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Udacity Machine Learning Nanodegree
Capstone Project Proposal

Find Nuclei in pathological images using CNNs

i. Domain Background

Accurate segmentation of nuclei has diagnostic significance in histopathological examinations.[1] At the moment, manual pathological examinations by humans serve as the gold standard for reliable morphological statistics in many clinical protocols. However, the manual segmentation and detection of nuclei structures is **expensive**, **error-prone**, and **time-consuming**. Therefore, automating nucleus detection and segmentation will improve the efficiency, reliability, and scalability of clinical analysis in different domains.

Existing work in the field can be classified into two categories: image processing methods and machine learning techniques.[2]–[5] Recent approaches in machine learning have focused on deep neural models. [6], [7] The most promising deep learning approach was proposed by Chen et al. in which they proposed a deep contour-aware network (DCAN) derived from an end-to-end fully convolution network (FCN) by fusing the complementary information of object appearances and contours.[8] The peculiar fact that finding nuclei in pathological images has a high impact on healthcare and is also an opportunity to learn more about image segmentations forms the basis of my attraction to the challenge.

ii. Problem Statement

Development of an algorithm for segmenting nuclei in pathological images continues to pose interesting challenges. One should prioritize computing the correct number of objects rather than morphological accuracy since improved morphological accuracy can be achieved with a refinement step or additional post-processing. This is a quantifiable problem and can be formulated by coordinates set of pixels inside a specific region of the image. To measure this problem, the mean average precision (mAP) is the standard for object detection and image segmentation which can be easily applied here. Furthermore, the problem is replicable in various domains such as medical image analysis and biology research labs.

iii. Datasets and Inputs

The dataset contains 670 training images and 65 testing images of microscopic images of varying size showing ensembles of cells and their nuclei. For the training images the nuclei are segmented by humans such that we know their number and location within each image. The dataset is provided by Booz Allen Hamilton's *2018 Data Science Bowl: Find the nuclei in divergent images to advance medical discovery* challenge under Creative Commons license.[9] The images were acquired under a variety of conditions and vary in the cell type, magnification, and imaging modality (brightfield vs. fluorescence). The dataset is designed to challenge an algorithm's ability to generalize across these variations.

Each image is represented by an associated Image Id. Files belonging to an image are contained in a folder with this Image Id. Within this folder are two subfolders of images and masks, contains the segmented masks of each nucleus. Each mask contains one nucleus. Masks are not allowed to overlap (no pixel belongs to two masks).

iv. Solution Statement

A possible solution is a U-Net neural network consisting of several convolutional and max-pooling layers. The algorithm uses TensorFlow as its backend and Keras as the framework. The input of the network are images of quantifiable shape (height, width, channels) while the output are corresponding binary masks of shape (height, width, 1).[10] The performance of an algorithm is measured on the mean average precision at different intersection over union (IoU) thresholds. The algorithm is replicable, and the trained network will be saved and is reusable.

v. Benchmark Model

There is one benchmark model that the solution may be compared to; Chen et al. proposed FCN methods with mAP of 74% in which a deep contour-aware network (DCAN) derived from an end-to-end fully convolution network (FCN) by fusing the complementary information of object appearances and contours as shown in Figure1 below.[8] Chen et al provide an appropriate benchmark model, given the benchmark is within the same domain of deep learning so is the solution, moreover it uses the same evaluation metric of mAP in object instance segmentation of histology images, thus easily comparable to the solution.

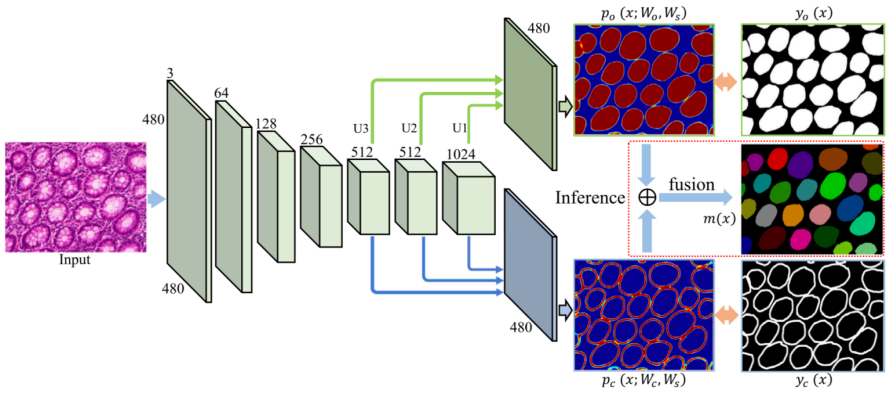

Fig. 5. The overview of the proposed deep contour-aware network. (For interpretation of the references to color in this figure, the reader is referred to the web version of this article).

Figure1: Chen et al DCAN model.[8]

vi. Evaluation Metrics

This project will be evaluated on the mean average precision at different intersection over union (IoU) thresholds as proposed by Booz Allen Hamilton's *2018 Data Science Bowl: Find the nuclei in divergent images to advance medical discovery* challenge. The IoU of a proposed set of object pixels and a set of true object pixels is calculated as:

$$\text{IoU}(A,B)=\frac{A\cap B}{A\cup B}$$

The metric sweeps over a range of IoU thresholds, at each point calculating an average precision value. The threshold values range from 0.5 to 0.95 with a step size of 0.05. In other words, at a threshold of 0.5, a predicted object is considered a "hit" if its intersection over union with a ground truth object is greater than 0.5. At each threshold value t, a precision value is calculated based on the number of true positives (TP), false negatives (FN), and false positives (FP) resulting from comparing the predicted object to all ground truth objects:

$$\frac{\text{TP(t)}}{\text{TP(t)}+\text{FP(t)}+\text{FN(t)}}$$

A true positive is counted when a single predicted object matches a ground truth object with an IoU above the threshold. A false positive indicates a predicted object had no associated ground truth object. A false negative indicates a ground truth object had no associated predicted object. The average precision of a single image is then calculated as the mean of the above precision values at each IoU threshold:

$$\frac{1}{|\text{thresholds}|}\sum\frac{\text{TP(t)}}{\text{TP(t)}+\text{FP(t)}+\text{FN(t)}}$$

Lastly, the score returned by the competition metric is the mean taken over the individual average precisions of each image in the test dataset.

vii. Project Design

The goal is to find the correct number and location of all nuclei shown in the test images. For the task we implement a deep neural network of the U-Net type consisting of several convolutional and max-pooling layers. Prior to training the network we resize, normalize and transform the images. I may use 10% of the training data for validation. Furthermore, I may implement data augmentation by making use of translations, rotations, horizontal/vertical flipping and zoom. Choosing an image size of 256x256 pixels the network and roughly 10 training epochs before the training is expected to converge. Some score discrepancies between training/testing data should be expected and can be explained by overlapping/touching nuclei that are identified as a single nucleus by the current implementation. Furthermore, there will be a lot of room for improvement by using the hyperparameters

The network uses TensorFlow backend and Keras framework. The input of the network are images of shape (height, width, channels) while the output are corresponding binary masks of shape (height, width, 1). The pseudocode of the network:

```
# Build U-Net model
inputs = Input((HEIGHT, WIDTH,CHANNELS))
s = Lambda(lambda x: x / 255) (inputs)

c1 = Conv2D(16, (3, 3), activation='elu', kernel_initializer='he_normal', padding='same') (s)
c1 = Dropout(0.1) (c1)
c1 = Conv2D(16, (3, 3), activation='elu', kernel_initializer='he_normal', padding='same') (c1)
p1 = MaxPooling2D((2, 2)) (c1)
.
.
.
u9 = Conv2DTranspose(16, (2, 2), strides=(2, 2), padding='same') (c8)
u9 = concatenate([u9, c1], axis=3)
c9 = Conv2D(16, (3, 3), activation='elu', kernel_initializer='he_normal', padding='same') (u9)
c9 = Dropout(0.1) (c9)
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(metrics=[mean_iou])
model.summary()


#Fit model
Stopper = EarlyStopping()
Checkpointer = ModelCheckpoint()
Results = model.fit (X, Y, validation_split=0.1, batch_size, epochs=10, callbacks)
#predictions
.
.
.
#sanity checks on random images
```

References

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