Deep learning for cellular image analysis

This review article written by Erick Moen, Dylan Bannon, Takamasa Kudo, William Graf, Markus Covert and David Van Valen provides a superb overview of both deep learning and traditional cellular image analysis and the methods in which deep learning can be applied to this domain to the four tasks: image classification, image segmentation, object tracking and augmented microscopy. This article additionally highlights Deep learning-based ready-to-use frameworks and tools for these tasks in this domain.

Typical tasks in the field of medical and biomedical image analysis include unsupervised image exploration, image classification, image segmentation and object tracking. There have been numerous developments using non-Deep Learning-based techniques for the aforementioned tasks and their direct implementations can be found in Python and MATLAB. Tools such as SuperSegger, Oufti can be used for single-cell bacteria analysis; CellProfiler, Ilastik for single-cell mammalian cell analysis. Concurrently, Deep learning has also been developing rapidly for solving precisely the same set of tasks that are required for the field of cellular image analysis. The model architectures that have been developed starting with AlexNet, LeNet, Inception, right upto Vision Transformers, EfficientNets have predominantly focused on achieving state-of-the-art performance on the ImageNet dataset. Researchers have tried implementing Transfer Learning techniques to use these excellent models on medical imaging datasets that has led to good results. To effectively engender the research of Deep learning techniques for this field, both the quality and quantity of annotated data is a crucial requirement and needs to be jointly developed alongwith new algorithms, which has been referred to in this article as Software 2.0.

To successfully apply Deep learning techniques to the domain of biomedical image analysis, following are the three primary requirements: Development of high-quality annotated training dataset, application of Deep learning techniques on this dataset, and the robust deployment of

the trained models on unseen data. Getting access to high-quality data or extracting data in the desired format oftentimes takes roughly the same time as required for developing and deploying the Deep learning models on that data and is hence a very important step. Generally, if the amount of training data available is limited (which normally is the scenario), techniques such as on-the-fly data augmentation, Transfer Learning have been successfully implemented. The data can also be manually generated by experts, through crowdsourcing and gamification. In short, an easy access to high quality data, specifically for this field, such as a 'Cellular ImageNet' would greatly help researchers develop robust systems by being able to focus more time on actually developing solutions than collecting the required data.

Python is the most popular programming language when it comes to implementing Deep learning models and existing open-source, constantly updated frameworks such as Tensorflow-Keras, PyTorch, MXNet, CNTK, Theano and Caffe are available for Python. All these frameworks construct computation graphs, automatically perform derivatives and efficiently harness the computing power of GPUs and Tensor Processing Units (TPUs). They also consist of common, required mathematical objects, algorithms which the users can directly use without having to develop them again from scratch. These frameworks also provide support for easy deployment of these models using well-documented APIs. With the use of containerization technologies like Docker, it is easier than ever before to reuse and adapt existing models to the desired tasks. Cloud computing has also played a major role in providing easy access to remote GPUs and production environments for researchers and developers to train, test and develop these models.

For biomedical image classification and image segmentation tasks, Transfer learning has played a major role in using existing state-of-the-art model architectures pre-trained on large datasets like ImageNet and adapting them for datasets in this domain, which are often available in limited quantity. Deep learning-based Image classifiers have been used to identify changes in cell state, to classify spatial patterns in fluorescence images, to determine protein localization, to sort cells based on image activations, and to isolate cells based on protein localization and inter-cell

interactions. Both semantic and instance segmentation tasks have been successfully solved for other domains using Deep learning-based techniques; but the latter proves to be challenging in the biomedical domain. Single-cell segmentation has been implemented using multiple ways: pixel-level classification with U-Net and DeepCell, by learning a distance transform and feeding it to a watershed transform, using Object detection-based methods such as Faster R-CNN, RetinaNet, and Mask R-CNN, using generative approaches and vector embeddings.

Object tracking is a challenging task in this domain, as objects can touch, disappear, merge, or split over a period. In object tracking, objects are represented as points and their centroids are used to track them. Techniques such as nearest-neighbor search, state-space models, and linear programming are used. Non-Deep learning-based software packages such as uTrack, CellProfiler, TrackMate have been successfully used for this task, but recently Deep learning-based approaches like DeepLabCut, LEAP, idtracker.ai have been also developed, but not yet been majorly adapted for cellular image analysis. The task of augmented microscopy to identify cellular nuclei within bright-field images was transformed to a traditional supervised learning problem. Researchers at the Allen Institute and Google have developed conditional generative models and pixel-based prediction techniques respectively. Deep learning has also been used to implement content-aware image denoising to improve image resolution and eliminate axial under sampling.

In this way, deep learning has been applied to the field of cellular image analysis and the authors encourage development of larger, publicly available datasets with curated metadata that will benefit researchers make use of them effectively. Tools like Tensorflow Hub, that provide ready-to-use deep learning models with pre-trained weights have been valuable. Innovative solutions like neural architecture search can be used to look for the best architectures for this domain. The authors end the article with a recommendation for both the data scientists and data curators to work together to better develop robust pipelines and models.