Unsupervised Domain Adaptation for Cell Detection Across Histopathological Stains

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Introduction
Deep learning models trained on hematoxylin and eosin (H&E) stained images often fail to generalize to immunohistochemistry (IHC) stains due to domain shifts. The scarcity of annotated IHC datasets limits the applicability of supervised learning. To address this challenge, we propose an unsupervised domain adaptation approach that enables CellNuc-DETR to generalize from H&E to IHC without requiring additional manual annotations.

Material and methods
We leverage Adversarial Query Transformers (AQT) to align feature representations between H&E and IHC domains, enhancing generalization without explicit supervision. The model is pre-trained on PanNuke (H&E) and fine-tuned using unannotated IHC patches from 93 WSIs across four stains: ER, PR, Ki-67, and HER2. Performance is evaluated using F1-score on annotated test patches.

Results and discussion
The AQT-adapted CellNuc-DETR significantly outperforms the source-only model, improving F1-score from 0.42 to 0.74, 0.46 to 0.80 and 0.46 to 0.80 on Ki-67, ER and PR, demonstrating strong cross-stain generalization. Compared to CycleGAN-based stain translation, AQT achieves a 20% improvement in F1-score. Additionally, we find that adapting to all IHC stains at once leads to better generalization than adapting to each stain individually, suggesting that learning shared stain-invariant features is more effective than stain-specific adaptation. However, adaptation remains challenging for HER2, where the stain highlights cell membranes rather than nuclei, leading to poor performance and indicating the need for further adaptation techniques.

Conclusion
Our results highlight the potential of adversarial domain adaptation to extend deep learning models to new histological stains without requiring extensive re-annotation. This approach enables scalable, generalizable computational pathology workflows, improving automated biomarker quantification across different staining modalities.

Key words: Cell Detection, Unsupervised Domain Adaptation, Deep Learning, Transformers