

Reply to reviewers:

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: Machine learning become a widely used tool for prediction in clinical medicine gradually. ML methods have shown exciting performance in data predication. However, a big cause for concern is that all kind of ML methods have the problem of over-fitting. These over-fitting considerations provided in this letter are worthy of our attention and discussion.

We would like to thank you for your comment.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: Interesting paper, although the review of existing literature and possible approaches is very limited. Some other references that can be considered, also involving topics of interest of the present journal are on the automatic classification of Potentials in Celiac Disease, recently published in Scientific Reports (Nature group).

Thank you for the comment. In our Letter to the Editor, we aimed to inform the readership about the importance of cross-validation, regardless of which machine learning algorithm is being used, and its use to counteract the danger of over-fitting. Given the space limitations of a letter, the intention was not to extensively review the literature, but to provide a quick overview and convey the importance of nested cross-validation techniques and their caveats, when performing hyper-parameter tuning in machine-learning algorithms.

Reviewer #3:

Scientific Quality: Grade E (Do not publish)

Language Quality: Grade D (Rejection)

Conclusion: Rejection

Specific Comments to Authors: 1. My major concern is that the authors did not well clarify which are the new findings of their work. I invite then the authors to accomplish

this task both in the Introduction and in the Conclusion section. 2. The Observations in manuscript should be backed up with Figures 3. More analysis is required with respect to different statistical comparison and experimental results are insufficient 4. The overall organization in terms of page format is not good

Dear Reviewer,

We prepared a Letter to the Editor, in response to the article “*Deep learning vs conventional learning algorithms for clinical prediction in Crohn's disease: A proof-of-concept study*”. In this letter we aimed to inform the readership about the importance of cross-validation, regardless of which machine learning algorithm is being used, and its use to counteract the danger of over-fitting. Given the space limitations of a letter, the intention was not to extensively review the literature, but to provide a quick overview and importance of nested cross-validation technique, and their caveats, when performing hyper-parameter tuning in machine-learning algorithms.

Reviewer #4:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: This is a commentary paper on earlier publication in the Journal. It is delivered in a competent, robust manner, and is well structured.

Thank you for the comment.