

Supplementary Material

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1 Algorithm

Algorithm 1 PID module in end-to-end PID-LRSC

Input: Feature clusters $\mathbf{Z} = \{\mathbf{Z}_1, \mathbf{Z}_2, \mathbf{Z}_3\}$, Prototype features \mathbf{Z}^{PI}

Output: Final bag feature \mathbf{Z}_{WSI} and label map **label**

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1: for  $k = 1$  to 3 do
2:    $d_k \leftarrow D(\mathbf{Z}_k, \mathbf{Z}^{\text{PIs}})$  ▷ Distribution-aware CFD metric
3: end for
4:  $\{w_k\}_{k=1}^3 \leftarrow 1 - \text{Normalize}(\{d_k\})$ 
5:  $\text{order} \leftarrow \text{argsort}(\{w_k\}, \text{descend})$ 
6:  $\text{label}[\text{TIs}] \leftarrow \mathbf{Z}_{\text{order}[1]}, \dots, \text{label}[\text{BGIs}] \leftarrow \mathbf{Z}_{\text{order}[3]}$ 
7:  $\mathbf{Z}_{\text{final}} \leftarrow \mathcal{A}\left(\text{concat}\left(\sum_{k=1}^3 w_k \mathbf{Z}_k, \mathbf{Z}^{\text{PI}}\right)\right)$ 
8: return  $\mathbf{Z}_{\text{WSI}}, \text{label}$ 
```

2 Datasets and Configurations

Datasets: We conduct experiments on two private datasets collected from some institution for squamous cell carcinoma pathological grading. **AMU-LSCC** is for laryngeal squamous cell carcinoma pathological grading and **AMU-CSCC** is for cervical squamous cell carcinoma. **AMU-LSCC** dataset includes 342 whole slide images that was divided by a 6:4 training-validation ratio for each category. Specially Grade I contains a total of 89 WSIs, Grade II contains 152 WSIs and Grade III includes 101 WSIs. **AMU-CSCC** dataset includes 262 whole slide images, where Grade I contains a total of 27 WSIs, Grade II contains 127 WSIs and Grade III includes 108 WSIs. 961 patches were grid cropped from each WSI on two datasets. Besides, we validate generalization of proposed PLoRC on two public datasets, where **DHMC-LUNG** [9] is for lung adenocarcinoma classification and **DHMC-KIDNEY** [13] is for renal cell carcinoma sub-types classification.

Compared MIL Models: Eleven SOTA models are implemented for comparison. They are ABMIL [4], CLAMs [6], TransMIL [7], DTfD-MIL [11], IBMIL [5], ILRA-MIL [10], S4MIL [3], FRMIL [1], DGRMIL [14], ACMIL [12], RRT-MIL [8]

and MFC-MIL [2]. We report metrics Accuracy and Area Under Curve (AUC) for evaluation.

Implementation: For end-to-end training, we employ Rmsprop optimizer and the learning rate schedule sets: 1×10^{-5} for epochs 1–50, 5×10^{-6} for epochs 51–75, and 1×10^{-6} for epochs 76–100. Models on two private datasets were trained with a batch size of 2 and 100 epochs. For two public datasets, batch size is set 1. The random seed was fixed 0 across all stages to ensure reproducibility. The input resolution of PLoRC was $96 \times 96 \times 3$. The hyper-parameter in loss function setting is $\gamma_1 = \gamma_2 = 0.1$, $\gamma_3 = 1 \times 10^{-4}$. The low rank hyper-parameter $r = 384$ when parameterizing \mathbf{A} . Patches were grid cropped from each WSI in 10x magnification and we filtered out instances with blank areas. All models are employed under the same experimental configurations with four *NVIDIA A10 Tensor Core 24GB* GPUs. The peak GPU memory usage is reported 10GB.

References

1. Chikontwe, P., Kim, M., Jeong, J., Sung, H.J., Go, H., Nam, S.J., Park, S.H.: Fr-mil: Distribution re-calibration based multiple instance learning with transformer for whole slide image classification. *IEEE Trans. Med. Imaging* (2024)
2. Cui, X., Chen, W., Su, J.: A multiscale frequency domain causal framework for enhanced pathological analysis. In: *The Thirteenth International Conference on Learning Representations* (2025)
3. Fillioux, L., Boyd, J., Vakalopoulou, M., Cournède, P.H., Christodoulidis, S.: Structured state space models for multiple instance learning in digital pathology. In: *International Conference on Medical Image Computing and Computer-Assisted Intervention*. pp. 594–604. Springer (2023)
4. Ilse, M., Tomczak, J., Welling, M.: Attention-based deep multiple instance learning. In: *International Conference on Machine Learning*. pp. 2127–2136. PMLR (2018)
5. Lin, T., Yu, Z., Hu, H., Xu, Y., Chen, C.W.: Interventional bag multi-instance learning on whole-slide pathological images. In: *Proceedings of the IEEE/CVF Conference on Computer Vision and Pattern Recognition*. pp. 19830–19839 (2023)
6. Lu, M.Y., Williamson, D.F., Chen, T.Y., Chen, R.J., Barbieri, M., Mahmood, F.: Data-efficient and weakly supervised computational pathology on whole-slide images. *Nat. Biomed. Eng.* **5**(6), 555–570 (2021)
7. Shao, Z., Bian, H., Chen, Y., Wang, Y., Zhang, J., Ji, X., Zhang, Y.: Transmil: Transformer based correlated multiple instance learning for whole slide image classification. *Advances in Neural Information Processing Systems* **34**, 2136–2147 (2021)
8. Tang, W., Zhou, F., Huang, S., Zhu, X., Zhang, Y., Liu, B.: Feature re-embedding: Towards foundation model-level performance in computational pathology. In: *Proceedings of the IEEE/CVF Conference on Computer Vision and Pattern Recognition*. pp. 11343–11352 (2024)
9. Wei, J.W., Tafe, L.J., Linnik, Y.A., Vaickus, L.J., Tomita, N., Hassanpour, S.: Pathologist-level classification of histologic patterns on resected lung adenocarcinoma slides with deep neural networks. *Scientific reports* **9**(1), 3358 (2019)
10. Xiang, J., Zhang, J.: Exploring low-rank property in multiple instance learning for whole slide image classification. In: *The Eleventh International Conference on Learning Representations* (2023)

11. Zhang, H., Meng, Y., Zhao, Y., Qiao, Y., Yang, X., Coupland, S.E., Zheng, Y.: Dtf-d-mil: Double-tier feature distillation multiple instance learning for histopathology whole slide image classification. In: Proceedings of the IEEE/CVF Conference on Computer Vision and Pattern Recognition. pp. 18802–18812 (2022)
12. Zhang, Y., Li, H., Sun, Y., Zheng, S., Zhu, C., Yang, L.: Attention-challenging multiple instance learning for whole slide image classification. In: European Conference on Computer Vision. pp. 125–143. Springer (2024)
13. Zhu, M., Ren, B., Richards, R., Suriawinata, M., Tomita, N., Hassanpour, S.: Development and evaluation of a deep neural network for histologic classification of renal cell carcinoma on biopsy and surgical resection slides. *Scientific reports* **11**(1), 7080 (2021)
14. Zhu, W., Chen, X., Qiu, P., Sotiras, A., Razi, A., Wang, Y.: Dgr-mil: Exploring diverse global representation in multiple instance learning for whole slide image classification. In: European Conference on Computer Vision. pp. 333–351. Springer (2024)