FINAL PROJECT – PROGRESS DRAFT

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Topic: Find the nuclei in divergent images to advance medical discovery

Abstract

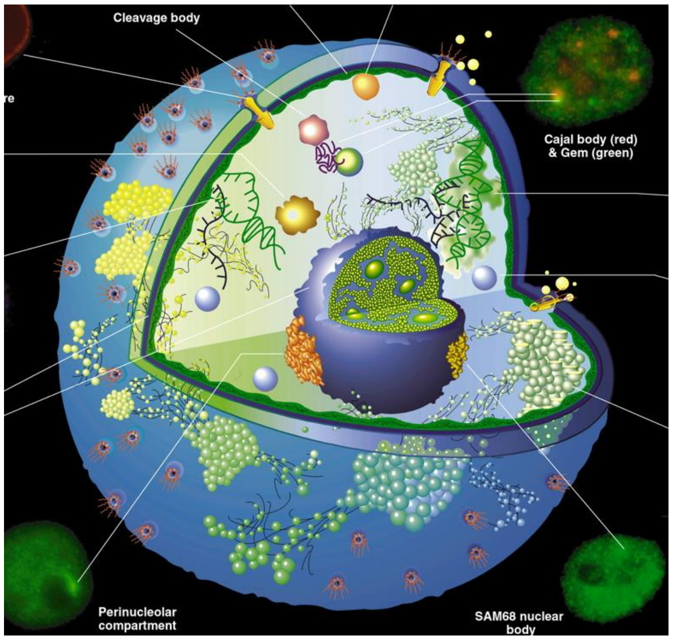
The idea of this project is to spot nuclei to speed up curing process for every disease. The aim is to create an algorithm to automate nucleus detection. The detection of nucleus is the first stage for most analyses as most of the human body's 30 trillion cells contain a nucleus full of DNA, the genetic code that programs each cell. Identifying nuclei allows researchers to identify each individual cell in a sample, and by measuring how cells react to various treatments, the researcher can understand the underlying biological processes at work.

Steps in medical diagnosis

1. Locate cells in varied conditions by spotting nuclei
2. Develop drugs
3. Improve health and quality of life

Cell and nucleus

The nucleus is a highly specialized organelle that serves as the information processing and administrative center of the cell. This organelle has two major functions: it stores the cell's hereditary material, or DNA, and it coordinates the cell's activities, which include growth, intermediary metabolism, protein synthesis, and reproduction (cell division).



Data

Data source: https://www.kaggle.com/c/data-science-bowl-2018/data

The dataset contains many segmented nuclei images. Images were acquired under a variety of conditions and vary in the cell type, magnification and imaging modality. The dataset is split into train and test images. There are 670 train samples and around 4000 test samples. This dataset split shows there are more test samples than train ones.

Exploratory Data Analysis

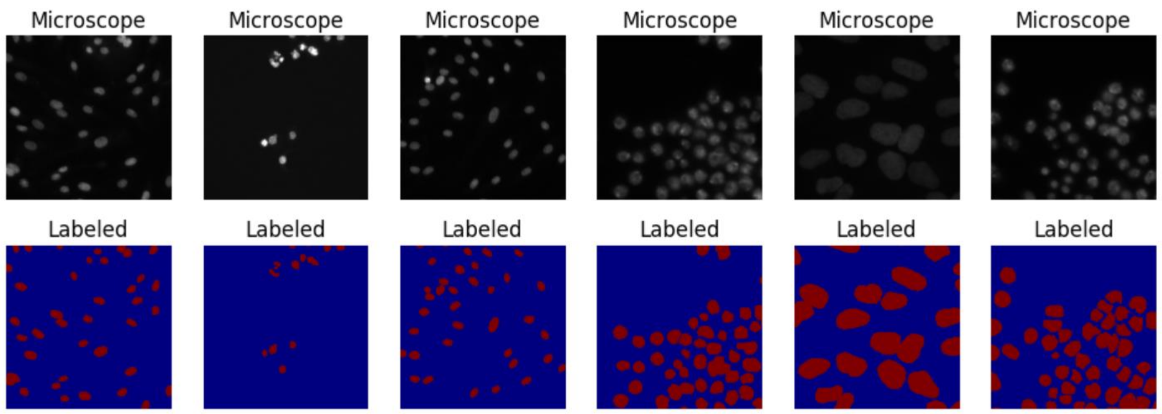
Displayed below are the image id's in stage 1 train folder. The train image id's with the label's encoded pixels are displayed in a tabular format. Nuclei are depicted as encoded pixel values. Each image in the train set has 40 masks on an average which brings the total count of train image size of around 30,000.

	ImageId	EncodedPixels
18480	a022908f1b7880838dbc0411e50828e64b4f5e0263afdf...	[52841, 7, 53094, 11, 53349, 13, 53604, 14, 53...
19560	a65bbfc5673e8053b6ce49f39c79cf3a846fe5cc46dd93...	[63093, 9, 63609, 16, 64127, 20, 64646, 23, 65...
15212	7b5987a24dd57325e82812371b3f4df7edc528e0526754...	[27915, 6, 28169, 9, 28424, 12, 28679, 14, 289...

The images are accessed by splitting the path using slash \ for train and test.

	path	ImageId	ImageType	TrainingSplit	Stage
22502	D:/Kaggle/Nuclei/input\stage1_train\b98681c748...	b98681c74842c4058bd2f88b06063731c26a90da083b1e...	masks	train	stage1
27649	D:/Kaggle/Nuclei/input\stage1_train\e7a3a7c994...	e7a3a7c99483c243742b6cfa74e81cd48f126dcef00401...	masks	train	stage1

The images from microscope and the labeled masks are shown in the following figure:



The following are some statistics describing mask counts, minimum nuclei size, maximum nuclei size, mean nuclei size and standard deviation of nuclei size

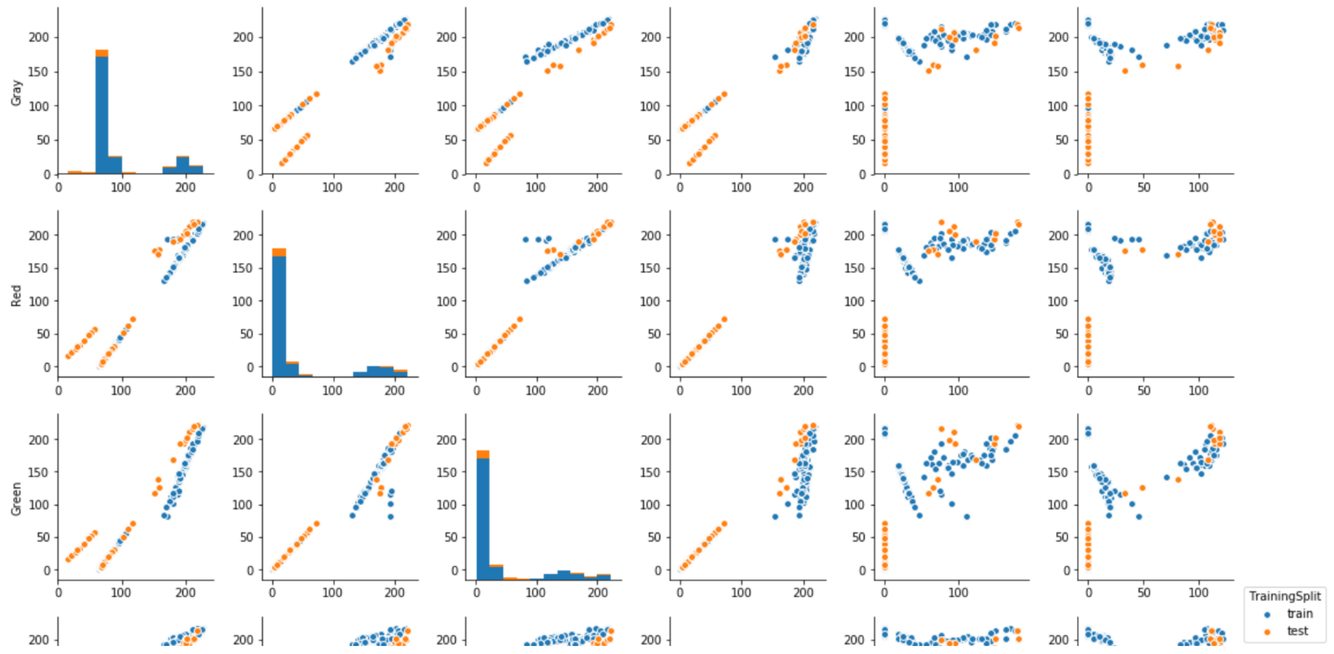
	mask_counts	nuclei_size_min	nuclei_size_max	nuclei_size_mean	nuclei_size_std
count	670.000000	670.000000	670.000000	670.000000	670.000000
mean	43.971642	69.270149	1243.029851	560.483462	306.627435
std	47.962530	197.402043	1346.599675	634.752932	359.936976
min	1.000000	21.000000	26.000000	26.000000	0.000000
25%	15.250000	24.000000	287.250000	150.521825	65.940617
50%	27.000000	33.000000	634.500000	265.434343	148.111038
75%	54.000000	63.000000	1733.000000	674.434370	394.974610
max	375.000000	4367.000000	11037.000000	7244.071429	1965.426189

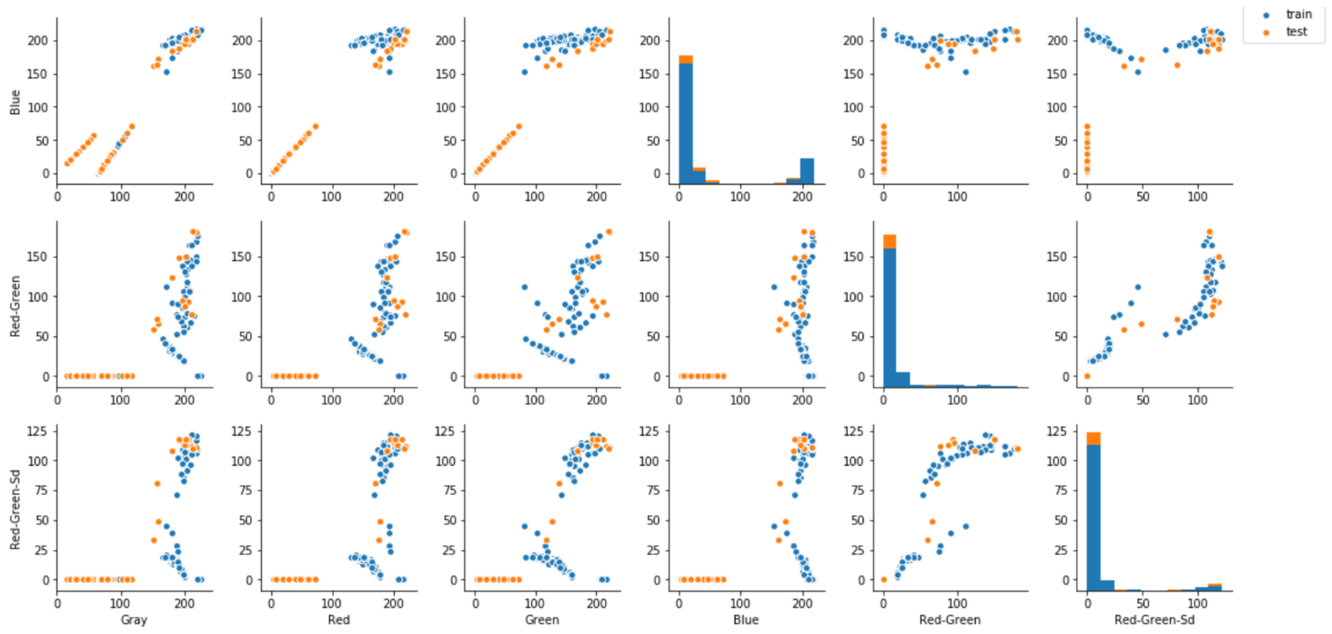
The following is the value counts of images in train set. This analysis shows that 50% of the images have 256, 256 size and rest 50% have different sizes. Images must be resized for further steps.

```
[11]: train_img_df['images'].map(lambda x: x.shape).value_counts()
```

```
:[11]: (256, 256, 3)      334
       (256, 320, 3)      112
       (520, 696, 3)       92
       (360, 360, 3)       91
       (1024, 1024, 3)     16
       (512, 640, 3)       13
       (603, 1272, 3)       6
       (260, 347, 3)        5
       (1040, 1388, 3)      1
       Name: images, dtype: int64
```

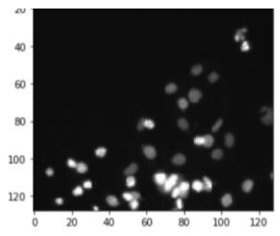
I used pair plots to observe the intensity of train and test images and also to identify different color groups in the dataset. This shows the color intensity for train and test are different and images are predominantly red, green, gray and blue.



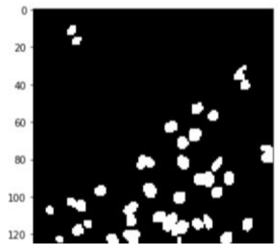


Train image and mask after resizing

The last step of data preprocessing is image resizing. I used skimage's resize to resize train and test images and masks.



IMAGE



MASK

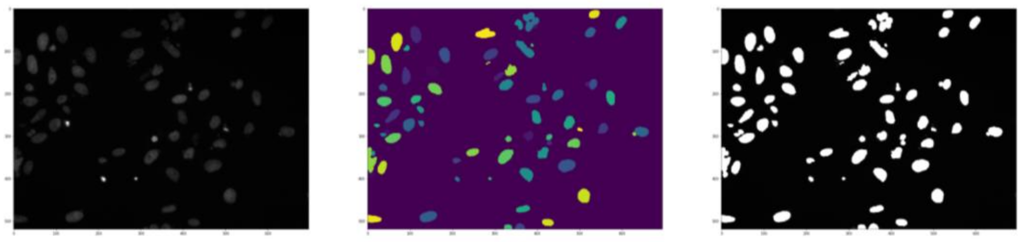
Image Segmentation

The technology of image segmentation is widely used in medical image processing, face recognition pedestrian detection, etc. The current image segmentation techniques include region-based segmentation, edge detection segmentation, segmentation based on clustering, segmentation based on weakly-supervised learning in CNN, etc.

Segmentation has two objectives. The first objective is to decompose the image into parts for further analysis. In simple cases, the environment might be well enough controlled so that the segmentation process reliably extracts only the parts that need to be analyzed further. For example, in the chapter on color, an algorithm was presented for segmenting a human face from a color video image. The segmentation is reliable, provided that the person's clothing or room background does not have the same color components as a human face.

The second objective of segmentation is to perform a change of representation. The pixels of the image must be organized into higher-level units that are either more meaningful or more efficient for further analysis (or both). A critical issue is whether or not segmentation can be performed for many different domains using general bottom-up methods that do not use any special domain knowledge.

Sample Image Segmentation

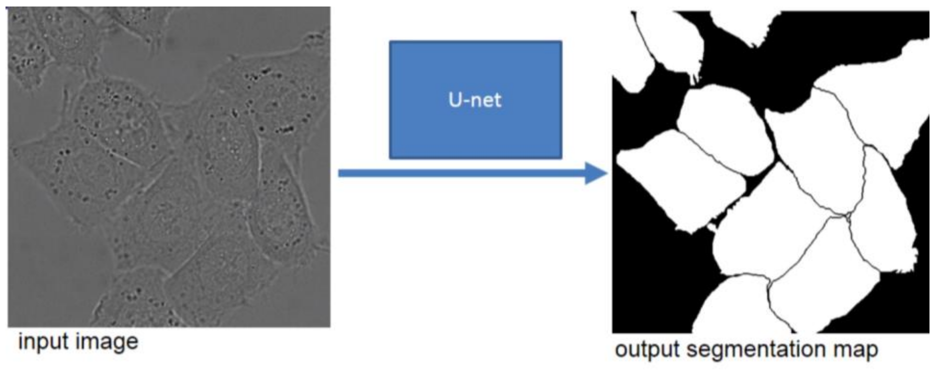


Suggested models

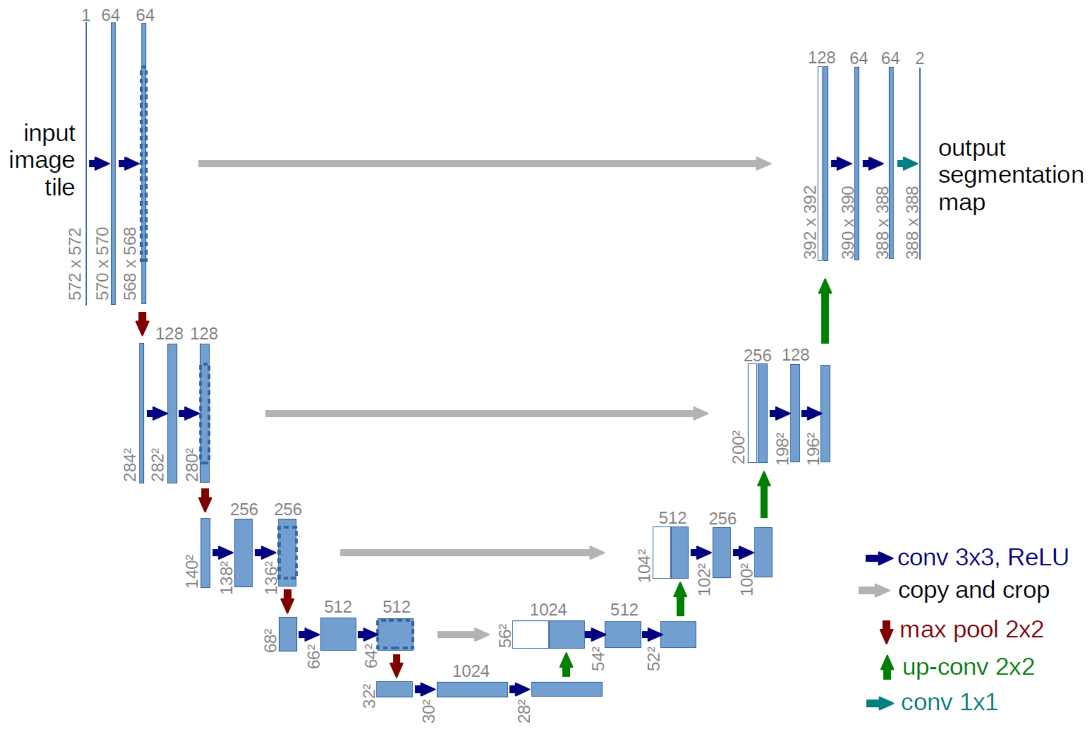
1. U-Net: CNN - for faster image segmentation

U-Net implementation is proposed by Ronneberger et al. developed along with tensorflow. The code has been developed and used for Radio Frequency Interference mitigation using deep convolutional neural networks. The network can be trained to perform image segmentation on arbitrary imaging data. The model starts with blocks of convolution layers and max pooling layers followed by deconvolution layers and recreating the image step by step. The output is similar to input image size with segmented or labeled masks.

Input image and Output image in U-Net



U-NET ARCHITECTURE



U-Net: Convolution layers

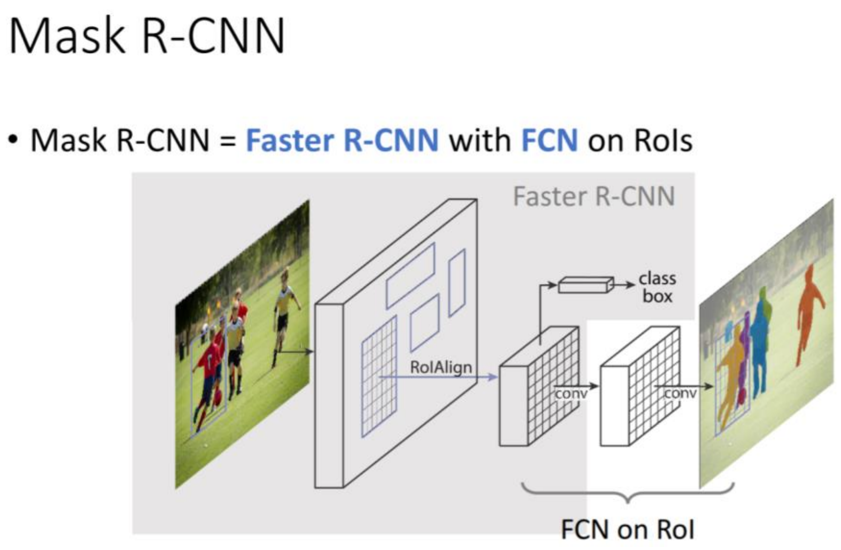
These layers convolve through the image and get a detail observation of the image. The model can be made more detail by increasing the convolution layers. I used 12 layers of convolution and few maxpooling layers to consider maximum values and to reduce architecture size.

U-Net: Deconvolution layers

These layers are generated by using conv transpose function in tensorflow which performs the reverse of convolution. The output is generated by gradually recreating the image using convolution layers used previously.

2. Mask RCNN

Mask R-CNN extends Faster R-CNN by adding a branch for predicting an object mask in parallel with the existing branch for bounding box recognition. Mask R-CNN is simple to train and adds only a small overhead to Faster R-CNN, running at 5 fps. Moreover, Mask R-CNN is easy to generalize to other tasks, e.g., allowing us to estimate human poses in the same framework. When run without modifications on the original Faster R-CNN architecture, the Mask R-CNN authors realized that the regions of the feature map selected by RoIPool were slightly misaligned from the regions of the original image. Since image segmentation requires pixel level specificity, unlike bounding boxes, this naturally led to inaccuracies.



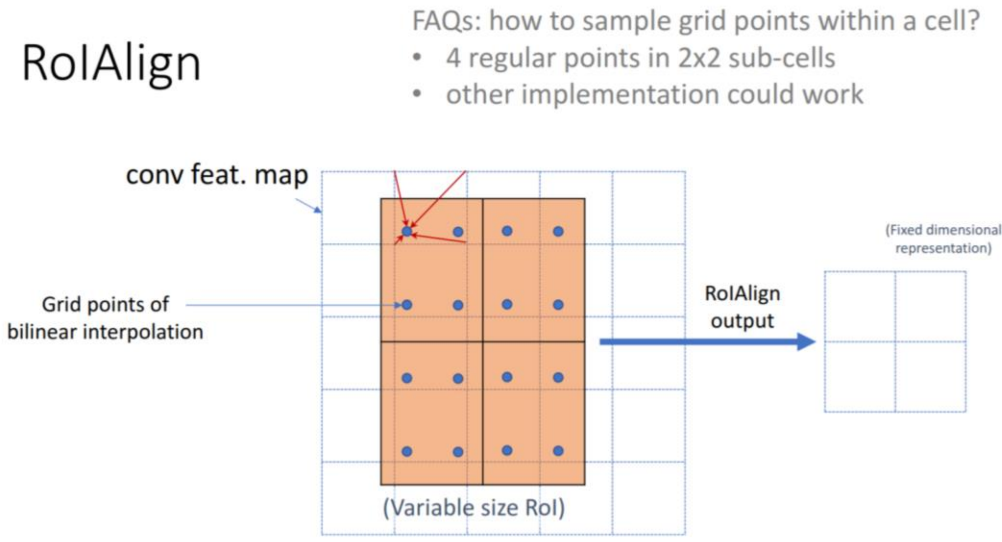
Faster R-CNN

Faster R-CNN has two networks: region proposal network (RPN) for generating region proposals and a network using these proposals to detect objects. The main different here with Fast R-CNN is that the later uses selective search to generate region proposals. The time cost of generating region proposals is much smaller in RPN than selective search, when RPN shares the most computation with the image segmentation network.

FCN – Fully convolutional network

Convolutional networks are powerful visual models that yield hierarchies of features. We show that convolutional networks by themselves, trained end-to-end, pixels-to-pixels, exceed the state-of-the-art in semantic segmentation. Fully convolutional networks take input of arbitrary size and produce correspondingly-sized output with efficient inference and learning.

ROI (Region of interest) Align

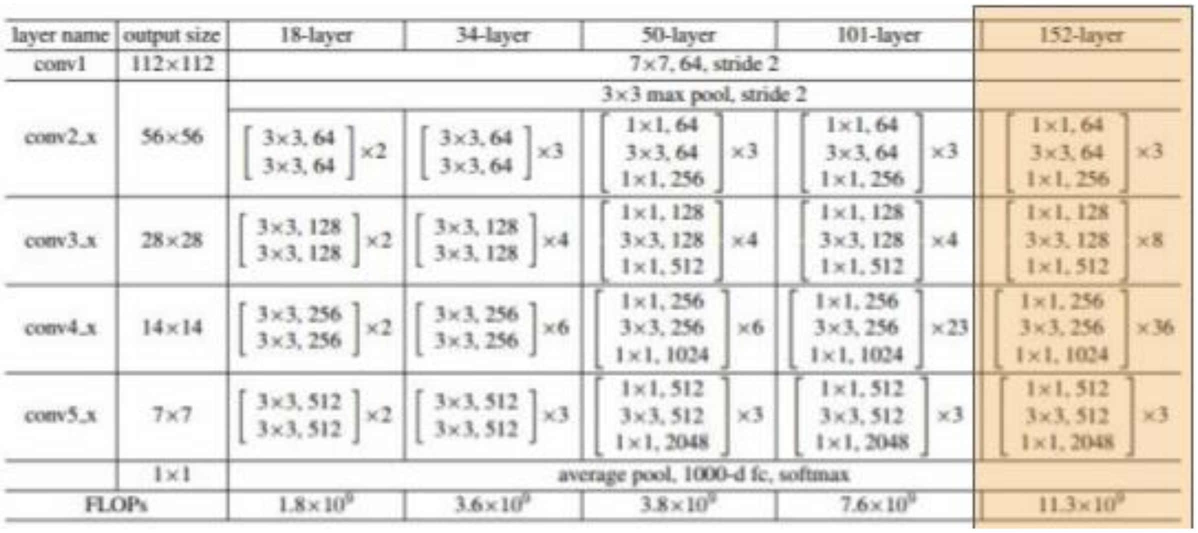

RoIAlign
FAQs: how to sample grid points within a cell?
• 4 regular points in 2x2 sub-cells
• other implementation could work
conv feat. map
Grid points of bilinear interpolation
RoIAlign output
(Fixed dimensional representation)
(Variable size RoI)

A region of interest (often abbreviated ROI), are samples within a data set identified for a purpose. The concept of a ROI is commonly used in many application areas. For example, in medical imaging, the boundaries of a tumor may be defined on an image or in a volume, for the purpose of measuring its size

3. Resnet – 101

Deeper neural networks are more difficult to train. A residual learning framework to ease the training of networks that are substantially deeper than those used previously. The layers are reformulated as learning residual functions with reference to the layer inputs, instead of learning unreferenced functions. On the ImageNet dataset evaluate residual nets with a depth of up to 152 layers---8x deeper than VGG nets but still having lower complexity. An ensemble of these residual nets achieves 3.57% error on the ImageNet test. The depth of representations is of central importance for many visual recognition tasks. Solely due to our extremely deep representations, we obtain a 28% relative improvement on the COCO object detection dataset.

RESNET ARCHITECTURE



layer name	output size	18-layer	34-layer	50-layer	101-layer	152-layer
conv1	112×112	7×7, 64, stride 2				
conv2_x	56×56	3×3 max pool, stride 2				
		[3×3, 64; 3×3, 64] ×2	[3×3, 64; 3×3, 64] ×3	[1×1, 64; 3×3, 64; 1×1, 256] ×3	[1×1, 64; 3×3, 64; 1×1, 256] ×3	[1×1, 64; 3×3, 64; 1×1, 256] ×3
conv3_x	28×28	[3×3, 128; 3×3, 128] ×2	[3×3, 128; 3×3, 128] ×4	[1×1, 128; 3×3, 128; 1×1, 512] ×4	[1×1, 128; 3×3, 128; 1×1, 512] ×4	[1×1, 128; 3×3, 128; 1×1, 512] ×8
conv4_x	14×14	[3×3, 256; 3×3, 256] ×2	[3×3, 256; 3×3, 256] ×6	[1×1, 256; 3×3, 256; 1×1, 1024] ×6	[1×1, 256; 3×3, 256; 1×1, 1024] ×23	[1×1, 256; 3×3, 256; 1×1, 1024] ×36
conv5_x	7×7	[3×3, 512; 3×3, 512] ×2	[3×3, 512; 3×3, 512] ×3	[1×1, 512; 3×3, 512; 1×1, 2048] ×3	[1×1, 512; 3×3, 512; 1×1, 2048] ×3	[1×1, 512; 3×3, 512; 1×1, 2048] ×3
	1×1	average pool, 1000-d fc, softmax				
FLOPs		1.8×10^9	3.6×10^9	3.8×10^9	7.6×10^9	11.3×10^9

Training steps

Metric - Intersection over union

Intersection over union IoU is a common metric for assessing performance in semantic segmentation tasks. In a sense, IoU is to segmentation what an F1 score is to classification. Both are non-differentiable, and not normally optimized directly. Optimizing cross entropy loss is a common proxy for these scores, that usually leads to decent performance, provided everything else has been setup correctly, e.g regularization, stopping training at an appropriate time.

$$I(X) = \sum_{v \in V} X_v \times Y_v$$

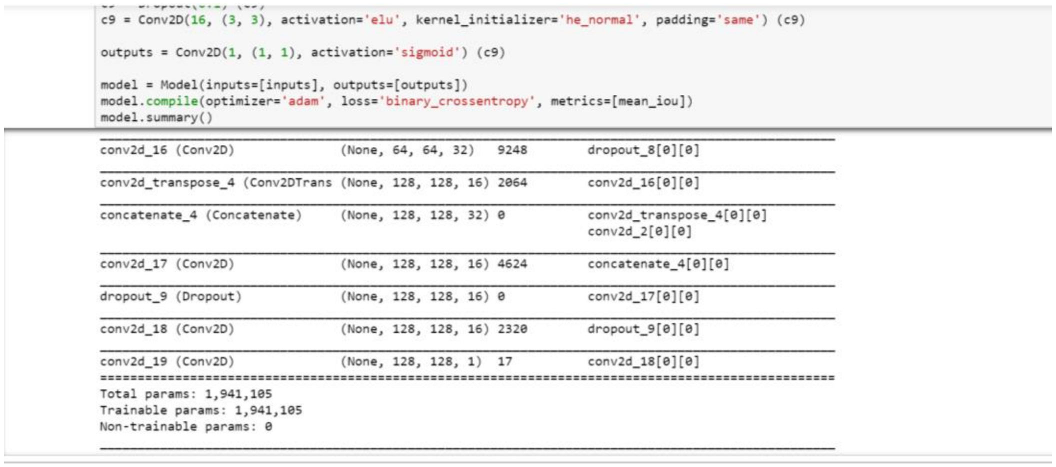
$$U(X) = \sum_{v \in V} X_v + Y_v - X_v \times Y_v$$

$$IoU = \frac{I(X)}{U(X)}$$

$$loss = 1.0 - IoU$$

U-Net efficiency

By far, U-Net has the best efficiency validation mIOU value 83%. I used 19 layers of convolution and 4 deconvolution layers to attain this efficiency.



```
c9 = Conv2D(16, (3, 3), activation='elu', kernel_initializer='he_normal', padding='same') (c9)

outputs = Conv2D(1, (1, 1), activation='sigmoid') (c9)

model = Model(inputs=[inputs], outputs=[outputs])
model.compile(optimizer='adam', loss='binary_crossentropy', metrics=[mean_iou])
model.summary()
```

```
________________________________________________________________________________
conv2d_16 (Conv2D)              (None, 64, 64, 32)   9248        dropout_8[0][0]
________________________________________________________________________________
conv2d_transpose_4 (Conv2DTrans (None, 128, 128, 16) 2064        conv2d_16[0][0]
________________________________________________________________________________
concatenate_4 (Concatenate)     (None, 128, 128, 32) 0           conv2d_transpose_4[0][0]
                                                                 conv2d_2[0][0]
________________________________________________________________________________
conv2d_17 (Conv2D)              (None, 128, 128, 16) 4624        concatenate_4[0][0]
________________________________________________________________________________
dropout_9 (Dropout)             (None, 128, 128, 16) 0           conv2d_17[0][0]
________________________________________________________________________________
conv2d_18 (Conv2D)              (None, 128, 128, 16) 2320        dropout_9[0][0]
________________________________________________________________________________
conv2d_19 (Conv2D)              (None, 128, 128, 1)  17          conv2d_18[0][0]
================================================================================
Total params: 1,941,105
Trainable params: 1,941,105
Non-trainable params: 0
________________________________________________________________________________
```

Conclusion

This project gave me an in-depth exposure of image segmentation. I tried out several architectures starting from CNN, FCN, U-Net, Mask RCNN, Resnet-101. I am learning the architectures and plugging in this model. It is a very good learning experience.

References

[1] http://kaiminghe.com/iccv17tutorial/maskrcnn_iccv2017_tutorial_kaiminghe.pdf

[2] https://github.com/KaimingHe/deep-residual-networks

[3] https://github.com/matterport/Mask_RCNN

[4] https://lmb.informatik.uni-freiburg.de/people/ronneber/u-net/

[5] https://github.com/shelhamer/fcn.berkeleyvision.org