Managing Editor
Plos One

12-Jan-2026

Dear Editor:

We are submitting our manuscript entitled “Toward reliable false discovery rate control in classification problems under distribution shift” for consideration for publication in *Plos One* as ***original research article***.

We note that we are affiliated to a Russian University, our institution is not under sanctions and we are not involved in any research related to the Russian military, etc. We will pay APC from a European bank card.

We present our study on controlling false discovery rates (FDR) under data distribution shift in classification problems in the biomedical domain. In this study, we draw attention to a very important but often neglected problem; namely, the performance of deep-learning based classifiers is assumed to be the same in application. However, it often can be much worse than thought due to data distribution shift (a.k.a. covariate shift), data label distribution shift, batch effects caused by some confounding factors, and overfitting. This performance drop of a machine learning system often remains undetected, resulting in risk for people in health care and clinical applications.

In this manuscript, we present a simple, fast and robust method to adjust the test prediction scores so that the latent test null distribution will be more similar to the train null distribution. This will result in more accurate FDR control.

Our method operates in the 1-dimensional prediction score space. Therefore, it is not hindered by high-dimensional space, data sparsity (i.e. curse-of-dimensionality), and correlated features. In addition, our method does not rely on data clustering or graphical causal models.

We tested our method with four public benchmark datasets commonly used in biomedical image analysis: PatchCamelyon (PCam), Chest x-ray (CheXpert), TissueNet, and Breast Cancer Semantic Segmentation (BCSS). With our method, we obtained much more accurate FDR control under data distribution shifts in the test data compared to a recent algorithm, called Learn-then-test, developed by Michael Jordan’s lab from Stanford University.

A declaration of any potential competing interests:

None.

Confirmation that all authors have approved the manuscript for submission:

This manuscript has been approved by both authors.

Confirmation that the content of the manuscript has not been published:

This manuscript has never been submitted to any other journals. We have not interacted with PLOS regarding this manuscript before. The manuscript will be properly formatted for the journal if it is needed for the reviewing stage or once it is accepted. We did not use AI chat bots in manuscript preparation or in this study in general.

Suggested Academic Editors:

1. Musa Aydin, Turkey, orcid.org/0000-0002-5825-2230
2. Hong-Seng Gan, Malaysia, orcid.org/0000-0003-3777-3640
3. Zeyneb Kurt, UK, orcid.org/0000-0003-3186-8091
4. Xiaohui Zhang, USA, orcid.org/0000-0002-7990-1594
5. Anybody with a background in machine learning classification, error control, image processing would suffice.

Suggested reviewers:

1. Nikita Moshkov, PhD, Institute of Biochemistry, Biological Research Center. Szeged, Hungary, Deep Learning specialist in biological image analysis, cell segmentation, etc. nikita.moshkov@brc.hu
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Opposed reviewers:

None.

We hope that this manuscript provides a useful and interesting study for the readers of Plos One.

Best regards,

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