Pathology Images Classification - Project Proposal

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1 Project Summary

Medical image analysis is used to diagnose and track diseases that cannot be seen by the naked eye. However, performing this analysis manually relies on a rigorous set of predefined benchmarks, to which expert judgment is applied. This analysis can be prone to errors in human judgment, as well as being extremely tedious to identify. Early methods include semi-quantitative and quantitative methods which may lead to huge plaque burden bias. They are also limited by their lack of stability and time-consuming.

Fortunately, deep learning methods, especially convolutional neural networks (CNNs), can achieve expert-level performance in image analysis. CNNs are easily capable of handling complex recognition tasks, and are able to learn patterns in visual data without the need for predefined benchmarks. They have been proved to be effective in lots of medical image analysis scenarios, including the diagnosis of skin and breast cancer. This project will focus on using CNNs for classification of Alzheimer's Disease (AD), which is often characterized by the hallmark proteins in brain tissue or specific biomarkers in whole slide image (WSI).

However, deep learning models have been doubted for their low interpretability and dependency on enormous annotated datasets. We recognize that these features pose considerable obstacles to the creation of viable neuropathology tools. Using deep learning introspection methods: Guided Grad-CAM and feature occlusion analysis , we will try to show that trained models learn relevant aspects of each of the classes, providing visual proof that the model is interpretable. Through this project, we hope to gain a greater understanding of the strengths and weaknesses of deep learning in this classification setting.

2 Project description

The connection between AD and cognitive difficulties has been recognized for a long time. Numerous efforts have been taken in order to make progress in AD diagnosis. Neuropathologists use hallmark proteins [1, 2] or biomarkers for disease recognition and classification. The existence and distribution of these proteins are the basis of the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) schemes. For neuropathologic diagnosis, early methods include semi-quantitative[3] and quantitative methods. On one hand, the standard semi-quantitative method assesses beta-amyloid burden through the highest density of neocortical neuritic plaques, which fails to include the diffuse plaque and may lead to over 50% of plaque burden bias. On the other hand, the quantitative methods, such as positive pixel count algorithm [4] and manual counts methods [5] are limited by their lack of stability or time-consuming nature.

Over the past decades, neuroimaging data have been introduced to disease diagnosis. A variety of studies have been proposed to integrate WSI processing pipelines with machine learning algorithms. In addition to conventional machine learning methods, such as support vector machines and random forests, deep learning methods have recently gained attention in digital biomedical image processing. For example, deep learning methods have been used in neuropathology to classify pathophysiology in magnetic resonance and positron-emission tomography images [6, 7]. Medical image analysis has been changed by deep learning [8, 9]. Expert-level performance has been attained by CNNs in complicated visual identification tasks [10, 11]. Harshita Sharma et al. [12] applied deep neural networks for classification in WSI of gastric carcinoma. Algorithms like this have been shown to outperform many traditional handcraft features. These adaptable models can recognize complex patterns directly from visual input without the use of manually defined image features or expert-provided templates, and they can accommodate for non-trivial differences in image quality and color. For example, Nitika Goenka et al. [13] used a neuroimaging biomarker called T1w-MRI to test AD into three classifications using volumetric ConvNet and a 3D subject-based method – and achieved accuracy of 98.26%. The model is evaluated with several neuroanatomical extraction techniques, revealing that 3D-subject based ConvNet obtains the best accuracy over 3D-patch based ConvNet, and slice level approach.

Despite the excellent prediction capability of CNNs, deep learning models have been doubted for their low interpretability and dependency on enormous annotated datasets [14]. We recognize that these features pose considerable obstacles to the creation of viable neuropathology tools. A neuropathology-specific strategy would necessitate:

1) a clear definition of the machine learning objective

2) the creation of a curated image dataset with expert annotations at high resolution

3) extensive model interpretability

We hypothesize that CNN models might be used to recognize and classify pathological images; at the same time, we have a goal of producing reliable, scalable, and interpretable measurements. We feel it is crucial that predicted performance come from learning meaningful patterns within the images in order to create a useful tool.

In order to investigate the CNN model's basic logic, we will conduct two tests to examine the role of morphological features in contributing to correct predictions. First, we will use guided gradient-weighted class activation mapping (Guided Grad-CAM)[15] to find key visual cues that underpin the model's predictions. Guided Grad-CAM establishes an activation map by following the CNN's gradient flow from individual tasks back onto the original image tile, highlighting the input features most relevant to each CNN prediction. Second, we will perform a feature occlusion analysis [16] on the same instances. A small occlusion patch is pushed over the image, and the model predicts the occluded image at each increment.

In this study, we want to design a pipeline for the neuropathological analysis of pathology images. We aim to train a CNN model that result in high-performing classifiers capable of distinguishing different classes. Using deep learning introspection methods, we will try to show that trained models learn relevant aspects of each of the classes, providing visual proof that the model is interpretable.

3 Collaboration plan

1. Reading papers

   - Materials:

     * Interpretable classification of Alzheimer's Disease pathologies with a convolutional neural network pipeline [17]
     * Deep learning in medical image analysis [8]
     * A survey on deep learning in medical image analysis [9]
     * Deep convolutional neural networks enable discrimination of heterogeneous digital pathology images [11]
     * End-to-end text recognition with convolutional neural networks [18]
     * A deep learning model for the classification of indeterminate lung carcinoma in biopsy whole slide images
     * Early diagnosis of Alzheimer's disease with deep learning [19]
     * Deep convolutional neural networks for automatic classification of gastric carcinoma using whole slide images in digital histopathology [12]
     * A visualization method based on the Grad-CAM for medical image segmentation model [20]

    - View of A Deep Learning Model in the Detection of Alzheimer Disease [21]
    - Alzheimer Detection Using Deep Convolutional GAN [22]
  - Leader: Boyang Li, Jiaping Zhu
  - Deadline: 4/1/2022
  - Importance: Normal
  - Challenges: Understanding and synthesizing the methods that we are trying to implement

2. Implementing pathology classification method
   - Leader: Jia Yin
   - Deadline: 4/13/2022
   - Importance: Important
   - Challenges: Issues with implementing CNN pipeline; general code debugging issues

3. Using metrics to compare results with baseline
   - Leader: Avery Peiffer
   - Deadline: 4/20/2022
   - Importance: Important
   - Challenges: Issues with comparing metrics; Suboptimal Results; Model fine-tuning;

4. Synthesizing results into report and presentation
   - Leader: Jiaping Zhu, Boyang Li
   - Deadline: 4/30/2022
   - Importance: Important
   - Challenges: Writing format; Writing style

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