Comments for Reviewer 9snc

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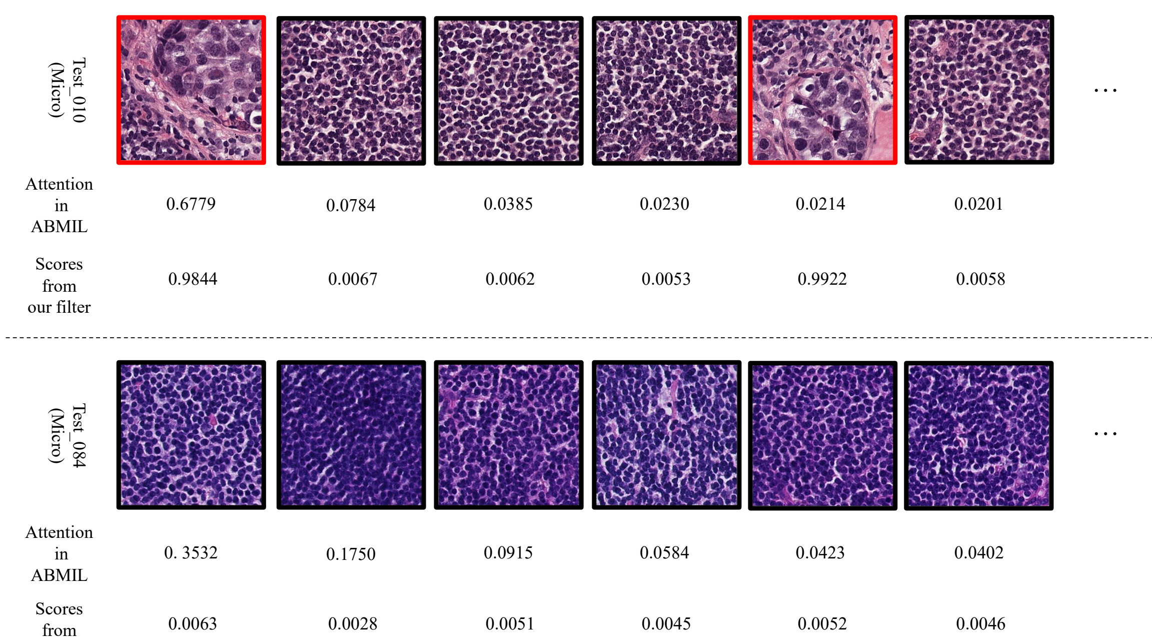
1 Comments

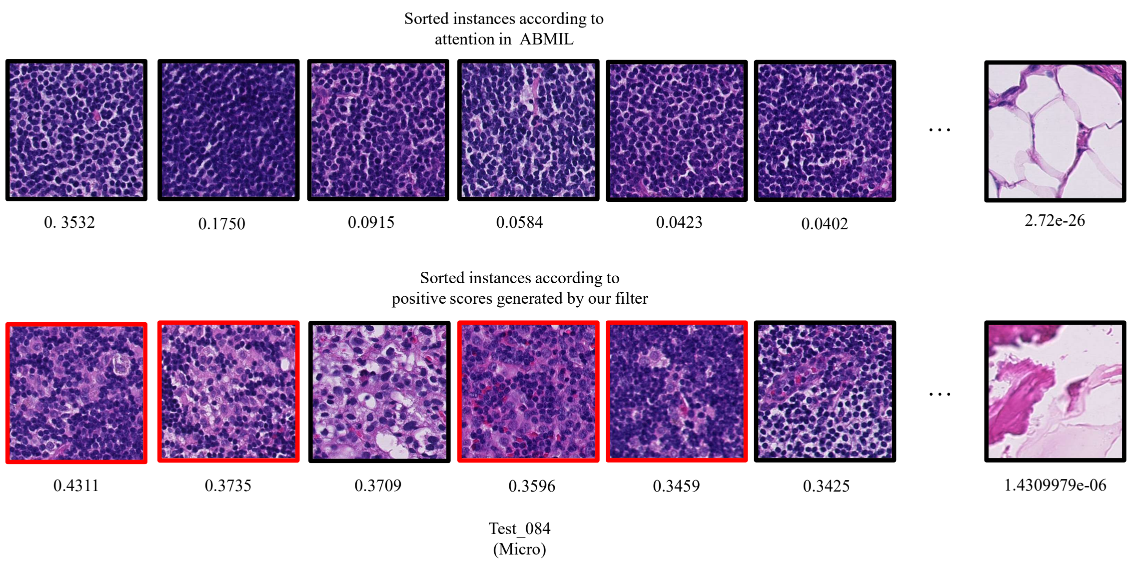
Thank you for your invaluable feedback and comments. We are sorry that the lack of specificity in the writing confused you. We hope the following statements address your concerns:

- **Filtering of irrelevant instances and upper bounds on the capacity of the attention mechanism.** For issue 1.1: Before feature extraction, our method is consistent with other baseline methods, which all use the OTSU algorithm to remove background patches including blank areas, fat areas, etc. While filtering of instance-level features occurs between extraction and aggregation. Conventional embedding-level methods extract high-dimensional features from patches, which will all be considered by the aggregator. However, our proposed method first sorts all patches using positive scores, and then filters out the top k ones (regarded as potential positive instances) and the negative top k ones (which are regarded as potential negative instances) as input to the aggregator, which helps reduce the noisy signal brought by too many negative instances [YSJ+23]. To further prove the effectiveness of our proposed method, we consider the Camelyon16 dataset, which is a binary classification task of WSI distinguishing the presence and absence of cancer, in which the WSI with cancer is regarded as a positive bag (patches with cancer are regarded as positive instances), the non-cancer WSI is regarded as a negative bag (patches without cancer are regarded as negative instances), and the attention mechanism-based methods will give each instance a positive-related importance score. However, in practice, they will mistakenly give high scores to negative instances sometimes. As shown in the figure below. We demonstrate the attention scores assigned to instances by ABMIL and the positive scores



assigned to instances by our classifier (filter) in two micro-metastatic cancer slides. Negative instances are highlighted with black frames, while positive ones are marked in red. Instances are sorted in descending order from left to right by attention. For ease of observation, the attention is scaled by the softmax operator. In Test_10, three negative instances are assigned the second to fourth highest attention, but our method successfully eliminated these negative examples and correctly classified the WSI. In Test_84, negative instances containing a large number of lymphocytes received high attention in ABMIL, while positive instances were not in the high attention list, resulting in misclassification. Our method tended to eliminate these negative instances.

For issue 1.2: As shown in the following figure, for Test_84, irrelevant instances (negative instances) are fed into the aggregator of ABMIL, but the attention mechanism considers them relevant and leads to misclassification. We also show the results of ranking the positive scores generated according to our filter, where a large number of positive instances remain in the higher ranks despite the lower scores. These relevant instances are encapsulated in the new pseudo-bag.



- **Results of baseline methods.** We do not reproduce the results reported in the original article using the baseline model on the CAMELYON16 dataset for several reasons. Firstly, our experimentation involved a 5-fold cross-validation, which differed from that used in the baseline article. To enhance the credibility of our study, we provide detailed information regarding the division of the 5 folds, which can be accessed at `https://github.com/polyethylene16/NcIEMIL/tree/main/fold`. Secondly, despite employing the same preprocessing strategy, we did not generate the same number of patches as reported in the other articles. Finally, we did not employ any additional techniques during training; for instance, in the comments section of `https://github.com/szc19990412/TransMIL/issues/25`, a commenter only achieved slightly lower results by employing a trick (early-stop) not mentioned in the original article. During experiments, We directly used the training code provided by the authors and conducted with our partitioned dataset.

- **Modifications of the abstract.** We have updated the abstract to address poor readability, and in the following, the red font is the revised section: "On account of superiority in annotation efficiency, multiple instance learning (MIL) has proved to be a promising framework for the whole slide image (WSI) classification in pathological diagnosis. However, current methods employ fully- or semi-decoupled frameworks to address the trade-off between billions of pixels and limited computational resources. This exacerbates the information bottleneck, leading to instance representations in a high-rank space that contains semantic redundancy compared to the potential low-rank category space of instances. Additionally, most negative instances are also independent of the positive properties of the bag. To address this, we introduce a weakly annotation-supervised filtering network, aiming to restore the low-rank nature of the slide-level representations. Additionally, we design a parallel aggregation structure that utilizes spatial attention mechanisms to model inter-correlation between instances and simultaneously assigns corresponding weights to channel dimensions to alleviate the redundant information introduced by feature extraction. Extensive experiments on the private gastrointestinal chemotaxis dataset and CAMELYON16 breast dataset show that our proposed framework is capable of handling both binary and multivariate classification problems and outperforms state-of-the-art MIL-based methods. The code is available at: https://github.com/polyethylene16/NcIEMIL."

In response to the poor readability of this paper, we will adjust the paragraphs, including the abstract, in the final version of the paper. Thanks again for your comments!

References

[YSJ+23] Renao Yan, Qiehe Sun, Cheng Jin, Yiqing Liu, Yonghong He, Tian Guan, and Hao Chen. Shapley values-enabled progressive pseudo bag augmentation for whole slide image classification. *arXiv preprint arXiv:2312.05490*, 2023.