Abstract:

Whole slide images (WSIs) are high-resolution digital representations of histopathological tissue and are widely used in computational pathology. Despite recent advances in deep learning for WSI analysis, existing models often struggle with robustness and generalization due to artifacts, staining variability, limited annotations, and distribution shifts across datasets. These challenges limit the reliable use of automated methods in clinical settings.

This dissertation presents graph-based learning frameworks designed to improve the robustness and reliability of WSI analysis. By representing WSIs as graphs of spatially connected tissue regions, the proposed methods capture both local features and global tissue structure while enabling efficient slide-level analysis. The work addresses key challenges in computational pathology, including adversarial robustness, out-of-distribution (OOD) generalization, uncertainty estimation, and stain normalization.

First, robustness to imaging artifacts and adversarial perturbations is addressed through graph-based models that improve stability at both the image and graph levels. Second, to handle distribution shifts, an explainability-based graph augmentation framework is introduced to improve generalization to unseen data. Third, a multi-head graph neural network framework is developed for uncertainty estimation, providing more reliable predictions and improved interpretability. Fourth, a graph-based diffusion model is proposed for stain normalization, preserving tissue structure while reducing staining variability. Finally, a slide-specific untrained graph autoencoder is introduced for denoising and OOD detection, achieving strong performance without requiring large-scale training.

Experimental results across multiple datasets demonstrate improved robustness and generalization compared to existing methods, with consistent performance under distribution shifts and challenging real-world conditions.