Using transfer learning to classify breast cancer cells with fluorescence imaging

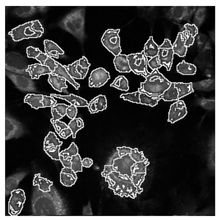
Zijie (Jay) Wang, Tiffany M Heaster, Quan Yin, Alex J Walsh, Melissa C Skala, Anthony Gitter

1 Introduction

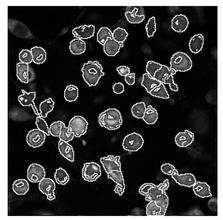
Tumor heterogeneity may have effects on cancer growth and therapy resistance. However, studying tumor heterogeneity by analyzing protein or gene expression levels over thousands of cells is very challenging. In this project, we instead use a transfer learning approach to classify cancer cell types solely based on fluorescence imaging.

2 Preparation

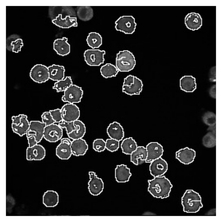
High resolution fluorescence images were made on two breast cancer cell lines MDA-MB-231 and SKBr3 being co-cultured in different proportions. We cropped out single cells and gave each individual cell a manual classification label. To avoid model selection bias, we only used about 60% of total images for training and evaluation of this model. The left 40% will be used to report the final performance.



100M:0S



50M:50S



0M:100S

Cropped MDA-MB-221 cell-line

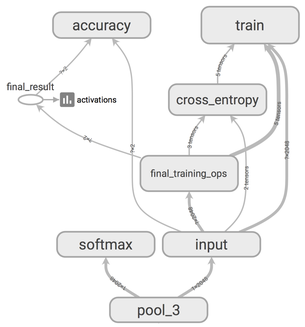
Cropped SKBr3 cell-line

	MDA-MB-221	SKBr3
Train + Validation	358	165
Test	147	90

3 Method

Due to the limited size of training data, we took advantage of a pre-trained deep neural network, Inception v3, which was trained and fined-tuned on 10 million natural images with over 400 categories. While freezing all previous layers, we only trained on the last layer.

Original Inception v3 graph



Train the last laver

We trained this model using Tensorflow on HTCondor without GPU support. It took about 20 minutes to train 4000 epoches. The model converged quickly and finished with 98%-100% accuracy on the training set and 88% accuracy on the validation set. However, the model performed poorly on the test dataset with 68% accuracy.

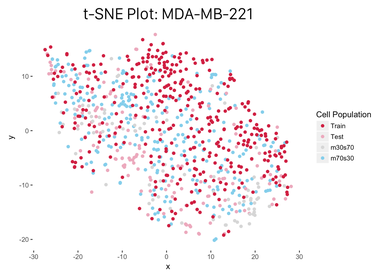
Truth \ Prediction	SKBr3 (-)	MDA-MB-221 (+)
SKBr3 (-)	27	55
MDA-MB-221 (+)	17	130

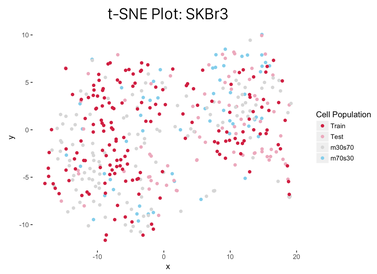
Confusion Matrix of Our Model Tested on 50M:50S

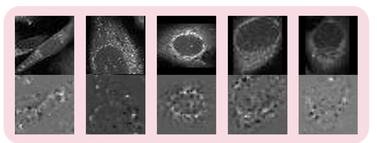
From the confusion matrix above, we found that the precision is about 70% and the recall is about 88%. Our model tends to predict MDA-MB-221 cell line. It might be caused by the disproportion of positive samples in the training set, but we also noticed that MDA-MB-221 outcompetes its counterpart in all co-cultured environments. There may also be morphological changes when the cells are co-cultured.

4 Diagnosis

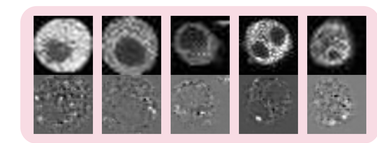
We first analyzed the features extracted by our model using T-distributed stochastic neighbor embedding (t-SNE) and saliency map.





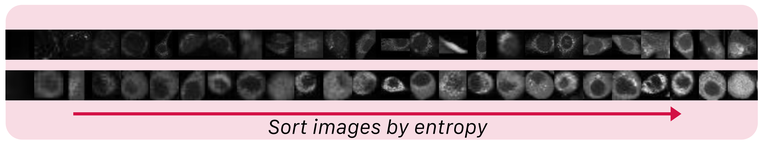


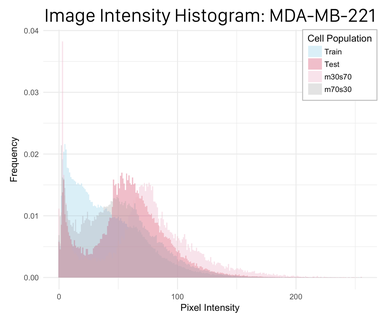
Saliency map of MDA-MB-221

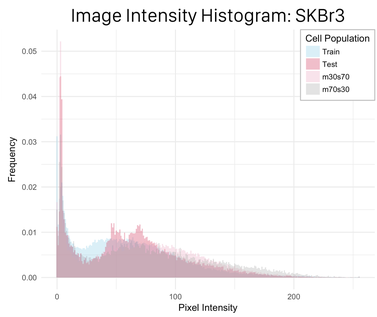


Saliency map of SKBr3

Then, we diagnosed the fluorescence images in a lower level with image entropy and intensity histogram.







5 Next Step

Based on the diagnosis, we will try to add weights based on image class and entropy in the model. We are also interested in computing the confidence score for individual predictions on the test set. Finally, we will test our model on other tumor dataset to examine its robustness.

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