CAMELYON17 CHALLENGE: SUBMISSION 3

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ABSTRACT

Grading whole slide images (WSIs) is an important task in digital pathology for treatment planning but it suffers from subjectivity and limited reproducibility. The grading of WSIs is also time consuming and therefore expensive. Designing a robust and automatic solution for decision support is a game changer. We propose a fully automatic pipeline from a set of patient whole slide images to pathologic N-stage prediction. Our approach consists of two steps: i) Segmentation of metastasis in whole slide images, ii) pathologic N-stage predictions from segmentations.

***Index Terms*—** segmentation, FCN, metastasis, breast lymph nodes.

0. UPDATES FROM SUBMISSION 1

This document is a copy of the submission 1 article except for this section. In this section the changes made from submission 1 to submission 3 are presented.

- To reduce the risk of overfitting the final pN-stage prediction has been changed to not include any learning algorithm. Its now only based on the length of the major axis for the largest segmented object. This final step now relies fully on the segmentation model and is as a result very close to the pathologist procedure.
- We have extended the training dataset to include the slides from CAMELYON16 Test set.
- The sampling of patches from the slides have been changed. We introduce a max limit per slide for each class. This way we can make sure there is no bias to slides with large tumors.
- Our mining strategy is now to introduce hard samples from a pre-trained network when training a new network from scratch.
- The number of weights in the network has been increased to approx 40000 weights.

1. INTRODUCTION

This work is focused on the prediction of pN-stage for breast cancer patients. The pN-stage assesment is based on the combined metastatic involvement of several lymph nodes and is one of the most important factors in deciding treatment of breast cancer. Common practice in current clinical settings is to assess metastatic involvement of the each lymph node specimen manually under a microscope. Although this task is routinely performed there is room for improvement since this procedure is highly subjective in nature and the task is difficult and time consuming.

The drawbacks of the current manual practice has created interest in automatic assessment of whole slide images for decision support. Automatic methods aim at reducing the subjectivity of current practices and limiting the time for slide assessment. Recent advances using machine learning methods such as convolutional neural networks for image analysis obtained excellent results for the analysis of histological slides [1][2]. The success and development of machine learning algorithms are largely driven by the availability and quality of annotated data. Due to the increased interest in the field several challenges such as TUPAC, AMIDA and CAMELYON [3, 4, 2] have been created in order to push forward scientific research in the field by providing annotated data.

Automatically assessing whole slide images has several challenging aspects. The nature of the task requires information about the specimen on cellular level, this leads to very high resolution i.e. very large images. Assessing the slide requires attention to image structures of approximately 10^4 pixels (a 100×100 pixel neighborhood) within large WSIs containing 10^{10} pixels. Future challenges include solving the subjectivity of annotations and variations in specimen staining (due to different practices regarding staining and slide preparation).

Recent results of previous challenges were focused on performing in slide predictions such as the detection of mitotic figures or segmentation of tumors. Although the state-of-the-art for these tasks is approaching and even surpassing [2] human-level performance these results have not been focused on the task of patient level assessment.

In the CAMELYON17 challenge the objective is to make a patient level prediction based on information from several

whole slide images.

Our proposed solution to the CAMELYON17 challenge is two fold. First we utilize previous data from CAMELYON16 to train a fully convolutional network segmentation model. This is followed by a gradient tree boosting model with features from the segmentation of the whole slides to predict the final pN-stages for each patient. We propose a new network architecture with few parameters and much lower computation time without compromising accuracy.

2. DATA

In this section we will present the data available and how it was used during the development of this model.

2.1. Available data

Two sources of data have been utilized during training of the model, the data from CAMELYON16 and CAMELYON17. The CAMELYON16 dataset was originally used in the 2016 edition of the Camelyon competition with the objective to detect and localize tumors in the whole slide images. The CAMELYON17 dataset was created for use in the 2017 edition of the Camelyon competition.

The CAMELYON16 dataset contains whole slide images with corresponding annotations of metastatic areas. A small subset of the data has not been exhaustively annotated.

The CAMELYON17 dataset contains whole slide images categorized by patient and clinical center. The annotations available are patient pN-stage and the largest tumor class for each slide. Additional annotations of metastatic areas are available for a subset of the data from each clinical center. The metastatic area annotations are of the same type as from the CAMELYON16 dataset.

2.2. Training data

The data used in training the segmentation model is mainly from the CAMELYON16 dataset with the addition of the subset of data from the centers in CAMELYON17 with annotation of the metastatic areas. The subset of the data that was not exhaustively annotated was not used in the training of the segmentation model. All data feed to our segmentation model is preprocessed using stain normalization [5].

The pN-stage prediction model was developed using the full camelyon17 dataset.

3. METHOD

In this section we will present an outline of our proposed model and how it was trained.

3.1. Metastasis segmentation

The segmentation model follows a U-Net like architecture with some modifications, for detailed graph see Figure 1. To compensate for the relatively low data diversity the number of weights in the network has been significantly reduced to approximately 30000 weights. To reduce the noise introduced by zero padding in the network we only make use of valid convolutions. As a result the network output is smaller than the input and the data have been sampled accordingly to assure dense predictions on the whole slide.

Each slide is divided into smaller patches and the network is applied convolutionally over each patch. The sampling of the patches from the slides are controlled in order to make sure we have a distribution of 80% healthy tissue and 20% tumor tissue for each batch. This sampling method results in one source of data limiting the size of each epoch. The samples from the other sources are randomized for each new epoch.

After initial training to convergence the resulting model is used to mine hard negative and hard positive samples. The network training is continued with the 40% mined samples for each batch. This results in an oscillating number of samples for each mine since the network adapts to the new batch distributions. The procedure is repeated iteratively with intermittent training until the oscillation has been reduced.

3.2. pN-stage prediction

The resulting predictions from the segmentation model are stitched into full predictions for each slide. Features are extracted from the largest tumor object for each slide using scikit-image [6] regionprops. The average value of the extracted features per slide for each patient are feed into a gradient tree boosting model [7] to predict the patient level pN-stage. The model parameters are optimized using cross validation on the patient level pN-stage in the CAMELYON17 dataset.

4. REFERENCES

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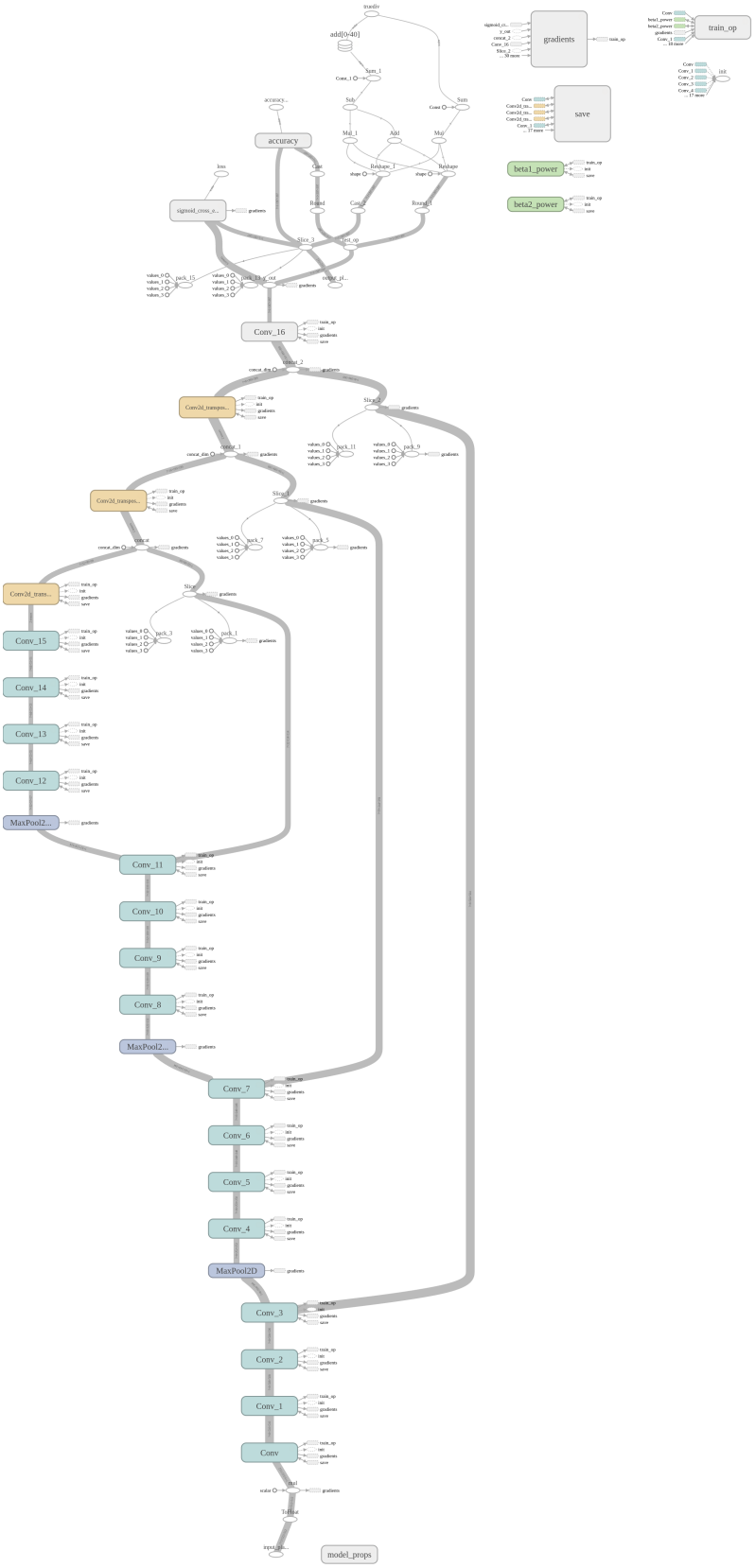

Fig. 1. The tensorflow model graph.