

Reviews in Computational Biology

3. Peer Reviewing



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January 25th, 2012

What is Peer-Review?

- Helps the authors improve their work

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Internal reports

manuscripts in progress

lecture material

websites

progress reports

progress reports

CVs

important correspondence

conference posters

talks & presentations

Publications

grants & funding applications

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What is Peer-Review?

- Helps the authors improve their work
- Independent evaluation of an academic article, usually by an anonymous expert
- Helps the editor decide what to publish

Why Peer-Review?

- Be a good citizen
- Stay at forefront of research
- Sharpen your critical thinking skills
- Impress the editor

Duties as Referee

- **Assess significance**
- **Verify accuracy**
- **Improve clarity**

Significance

- **Is the topic addressed important/interesting?** (Does the review say why?)
- **How original is the review?** (compared with existing reviews of field?)
- **Are the results reported significant?**

Accuracy

- Are all claims backed by evidence?
- Are the evidences relevant/reliable/sufficient?
- Are methods/results appropriate and well-described?
- Is important relevant work omitted?
- Does the review suffer from any bias?

Improve Clarity

- Is the review well organised?
- Do title/abstract accurately reflect content?
- Right level of detail?
- Language issues or typos?

Courtesy

- Criticise the work, not the authors
- Mention also positive aspects
- Offer constructive criticism
- Don't write things that you would not say in person

Reviewers' Questionnaire

- Some Journals only
- Ask for a ranking, out of 100
- Questions include...

On a scale of 1 to 5

0 Fails by a large amount

1 Fails by a small amount

2 Succeeds by a small amount

3 Succeeds by a large amount

4 Not applicable

*The subject addressed in this article
is worthy of investigation?*

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The information presented was new?

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3 Succeeds by a large amount

4 Not applicable

The conclusions were supported by the data?

Reviewers' Questionnaire

- Some Journals only
- Ask for a ranking, out of 100
- Questions include...

*Is there a financial or other conflict of interest between
your work and that of the authors?*

Reviewers' Questionnaire

- Some Journals only
- Ask for a ranking, out of 100
- Questions include...

Please give a frank account of the strengths and weaknesses of the article

Example

Reviews in Computational Biology – Lecture 3 Peer-Review

Example 1

This is a true example of a Peer-Review submitted to a journal that requires a questionnaire to be completed by each reviewer. For the avoidance of doubt, any references to the authors, reviewer and journal have been removed

Reviewer Recommendation Term:

Major Revision

Overall Reviewer Manuscript Rating:

55/100

Comments to Editor:

For each question, please use the following scale to answer (place an x in the space provided):

"To what extent does the article meet this criterion?"

- 0 Fails by a large amount**
- 1 Fails by a small amount**
- 2 Succeeds by a small amount**
- 3 Succeeds by a large amount**
- 4 Not applicable**

The subject addressed in this article is worthy of investigation.

0 _1 _2 _3 _X4

The information presented was new?

0 _1 _2 _X3 4

The conclusions were supported by the data?

0 _1 X2 _3 _4

Is there a financial or other conflict of interest between your work and that of the authors?

YES __ NO X

Comments to the Editor: Please give a frank account of the strengths and weaknesses of the article

While the subject is not without interest, the paper is very poorly written, both in terms of English usage and also in the clarity of presentation and drawing of meaningful conclusions.

There are various errors in the presented data - for example on p4, it gives the various [results] the wrong way round such that those with the [the modification] are labelled as those without - which make the paper very difficult to read and understand.

The layout is also poor in terms of repeated information - e.g. p6, Sections 2.4.1 and 2.4.2 say practically the same thing - and lack of data and explanation - e.g. it is unclear as to what experiments were undertaken to define conditions, what the parameters for those experiments were and how they were judged to have failed or succeeded.

The general presentation of the paper is sloppy, e.g. Sections 3.2 to 3.3 do not seem to exist, figures are referred to out of order (eg Figure 3c) and some figures are wholly unclear (e.g. figure 1, how can one tell which line represents which set of results?).

One of my major concerns here is that the [key findings] seem to be very selectively presented or not presented at all.

<...>

In general, as well as my more specific comments to the authors, I think the work is interesting but at present it lacks clarity, [clear] results and meaningful discussion.

I would therefore suggest the paper will require a major overhaul to be acceptable for publication.

Comments to the Author:

The authors have chosen an interesting subject for this paper and I looked forward to seeing their results. However, I find that there is a distinct lack of clarity, both within the construction of the argument and critically, within the presentation of results.

Unfortunately, the lack of clarity in the language used in the paper does in many cases prevent complete understanding. There are also many factual errors, which makes the paper difficult to understand, leaving the reader generally confused!

I have detailed some comments and questions below, which I hope will be helpful to the authors, but I should say that this represents a selection of the

issues I found, and is not a comprehensive list of the changes that should be generally made.

My greatest concern is that the data presented are rather selective and that the data for some samples are often omitted without explanation.

1. p1, <...>
2. p1, "successfully used chemically" should be "clinically" and some more up to date references should be given here.
3. p3, it is unclear as to the amount of [the reagent] that was actually used.
4. p3, the [result] should be shown (perhaps it is in Figure 2a?).
5. p4, the labels as presented in the first paragraph are the wrong way round, which makes the rest of the paper confusing if you happen to refer to that paragraph instead of Table 1.
6. p4, one problem I have a lot is that experiments are referred to where methods or chemical quantities were refined but no details are given as to what was being varied, what was being used as a parameter, or how conclusions were being drawn.
7. p5/6 Sections 2.4.1 and 2.4.2 share a lot of repeated information and should be rewritten to give a more concise section.
8. p7 Sections 3.2 and 3.3 do not seem to exist.
9. p7, I'm afraid many of the sentences need rewriting as at present it is very hard to understand the sense of this section. This is also another example of where other experiments <...> are referred to without any details being given.
- .
- .
- .
22. p14, I am unclear as to why the statistical analysis is now [applied]

Questions

1 If you were the Editor of the journal, what would your impressions be after receiving this?

2 Would you give the Author(s) the opportunity to revise the manuscript again?

Iteration Process

- Reviewers' comments to the Editor
- Authors make changes but respond with comments
- Revision with comments sent back to the reviewers
- Editor asks reviewers if they are happy?... If not repeat...

Normal Timescale

- Normally from 1 week to 1 month
- Repeated duration if iterated
- If delayed, the Editor might decide instead

Anonymity

- The rule not the exception
- Exceptionally some journals provide referees comments ...

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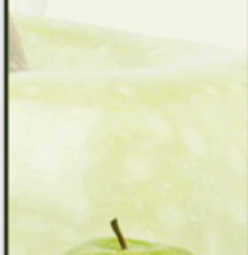
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Biology Direct operates on an open peer-review system, so each of the reviewers' comments accompanied by their name will be reproduced alongside the article, if published. The journal aims to publish all manuscripts that have attracted sufficient interest of Editorial Board members to result in 3 reviews. The reviews may be highly critical of the work or even outright negative, which in itself does not preclude publication should the authors decide to proceed. However, the reviewer also has the option to recommend rejection of manuscripts that have no scientific substance, or do not meet the standards of a scientific work.

Points to consider

Reviewers should refer to items under discussion using paragraph references (eg: Methods, third paragraph), rather than manuscript page numbers, as the pages numbers will not match the final version of the published article.

Reviewers are asked to mark minor comments (spelling, typographical errors, grammatical errors, stylistic suggestions etc) as "Minor issues not for publication" so that, once addressed, the author may remove them from the review.

1. Is the question posed original, important and well defined?

The research question posed by the authors should be easily identifiable and understood.

It is useful to both the editors and authors if reviewers comment on the originality and importance of the study within the context of its field. If the research question is unoriginal because related work has been published previously, please give references.

Reviewers should ask themselves after reading the manuscript if they have learnt something new and if there is a clear conclusion from the study.

2. Are the data sound and well controlled?

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Examples

Reviews in Computational Biology – Lecture 3 Peer-Review

Example 2

This is from "Biology Direct", a journal which has the unusual policy of publishing the peer-reviews alongside the article.

Piriyapongsa et al., *Biology Direct* 2011, 6:61
(<http://www.biology-direct.com/content/6/1/61/>)

Reviewer #1, Dr. Guillaume Bourque, McGill University, nominated by Dr. Jerzy Jurka, had the following comments:

This is an interesting paper that reports an over-representation of conserved TF binding motifs embedded in microRNA precursor sequences. Although this observation is not totally novel (see comment #1 below), the analysis is more comprehensive and the simulations designed to test the significance of this observation are non-trivial. One weakness of the paper in its current form is that it uses too many tables (there are 9) when I think that a few figures (there is currently only 1) would drive some of the points much better (see comment #2).

Comments

#1 I didn't see a reference to the paper "Genomic analysis of human microRNA transcripts", Saini et al. PNAS 2007 which should be cited. The figure 2 of that paper in particular is very similar to the main result of the current paper. You should explain how your work differs and expands on what was done previously.

Response: If you look closely at fig. 2 of the Saini et al paper, you will see that they characterized the regions UPSTREAM (+) and DOWNSTREAM (-) of the pre-miR sequence but they did NOT examine the pre-miR sequence itself! Nowhere in that paper do they demonstrate or even suggest the possibility that TF binding sites may reside within the pre-miR. However, we will add Saini et al to our reference list as providing prior supporting evidence for our own data showing that the regions immediately flanking the pre-miR are also enriched in TF binding sites (albeit to a lesser extent compared to within the pre-miR itself).

#2 There are many tables some with too little information (e.g. Table 3, Table 8), some with information that would be best represented by a figure (e.g. Table 7) and some with too much information that's not directly relevant to the main point (e.g. Table 9). I believe that many of these tables could be replaced by a few multi-panel figures (e.g. Table 3-4-5) that would greatly enhance the readability of the paper.

Response: We have now represented several of the tables by figures. Notably, we simplified the presentation of Table 1 and converted it to a figure (fig. 2) to make it more readable. We also reorganized and simplified some of the text throughout the paper to increase the readability.

#3 One of the first questions I had when I read the first section of the result section (e.g. on page 5) was whether the observation made for precursor sequences was restricted to the actual precursor sequences or extended to the flanking regions.

Could you show this directly in Table 1 (now fig. 2) or, even better, in a figure? I know that you talk about these things later in a different section on the properties of pre- miRNAs with motifs (page 7, par 2) but to me this goes earlier when you're trying to establish the association. Also, instead of Additional file 2, I think that a figure that shows where the motifs are relative to the precursors sequences and that the enrichment doesn't extend beyond those sequences would probably help significantly.

Response: These comments seem to imply that we are claiming that the TF binding sites are restricted to pre-miR sequences and NOT also enriched in flanking regions. However, as stated above, the enrichment does cover both the pre-miR and to a lesser extent, the flanking regions as well.

#4 Also about Table 1 (now fig. 2) and the enrichment, could you also include another control such as gene promoter sequences so that we can see the strength of the enrichment relative to a positive control?

Response: We appreciate the sentiment behind this request, but there are several problems with doing so. First, promoter sequences were used in the construction of the statistical model that defined motif matching and significance, so there is some circularity in using similar sequences for statistical testing. Second, the outcome of such a test is irrelevant to the point of our paper – it does not matter if the density of TF binding sites within pre-miRs is as great, greater than or less than the density within promoters. The fact that they are there AT ALL (much less in the majority of conserved pre-miRs) is surprising, unexpected and deserves to be acknowledged.

#5 Page 6, paragraph 2: Isn't this observation circular? You've looked for pre-miRNA sequences with conserved TFBS and you now observed that they are more conserved on a sequence-level... Wouldn't you have to look for any TFBS (whether conserved or not) and try to make that case?

Response: To some extent, what you are saying is true. However, the pre-miR sequences of highly conserved mature miRNAs do show significant drift in certain regions (e.g. the loop region). Since we showed that the TFBS sites are generally NOT co-located exactly with the mature miRNA sequence (Table 7, now fig. 4), there is no reason to assume that the set of conserved pre-miRs [defined by overall similarity across rat, mouse and human] should show the detailed conservation of exact TFBS motifs that it does, nor that it should extend

to other vertebrate classes. More importantly, we show in a separate analysis that TFBS are highly enriched in pre-miRs even when the analysis includes all non-conserved sites and non-conserved pre-miRs. This analysis also shows that the prevalence for TFBS is greater in conserved pre-miRs than in primate-specific pre-miRs.

#6 Page 7, paragraph 1: Are the cancer pathways enriched for these miRNAs? If not this is not really a critical observation.

Response: Correct. The point is not that they are enriched in cancer miRs, but that they affect many of the most-studied miRs and pathways that investigators care about.

#7 Page 12, par 1 and Page 21, Table 1: “TFBS with experimental support”, why do you mean here by experimental support? Do you mean that the motifs are experimentally supported? What is the source of the other ones? That wasn’t clear to me. Also in that table, what are the two numbers in each cell? Average and St Dev? This needs to be explained in the table caption. Do you mean 715 sets of 1000 sequences or 1000 set of 715 sequences (since that’s the number of human pre-miRNAs that you use).

Response: We have simplified Table 1, changed it to a figure (fig. 2), and rewritten the legend so that it is now clear. We removed the separate data for “with experimental support” as not being essential.

#8 Page 22, Table 2 (now fig. 3): The enrichment is more subtle based on this test (not even 2 fold). Can you comment on this discrepancy in the discussion? Response: There is no discrepancy here. In this case, we are examining all pre-miR sequences fully, rather than only conserved regions, so both the true hits and the baseline “noise” level of hits are higher than when only conserved hits were considered. For example, on the top line of Table 2 (now fig. 3), the average number of TFBS hits in the randomized set is 4016 with a SD of 97. Stated another way, the null distribution of hits expected by chance has a mean of 4016 and SD of 97. What we actually observed in human pre-miRs is an average of 4721 hits. $4721 - 4016 = 705$, which means the observed value is 7.268 SD away from the mean of the null distribution. This is extremely unlikely to have occurred by chance. What is important is the difference between pre-miRs and randomized pre-miR sequences, in terms of Standard Deviations – not the fold difference in hits.

Small comments

Page 3, par 2, line 1: “track is visible” -> “track is available”

Page 3, par 2, line 3: “398 transcription factor binding sites”, this is a bit confusing to me. Do you mean 398 transcription factor binding motifs? The term “binding site” is used to describe a specific instance of a binding motif.

Response: Done.

Page 10, par 2, line 11: “Importantly, since this paper was originally submitted for publication, Zhu et al have reported” -> “Consistent with our findings, Zhu et al. have recently reported”

Response: This erroneously implies that their observations predated ours.

Example 3

An example of a harsh, and not very constructive Peer-Review

This rather poorly written paper reports that an appropriate parallelization of the Farrar SSE2 vectorization of Smith-Waterman is fast on an IBM/CELL (Playstation PS3) processor. There are no novel algorithmic improvements, and the statements about the lack of threading for implementations of the Farrar algorithm (e.g. ssearch35) are incorrect. The paper adds almost nothing new, and misrepresents the current state of the art for the Farrar algorithm

The authors report an implementation of the Farrar Smith-Waterman vectorization for the IBM Cell processor used in the Playstation 3 (PS3). By distributing the vectorized computation across 6 Cell processors, they get speeds of about 50% that of a quad-core Intel processor. They do not compare their implementation to threaded versions of the Farrar algorithm (e.g. ssearch35_t). They also do not provide any detail about the actual algorithmic improvements (it is not clear that, other than threading and breaking up the query sequence, there were improvements).