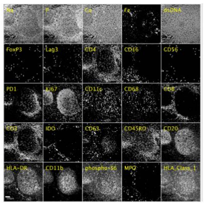
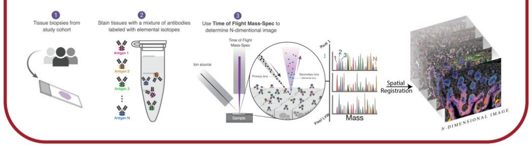
SuperMIBI: A convolutional neural network for prediction of upsampled mutliplexed imaging data from short acquisition times

Noah Greenwald and Erin McCaffrey
Computer Vision
Mentor: Shervine Amidi

Introduction



- Multiplexed Ion Beam Imaging (***MIBI, shown below***) is a novel imaging platform that allows biologists to image up to 40 proteins simultaneously in tissue[1]
- Images have far more channels than traditional RGB biological images (***shown left***).
- Increasing data acquisition increases quality, but at the cost of efficiency/time
- **Our Goal: Employ deep learning to upsample data collected at low scan times to higher quality, noise free MIBI images**



Data Description

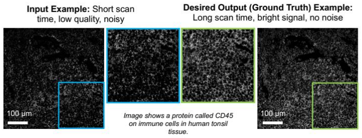
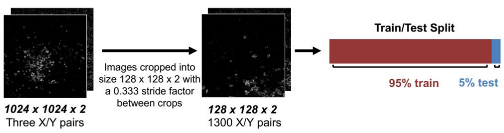


Image shows a protein called CD45 on immune cells in human tonsil tissue.

Data Overview

- Three x and y pairs, each with size 1024 x 1024 x 2
- Each channel with unique spatial distribution and dynamic range
- Data tends to be sparse with non-Gaussian distribution

Data Processing Workflow

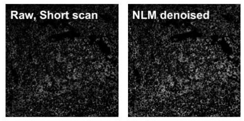


1300 X/Y pairs were produced by performing 128 x 128 crops on three 1024 x 1024 x 2 dimensional images. Only two channels were chosen in order to allow for quicker training and optimization of the model to the representative signal distribution of MIBI images.

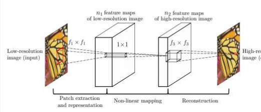
SuperMIBI Baseline & Network Architecture

Baseline: Non-local means denoising (NLM)

NLM denoising works by coloring pixels based on the signal of similar pixels[2]. Here we use the scikit-image fast-mode implementation of NLM denoising to act as a baseline to evaluate our model against qualitatively. It appears to modestly upsample data, but sufficiently reduce noise and smooth signal.



Super Resolution-CNN (SRCNN)[3]



Layer 1 $F_1(\mathbf{Y}) = \max(0, W_1 * \mathbf{Y} + B_1)$

Layer 2 $F_2(\mathbf{Y}) = \max(0, W_2 * F_1(\mathbf{Y}) + B_2)$

Layer 3 $F(\mathbf{Y}) = W_3 * F_2(\mathbf{Y}) + B_3.$

Super MIBI

SuperMIBI is built around the SRCNN architecture.

1. **Layer 1:** 128 filters of size 11 x 11, 'same' padding, stride of 1, batch norm, and ReLU activation
2. **Layer 2**: 64 filters of size 1 x 1, 'same' padding, stride of 1, batch norm, and ReLU activation
3. **Layer 3:** # filters = # input channels of size 5 x 5, stride of 1, batch norm, and ReLU activation

Implemented with Keras and Tensrorflow

Hyperparameter Tuning and Model Training

Loss: Mean-squared Error

$$L(\Theta) = \frac{1}{n}\sum_{i=1}^{n} ||F(\mathbf{Y}_i;\Theta) - \mathbf{X}_i||^2,$$

Parameter Initialization
Xavier

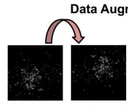
Filter number and sizes

- SRCNN uses a 9-1-5 structure for filter sizes across layers
- **Performance for SuperMIBI improved by increasing filter # to 11-1-5**
- Basic SRCNN uses 64 and 32 filters in layers 1 and 2, respectively
- **Performance for SuperMIBI improved by using 128 and 64 filters for layers 1 and 2, respectively**

Data Normalization

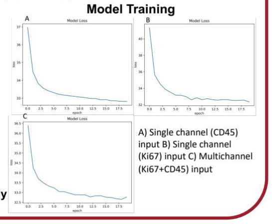
- $X_{norm} = X - \mu / \sigma$
- Performed on a per channel basis
- **Improved model performance significantly**

Data Augmentation



Images were flipped 180° between epochs using the Keras ImageDataGenerator[4]

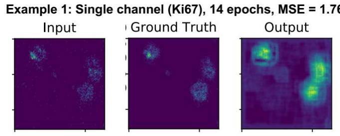
Model Training



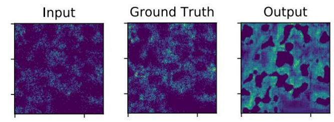
A) Single channel (CD45) input B) Single channel (Ki67) input C) Multichannel (Ki67+CD45) input

Results

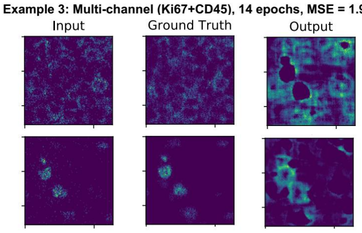
Example 1: Single channel (Ki67), 14 epochs, MSE = 1.76



Example 2: Single channel (CD45), 14 epochs, MSE = 2.63



Example 3: Multi-channel (Ki67+CD45), 14 epochs, MSE = 1.96



Discussion and Future Directions

- Normalizing the data set resulted in improved performance of the model.
- Larger filters better capture global features, but decrease the spatial accuracy of the predicted output, while smaller filter sizes result in upsampled noise, but better preservation of granular features.
- More training data and utilizing additional image channels may improve training.
- More complex architecture, such as those in the CARE-CNN[5] may improve network performance.

References and Acknowledgements

1. Keren, Leeat, et al. "A structured tumor-immune microenvironment in triple negative breast cancer revealed by multiplexed ion beam imaging." *Cell* 174.6 (2018): 1373-1387.
2. Buades, Antoni, Bartomeu Coll, and J-M. Morel. "A non-local algorithm for image denoising." *2005 IEEE Computer Society Conference on Computer Vision and Pattern Recognition (CVPR'05)*. Vol. 2. IEEE, 2005.
3. Dong, Chao, et al. "Learning a deep convolutional network for image super-resolution." *European conference on computer vision*. Springer, Cham, 2014.
4. https://keras.io/preprocessing/image/
5. Weigert, Martin, et al. "Content-aware image restoration: pushing the limits of fluorescence microscopy." *Nature methods* 15.12 (2018): 1090.

We would like to thank our mentor Shervine Amidi for all his help! Also the CS230 instructors, Andrew Ng and Kian Katanforoosh for a great course.