Deep Learning for Cellular Image Analysis - Paper Summary

Outline : This paper serves as a perfect kickstarter for anyone entering the domain of bio-medical applications of deep learning - image processing. It introduces terminology, architectural blocks of generic models, and builds onto talk about the most common issues faced while training these models and how to interpret and deal with each.It outlines all existing softwares and pre-trained models along with datasets available for multiple use cases and summarises the best working strategies in each case. It finally concludes on the steps required to build a strong open community to promote further research and accessibility to all researches across the globe.

Paper discusses **four major areas of study** :

- **Image Classification**
  Assigns a meaningful label to the overall image. Sample use cases : Running over a batch of images, classifying in which cases a specific protein is expressed in the cytoplasm or the nucleus based on the fluorescence. Or to identify changes in the cell state.

- **Image Segmentation**

  - **Semantic Segmentation** Partition into semantically meaningful parts and assign each part a class label - pixel - level annotation - "objectness" is not preserved. Two different adjacent nuclei might not be distinguishable. U-Net and DeepCell - make pixel level predictions
  - **Instance Segmentation** - Major focus Identify each instance. Single cell segmentation falls under this category and is one of its key applications. **Bounding Box Methods** - **Mask R-CNN** is the most accurate model, others include Faster R-CNN and Retinanet.
    Vector embedding approach - Discriminative loss function assigns pixels in the same object to the same vector and pixels of different objects to different vectors - works best even with overlapping objects.

- **Object Tracking - Object Detection & Object Linkage**
  Objects can be located and tracked across frames as points(centroid) using nearest neighbor searches, state-space models and linear programming.When that's not feasible, instance segmentation is performed on each frame. Linear programming helps with complex behaviors such as merging, disappearing and splitting.
  DeepLabCut shows impressive results even with less data by transfer-learning. Detecting plays a bigger role in tracking, improving detection should be our primary focus then linkage.

- **Augmented Microscopy** Extraction of latent features from biological images. Fluorescence images are used as ground truth and bright field images are used for prediction.

One of the major **road-blockers** in biological applications is the unavailability of large annotated data - Use of transfer learning, where a model pre-trained on a larger data set of images such as ImageNet is loaded, and by altering the last layer as per our use case, we can re-run on our small annotated data set to make decent predictions.

Addressing some commonly occurring pain-points -
Bias-Variance Trade-off & Model Capacity : Model capacity - Representational power of a deep learning model.Overfitting occurs when the model performs well on train but poorly on test data.Underfitting is when the model performs poorly on train data, unable to capture the variation with the training set. With high model capacity, performance is better on large datasets but prone to overfitting. With low model capacity, generalizes better but is prone to underfitting. With small datasets, overfitting is a major concern! To reduce Overfitting - Batch Normalization & dropout (either of these, not both to be used in the same model), Increasing the range of data augmentation, Pre-trained models & Use of models trained on **stochastic gradient descent with momentum** works best in terms of generalization.
Sources of Error - Improper image normalization, poor choice of learning rate, Dimension mismatch.
Class imbalance - Use of downsampling and upsampling or introduction of class weights.
Best evaluation metric of choice - Classification : Confusion matrix, Segmentation - pixel-level scores - Jaccard & Dice indices, Instance-level - precision, recall, and mean average precision Hyperparameter tuning - L2 Regularization, Talos (Keras) automates through grid search
Software Environments - Git - version control software & Docker - containerization tool that helps build reproducible programming environment are great tools
Future Scope: Since we are still in early stages in this domain, it is of great importance to improve the open accessibility and availability of curated datasets to ecourage open research community and cross learning across researchers. CellularImageNet should be open to public access.