainability in biomedical AI.

Short bio

Since November 1, 2006, Roberto Tagliaferri has been full Professor, at the University of Salerno. He is Director of the PhD School in Big Data Management and in Data Science, Accounting & Management, DISA MIS, University of Salerno. He had Master, Bachelor and PhD courses in Artificial Intelligence, Computational Intelligence and Neural Networks, Computer Architectures and Bioinformatics. He has been co-editor of several proceedings on international workshops on Neural Networks and Bioinformatics and special issues on international journals. He is Associate Editor of the IEEE Transactions on Cybernetics, of BMC in Bioinformatics and of the Journal of Translational Medicine. The scientific activity has been oriented to the design and analysis of models to describe complex systems using Neural Networks and Computational Intelligence methodologies, including Deep Learning, and to the design of architectures and of learning paradigms for Artificial Intelligence models. He is senior member of the IEEE "Computational Intelligence" and "System, Man and Cybernetics" societies and of INNS. He was Chair of the Italy Chapter of the IEEE CIS from 2013 to 2016.

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