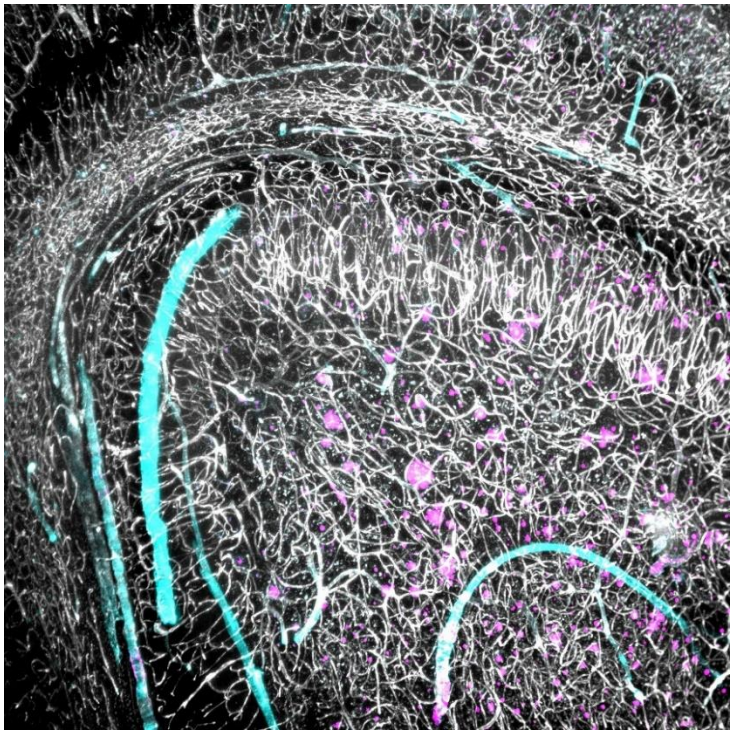
MASTER PROJECT: ANALYSIS OF LARGE DATASETS OF THE VASCULAR NETWORK IN HUMAN AD BRAIN

INTRODUCTION



Sporadic Alzheimer's disease (AD) is the most common neurodegenerative disease worldwide. The disease course is chronically progredient leading to loss of memory until loss of personal identity. In AD patients, the vascular network of the brain is directly affected by cerebral amyloid angiopathy and other pathological changes such as lacunae, microinfarcts, hemorrhage, and atherosclerosis. The goal of this project is to reconstruct and characterize the detailed cerebrovascular network of AD patients.

METHODS

We have developed a technique to process entire archival paraffinized human tissue blocks via deparaffination, clearing, staining, and 3D light sheet imaging. This procedure allows us to examine large structures like blood vessels and neighboring structures such as Aβ plaques in a large 3D volume across different brain regions of patients with distinct AD disease stages as well as control patients. A big challenge of this project is to process these datasets, each of them few TB large, in a computational pipeline.

DATA ANALYSIS PIPELINE

The 3D data consist of multiple tiles that are aligned and stitched to a common coordinate system. Then, blood vessels are segmented, and the vascular graph is constructed using the *TubeMap* vessel analysis pipeline (Kirst *et al., Cell* 2020; https://github.com/ChristophKirst/ClearMap2). Aβ plaques are segmented and counted using *ClearMap* (Renier *et al., Cell* 2016). The network of blood vessels is then be used for skeletonization and graph reconstruction. The vascular graph serves as the basis for further analysis and will be combined with information about the distribution of Aβ plaques.

The code is written in Python (with some contributions from Ilastik) and uses traditional machine learning as well as deep learning techniques based on PyTorch to process the datasets efficiently.

MASTER PROJECT DESCRIPTION

The Python code has been installed on a powerful local machine (80 cores, 1 TB RAM), and preliminary tests have already been carried out. However, it is still necessary to optimize parameters and improve the pipeline for correct processing. One aspect is to improve deep convolutional networks for vessel or Aβ plaques segmentation. If these image processing steps are successful, a potential second part of the project will be the analysis of the vascular network graph structure and the analysis of the localization of Aβ plaques concerning the vascular network.

The master student will be able to join a highly innovative project and to learn image processing methods for big datasets. The project is primarily located in the lab of Prof. Kist at FAU and will be co-supervised by an expert for AD, clearing, and light-sheet imaging (Dr. med. Dr. sc. nat. Anna Maria Reuss, Institute of Neuropathology, USZ/UZH). It will therefore be possible to gather experience both in machine learning / image processing and in the biological questions related to the vascular network of the human brain. The master project is estimated to last five months so that one month would be available to write the master's thesis.

YOUR PROFILE

We are searching for a highly motivated, committed master student with excellent programming skills who is eager to learn more about image processing of big datasets and who wants to work with data from human brains. The willingness to understand, use, and improve a complex state-of-the-art Python codebase for image processing is important. Successful work will result in a co-authorship on the final publication.

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