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Training-Free Style Augmentation with Histogram Matching for Domain Generalization in Histopathology

Content

Deep learning (DL) has demonstrated remarkable success in computer vision, yet its translation into clinical practice remains hindered by limited generalization across heterogeneous datasets. This challenge is particularly severe in digital histopathology, where variations in staining protocols and acquisition conditions introduce substantial domain shifts that undermine model robustness. While data augmentation is widely employed to address these issues, conventional techniques either fail to capture realistic staining variability or risk producing misleading samples. More advanced strategies, such as stain-specific normalization or domain-adaptive augmentation, often require access to target data during training and struggle to generalize to unseen staining protocols.

In our recent MICCAI 2024 work (Self-supervised Vision Transformers are Scalable Generative Models for Domain Generalization), we addressed this by proposing a generative style augmentation approach based on self-supervised Vision Transformers. By synthesizing histopathology images with diverse combinations of anatomical and stylistic characteristics across training samples on a patch-level, we achieved state-of-the-art performance on benchmark datasets (+2% on Camelyon17-wilds and +26% on an epithelium–stroma dataset). However, this approach introduced computational overhead and patch-boundary artifacts due to its patch-level synthesis.

Building on these findings, we revisit histogram matching as a classical yet overlooked alternative for style-based augmentation in histopathology. Histogram matching transfers the intensity or color distribution of one image to another, enabling efficient style adaptation without training, external data, or computationally intensive pipelines. Unlike generative methods, it preserves anatomical fidelity, avoids hallucinations, and operates in real time. Beyond training augmentation, we further explore its application at test time to align out-of-distribution samples with training distributions, improving robustness during inference.

We argue that re-evaluating classical image processing methods in this context offers a promising path toward scalable, reliable, and clinically translatable domain generalization in medical AI.

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