DRSE: A Novel Method for Drug Repurposing Based on Drugs Side-Effects Similarities

Dear Dr lakizadeh,

Thank you for submitting your manuscript to Informatics in Medicine Unlocked. I think this manuscript can be accepted soon. Ed

I have completed my evaluation of your manuscript. The reviewers recommend reconsideration of your manuscript following major revision.

When revising your manuscript, please consider all issues mentioned in the reviewers' comments carefully: please outline every change made in response to their comments and provide suitable rebuttals for any comments not addressed. Please note that your revised submission may need to be re-reviewed.

Editor and Reviewer comments:

Reviewer #1: The authors propose a matrix factorization-based approach of predicting drug-disease associations via a matrix factorization method. Also, they apply a random walk with restart to merge drug and disease features. Though the results look good, I have the following comments.

Major points

1. The writing logic of the introduction is bad. The research area of this problem is not reviewed well. This paper just simply mentions former methods, but has neither a summary of their advantages and disadvantages, nor the advantages of the proposed method. The originality of the article should be clarified better.

Intro has been changed but advantages and disadvantages has not

2. In Data sources, there is a lack of detailed description of data, such as the number of drugs, disease, genes, targets, etc. Moreover, it is better to give a couple of examples to illustrate the data they used.

It has mentioned in the abstract

3. In the methodology part, I'm confused how they handle the features. They should clarify the writing. Also, some terms should be standardized. For example, 'feature learning' is an unknown term in machine learning.

We changed feature learning into feature engineering

4. In the section of Result of the proposed method, before they make the comparison with other approaches, they should investigate how the parameters in their approaches influence the prediction and show the best values of these parameters.

Table 3 has been added

Minor points

1. Figures 3 and 4 are not referenced in the paper.

Figure 3 has been referenced twice. Table 1 had not been referenced thus we made the correction

2. The article clearly uses a variety of features, such as chemical structure of drugs and ontology characteristics of gens. But Abstract only mentions that this model uses the side-effect features of drugs.

انجام ندادم چون اصلا اسم روش رو بر اساس اسن انتخاب کردیم

Reviewer #2: In this paper, a new drug repurposing method, namely DRSE, has been proposed by using side effect similarities. To do so, DRSE first combines different sources of features for drugs and diseases and then computes the similarities of these features. After that, the diffusion component analysis is applied to mapping these similarity matrices into a low dimensional space, where the matrix factorization algorithm is adopted to predict the association between drug and disease. However, there are several major concerns to be addressed and thus the paper is not able to be accepted at this moment. Major concerns are listed as below.

1. The title of this paper indicates that the side-effects of drugs are used for drug repurposing. However, from Table 1, in addition to the similarity of side-effects, there are also another four kinds of similarity adopted by DRSE. Hence, the title has to be modified to better describe DRSE.

اسم رو باید خودتون تصمیم بگیرید چی بذارید

2. The formula of Jaccard index function is problematic, as the denominator should be Q\_{01}+Q\_{10}-Q\_{11} for the correct definition of Jaccard index function. Authors should clarify whether it is a typo.

این معادله رو چک کردم مال شما درست بود حالا واقعا نمی دونم

3. When applying DCA to do dimension reduction, how to determine the number of dimensions for the output? Is there any impact to the performance of DRSE? More analysis should be given in the revised version.

این مورد هم باید بررسی بشه که دقیقا چی مد نظرشون هست؟

4. From Table 2, we noted that several methods specifically proposed for drug repurposing had very poor performances in terms of AUPR. An in-depth analysis should be presented to explain this phenomenon. Moreover, regarding DRSE, it was not clear that how DRSE yielded a larger score of AUPR. Which step of DRSE contributed more to the better performance of DRSE in terms of AUPR?

دقیق باید مشخص کنید کدوم مرحله در این روش بهتر عمل می کنه

5. Grammar mistakes should be fixed in the revised version. For example, the percentage symbol was missed after 1.13 in the abstract.

همه چک شد