Increasing Trust in AI Using Explainable Artificial Intelligence for Histopathology – An Overview

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Abstract. Digital Pathology is an area that could benefit a lot from the automatic classification of scanned microscopic slides. One of the main problems with this is that the experts need to understand and trust the decisions of the system. This paper is an overview of the current state of the art methods used in histopathological practice for explaining CNN classification useful for histopathological experts and ML engineers that work with histopathological images. This paper is an overview of the current state of the art methods used in the histopathological practice for explain. The search was performed using *SCOPUS* database and revealed that there are few applications of CNNs for digital pathology. The 4-term search yielded 99 results. This research sheds light on the main methods that can be used for histopathology classification and offers a good starting point for future works.

Keywords: Histopathology, Trust, XAI, CNN

1. Introduction and Motivation

In the present paper we will discuss advantages and disadvantages for multiple XAI methods that can be applied to explain deep learning approaches. To increase trust in the results of using AI in clinical practice raises the need of explanation [1]. The intent is to give the reader a point of start in choosing the best technique that can be applied to a particular problem involving images based on the current practices. We will focus on articles that consider XAI applied to image classification.

1.1. Artificial intelligence in histopathology

To enable histopathology specialists to trust and use AI in their work we need to give them an insight into the model's decision. The model will likely be rejected or not used because they cannot understand why or how the decision is made.

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2. Methods

2.1. Search strategy

The search was done within the "Article title", "Abstract" and "Keywords" in Scopus database considering only the English language articles for the interval 2013-2023. Table 1 presents the initial results.

Table 1. Initial number of articles that resulted after Scopus database search

Description	Document type	No of articles
xai histopathology	Article, Review	5
explainable ai histopathology	Article, Review, Conference Paper	10
explainable deep learning histopathology	Article, Review, Conference Paper, Conference Review	25
classification explanations histopathology	Article, Review, Conference Paper, Conference Review	59

The second thing that could be noticed is that in explainable ai for histopathology area there are quite few articles available for review. As Table 1 displays, for the 4 search terms ("xai histopathology", "explainable ai histopathology", "explainable deep learning histopathology", "classification explanations histopathology") used we got 99 results. This shows that the area is still open for much research. The duplicated articles were removed. Table 2 presents the actual strings generated by the Scopus database to offer a better way to validate the review.

Table 2. Search strings

Search term	String
xai histopathology	TITLE-ABS-KEY (xai AND histopathology) AND PUBYEAR > 2012 AND PUBYEAR < 2023 AND (LIMIT-TO (DOCTYPE , "ar") OR LIMIT-TO (DOCTYPE , "re"))
explainable ai histopathology	TITLE-ABS-KEY (explainable AND ai AND histopathology) AND PUBYEAR > 2018 AND PUBYEAR < 2023 AND (LIMIT-TO (LANGUAGE , "English")) AND (LIMIT-TO (DOCTYPE , "ar") OR LIMIT-TO (DOCTYPE , "re") OR LIMIT-TO (DOCTYPE , "cp"))
explainable deep learning histopathology	TITLE-ABS-KEY (explainable AND deep AND learning AND histopathology) AND (LIMIT-TO (DOCTYPE , "ar") OR LIMIT-TO (DOCTYPE , "re") OR LIMIT-TO (DOCTYPE , "cp") OR LIMIT-TO (DOCTYPE , "cr")) AND (LIMIT-TO (LANGUAGE , "English"))
classification explanations histopathology	TITLE-ABS-KEY (classification AND explanations AND histopathology) AND PUBYEAR > 2012 AND PUBYEAR < 2024 AND (LIMIT-TO (DOCTYPE , "ar") OR LIMIT-TO (DOCTYPE , "re") OR LIMIT-TO (DOCTYPE , "cp") OR LIMIT-TO (DOCTYPE , "cr")) AND (LIMIT-TO (LANGUAGE , "English"))

We identified the XAI methods related to CNN image classification and their use. Initially we evaluated the abstract of each category to select the relevant results. We considered the results to be relevant if they met the criteria of histopathology classification using convolutional neural networks and also offered an explanation mechanism. We eliminated the proceedings that were returned and focused only on single relevant articles (aggregates or not). After eliminating the duplicate articles and checking the abstracts, resulted 42 final articles proposed for review. After full text reading, we have only 6 articles proposed for review. We considered these articles to be relevant containing both CNNs and XAI specifically applied on histopathology images. The final search status for articles (non-overlapping) are presented below:

We must note that for the aggregate articles we focused mainly on their conclusions. We also need to mention that no automatic retrieval system was used.

Table 3. Scopus articles selected after abstract review and full text reading.

Description	Document type	Nr of articles after abstract reading	Nr of articles after full text reading
xai histopathology	Article, Review	4	1
explainable ai histopathology	Article, Review, Conference Paper	6	1
explainable deep learning histopathology	Article, Review, Conference Paper, Conference Review	10	3
classification explanations histopathology	Article, Review, Conference Paper, Conference Review	21	1

2.2. XAI methods currently used specifically in histopathology

In this section we will present the most relevant methods that resulted from the review that are being used in histopathology.

One method is the rule-extracting from CNNs [2]. Even if the experts decide they do not like the decision, they could use the rules to get an easy English language understanding of the AI algorithms results. Another method will be the heatmap visualization. The Grad-CAM method was also used by [3]. A paper that refers to cancer diagnostics [4] emphasizes that the acceptance of deep learning is conditioned by the ability to understand what the algorithms are doing.

Several researchers used feature-extraction [5] to offer a better perspective for predicting survival in patients with lung cancer. Another team developed a report module that encompassed XAI [6]. An interesting development in this area is the presence of approximations for explanations [7] that offers a decrease in computational times for the explaining part (important for the emergency situations in medical area).

3. Results

After selecting and reading the articles, we found multiple methods for explainable artificial intelligence applied on CNNs, the most important categories being presented in the paragraph 2.2. From this review the conclusion is that each method offers some insight on the decision. For example Grad-CAM from [3] offers the gradients of any target concept flowing into the final convolutional layer of the CNN to produce a coarse localization map that highlights the important regions in the image for predicting the concept. From the methods described in this review we could infer that there is a need for multiple parameters to be understood by a histopathologist. Multiple methods that could offer different insights on the histopathological practice using deep learning could increase the trust the expert will have in the AI systems designed to support them.

Table 4. Summary of the three most relevant methods

Method name	Area of usage
Grad-CAM	Paratuberculosis
Feature-extraction	Nucleus classification
Explanation by approx.	Metastasis classification

4. Conclusion

In this article we presented the main options that can be applied for histopathology images explanations in the case of convolutional neural networks, CNNs. This information can be considered for further investigation on medical images. The database used is one of the most important available, but for future research the number of databases should be increased in order to gather more information about this topic. The current explainable artificial intelligence methods are only part of the solution. The low number of articles available for the histopathology area show that this area needs further exploration and research. For large-scale usage by the medical professionals, they will need accurate and precise explanations for each case (as global as well as local per each slide). The trust of histopathological experts in AI solutions will be increased by the explanations that can be received from the XAI methods. We consider that multiple methods should be used to offer different perspectives on the classification of images and in this way the trust of the histopathologists will be increased in AI methods. The way in which multiple methods could be used in collaboration will be considered as future research.

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