Data Intelligence Institute of Paris (diiP)
2024 **Masters-level Internship**

Biomarker prediction from images of histological slides of cancerous tissues using modern AI techniques: comparisons of different neural architectures

PROJECT INFORMATIONS

- **Keywords :** digital pathology, very large image analysis, deep learning, physicians' diagnosis
- **Investigators** : Nicolas Loménie, Zhuxian Guo, Camille Kurtz (LIPADE @ Université Paris Cité), Julien Calderaro (Henri Mondor University Hospitals)
- **Duration**: 6 months (standard stipend). To start between February and April 2024
- **Location**: 45 rue des Saints-Pères, 75006 Paris (LIPADE)
- **Application**: Please send a cover letter and a CV to Nicolas Loménie and Camille Kurtz (first.lastname@u-paris.fr). The position is opened until filled.

MOTIVATION

Digital Pathology is on the rise. Radiology paved the way a couple of decades ago since every patient exam is a digital scan that led to various automatic image processing solutions to ease physicians' diagnosis. In comparison, in anatomo-pathology, automatic image analysis and mining are outstandingly more challenging. Most exams are still done visually under the analogical microscope. But new scanners have emerged (Phillips, Hamamatsu, etc.) driving revolutionary changes at the clinical level. Given the rich information present in these images, a vast field of opportunity opens up for automated image analysis. This is especially pertinent in oncology where early and accurate diagnosis is paramount. Recent advances in deep learning, specifically convolutional neural networks (CNNs), have shown promise in (Whole Slide Images) WSI-based pathological tasks [1]. However, with the advent of transformer architectures, traditionally used in natural language processing tasks, there's an emerging interest in assessing its applicability for WSI image analysis. In collaboration between LIPADE and Henri Mondor University Hospitals (Julien Calderaro, PUPH, pathologist), as part of this project, we wish to take advantage of the opportunities offered by deep neural architectures to investigate how they can be used to the prediction of biomarkers on images of histological slides of cancerous tissues. The main challenges are linked to the very large dimension of the images and the extremely complex visual heterogeneity of this type of tumor from a phenotypic point of view. Within this vast field of opportunity is the specific task of slide-level or patient-level classification which has significant clinical implications. For Colorectal Carcinoma (CRC), Microsatellite instability (MSI) or Microsatellite stability (MSS) classification is pivotal. On the other hand, in the case of Hepatocellular Carcinoma (HCC), distinguishing between malignant and benign presentations at the slide or patient level is important. These tasks, requiring a combination of granular and broader analysis, make the case for innovative methods that build on existing AI technologies. The AI models aim to enhance early and accurate diagnoses by quickly analyzing vast amounts of data, ensuring consistent results, and highlighting critical areas on histological slides. As a middle-term goal, we aim to, in collaboration with Dr. Julien Calderaro, create an accessible web platform where medical professionals can upload a WSI and receive instant, comprehensive AI-driven analysis. This not only streamlines the diagnostic process but bridges the gap between intricate AI research and practical medical applications. **In this internship, we wish to study / compare**

different neural architectures with the aim of preparing the biological slide classification platform which can be deployed behind such a web service.

BACKGROUND & STATE-OF-THE-ART

Whole Slide Imaging in Oncology: WSI has become an instrumental tool in digital pathology, transforming the conventional microscope-based examination with high-resolution digital scans of tissue samples. It offers an unobstructed view of cellular structures and their interactions, making it indispensable in oncology [3].

Convolutional Neural Networks (CNN): CNNs, with their ability to automatically and adaptively learn spatial hierarchies of features from images, have marked their dominance in image processing tasks. Especially in the realm of pathology, CNNs have registered significant achievements [4].

Transformers in Medical Imaging: Transformers [5], initially devised for natural language processing tasks, have seen rising adoption in computer vision challenges [6]. Their self-attention mechanism, which captures long-range dependencies, has been identified as particularly beneficial. The prominent study, "Transformer-based biomarker prediction from colorectal cancer histology: A large-scale multicentric study," emphasizes the potential of transformers in predicting biomarkers from colorectal cancer histology images. Our team has previously developed a model known as HiTrans [9], a Hierarchical Transformer Encoder for Entire Neoplasm Segmentation. This model has been adapted for expanded patch-level classification, showcasing its adaptability and relevance for the challenges at hand.

In the context of oncology, these recent AI technologies have shown spectacular results for tissue slide classification. However, to our knowledge, **there are no comparative studies of the use and impact of the type of neuronal architecture considered in the specific case of tumoral tissue classification**. The hospital database collected by our partner hospital contains hundreds of diagnosed cases, with homogeneous clinical data, which offers the opportunity in this Master project to carry out such a comparative study.

PROPOSED WORK & IMPLEMENTATION

Dataset Selection:

- **Public Datasets**: The intern will leverage popularly available datasets. These datasets, known for their extensive collection of histopathological images, will provide a robust baseline for the study and can also be used for the pre-training of the considered neural models: CAMELYON16/17 for breast cancer, PAIP 2020 for colon cancer;
- **In-house hospital Dataset**: datasets for both CRC, HCC WSI images will be provided by our hospital partners.

Model Architectures:

- CNN: Multiple CNN architectures like ResNet, DenseNet, and VGG will be explored. Transfer learning will be explored using pre-trained weights from ImageNet to expedite training and potentially enhance performance.
- Transformer: Vision Transformer (ViT) [7] will be primarily used, exploring different configurations for image patches and attention heads. Due to the intricacies of histopathological images, customization of self-attention mechanisms and positional encodings will be considered.
- HiTrans [9] Adaptation for Slide-Level/Patient-Level Classification:
    - Model: Our modified HiTrans model, originally designed for entire neoplasm segmentation, will be incorporated for patch-level classification tasks. Its hierarchical transformer encoder structure is aptly suited to capture both local and global features in histological slides.
    - Slide-Level Aggregation: Slide-level or patient-level representation extracted by HiTrans will be processed through aggregation approaches. Techniques such as max pooling, average pooling, or more sophisticated methods like attention-based pooling might be considered to distill relevant features and information for slide-

level classification tasks.

Evaluation & Interpretation:

Comprehensive evaluation metrics including Accuracy, Precision, Recall, F1-Score, and AUC-ROC will be employed. Techniques such as Grad-CAM and SHAP will be used to understand the focus regions of both CNN and Transformer architectures, offering insights into how models make decisions [8].

Learning Experience: Selection and application of public datasets for benchmarking, Implementation and customization of complex architectures (CNN & Transformer), Practical evaluation strategies and model interpretability methods, Application and customization of our previously developed model, HiTrans, for slide-level or patient-level classification tasks.

The proposed work ensures a comprehensive approach towards comparing CNN and Transformer architectures in the context of WSI images. Integrating in-house datasets with public datasets allows for robust and generalizable conclusions, while the exploration of both architectures promises valuable insights into the nuances of each.

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