Peer Review of Papers and Proposals – How to Prepare an Constructive, Fair, Unbiased, Effective Review

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Pubmed Statistics

- Number of Manuscripts cited in Pubmed
- Number of Journals

- Year

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These are my thoughts, certainly biased, certainly incomplete

- 750,000 manuscripts are added to Pubmed per year
- Assume only 1‰ is relevant for your research area
- You’ll have 750 manuscripts to read per year to stay current in your field or about 2 per day!

Scientometrics (2010) 84:575–603
DOI 10.1007/s11192-010-0202-z

The rate of growth in scientific publication and the decline in coverage provided by Science Citation Index

Peder Olesen Larsen · Markus von Ins

Received: 3 September 2009 / Published online: 10 March 2010 © The Author(s) 2010. This article is published with open access at Springerlink.com
Roles of peer review

- Gate keeper to prevent publications of results that are premature
- Prevent publication of conclusions that are not supported by data
- Ensure that scientific content of a manuscript is readily consumable

- Bad papers (in high-impact journals) delay scientific progress
- Overreaching conclusions (even in good papers) delay scientific progress
Benefit of Being a Reviewer

- Acquire a detailed knowledge of the research done – select to review manuscripts that really interest you!

- Developing critical thinking skills – you have to actively search for flaws in the experimental setup and interpretation of data

- You will write better manuscripts and proposals as you learn to judge your own work through the eyes of reviewer
Accepting a Paper for Review

- Large honor but also large responsibility
- Accept only manuscripts that really interest you and where – based on the abstract – you truly are an expert for all or the major part of this manuscript.

- How many manuscripts should I review?
- Quality not quantity! Good reviews take time – don’t overdo it.
- Rule of thumb: 2-3 times the number of papers you publish
- Consider: Can you provide a timely review?
- If you have a conflict of interest, don’t accept the manuscript for review! (even if you would like to know the content)
Pipeline for Paper Review

Agree to Review and Receive Manuscript

First “unbiased” Read of Manuscript
- read the manuscript assuming it is a published paper
- sleep over it to process content thoroughly – no rush!

Critical Analysis with Collecting Notes
- take notes as they come to my mind over a period of up to one week
- return to original literature – cited and not cited – to confirm statements
- critically analyze whether the data presented indeed support the conclusions drawn

Second Read Detailing Notes, Confirming Critical Statements in the Manuscript, Major/Minor classification

Form Opinion based on number and severity of concerns
- Accept, minor revisions, major revisions, reject
- Clearly articulate concerns and provide constructive suggestion to address your concerns even if your verdict is “reject”
- Make sure to spell out aspects of the manuscript you liked

Write and Submit Review

Submit Review
Abstract

- What is the scientific question this manuscript answers?
- In what way is it novel?
- What does it add to the scientific field?
- What is the scientific approach?
- What is the single most important Result?
- What is the single most important Conclusion?

- An abstract should not be a review of the field ⇒ Introduction
- Is the abstract concise? 250 words – not more!
Introduction

- Is the research placed into context accurately?
- Is the scientific question laid out?
- Is the research cited the most relevant and not self-centric?
- Is original research cited, not just review papers?
- Are the critical findings in the original research papers accurately summarized?
- Is the scientific novelty of the work made clear at the end of the introduction?
- Why is this study needed?
- What does it add to the scientific field?
- Is the introduction concise? 750 words – not (much) more!
Methods

- Are the scientific procedures described sound?
- Do the scientific procedure adhere to accepted standards?
- With the information provided, can all experiments be repeated? (!) without contacting the authors
- Nowadays much of this Information will be in the Supplement

- Computational methods: “protocol capture” that contains example files, command lines, scripts
- Links to all databases and benchmark sets used
- Is the computer program source code available for new methods?
Results

- Are the results presented in an logical, easily to understand format – think about text vs. table vs. figure?
- Are the results complete and substantial? For example:
  - results from HTS experiment describing single compound not showing all hit compounds and all compounds screened
  - results of only a single mutants from a scanning analysis
  - computational protein folding simulation tested on one protein
- Is an appropriate error analysis done?
- Are appropriate control experiments described?
- Are the results complete? ⇔ Supplement
  - Coordinates for all structures or models discussed
  - Electronic versions of small molecule database with HTS hits

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Discussion

- Results need to be *critically* analyzed
- Which definite conclusions are supported by the data?
- Which hypothesis are supported but not all alternative explanations are ruled out?
- Which questions do the data not or inconclusively address and why?
- Possibly, what would be an experimental setup to answer such questions?
- Put the results in context of previous research. Which previous finding substantiated? Which previous findings are negated? Which previous findings are expanded?
- Are limitations of the present research clearly labeled?
Conclusion

- Check if indeed the most important findings are summarized
- Check if indeed the most important aspects of the discussion are highlighted
- Should be brief – not more than 250 words
- Can contain a future direction statement
Supplement

- Supplements can often be assessed without downloading the complete manuscript!
- The supplement should therefore
  - Have a title page with manuscript title, authors, contact, place published etc.
  - provide minimal context for all items provided – not just a collection of figures and tables that did not fit into the manuscript
- The supplement should be inclusive – does not need to be text only:
  - self-written scripts or programs, command lines
  - detailed experimental protocols, vendors
  - data and experiments “not shown” in the main text
  - approaches that were tested but failed
  - kinks in the protocol that took tie to work out but were critical
  - databases of for example compounds
  - coordinates for all structures discussed in the manuscript
Final Verdict – Is the Journal a Good Home for this Manuscript?

- Is the audience the group of scientists that needs to hear about this research?
  - Less of a factor nowadays where most people can search and access articles online
  - However, still important – I for example read at least title of articles in selected journals
  - Journal with broad scope (Biochemistry, PLOS ONE, Protein Science, Structure, JACS, …) and sometimes high impact (Nature, Science, Cell) versus focused journals (Journal Bimolecular NMR, Journal of Chemical Information and Modeling)

- Is the research described in an appropriate way for the audience of the journal
  - Level of detail? Knowledge the reader is assumed to possess?
Final Verdict – be Constructive!

- Be constructive. Not just list your concerns but indicate what is needed to address these concerns even if you ultimately reject the manuscript.
- Never get personal! – always provide a fair and objective review of the actual science done.
- The authors invested much work and thought into compiling the manuscript – even if you find major flaws.
- In particular for interdisciplinary projects you find authors miss citations, experiments, conclusions as their expertise is biased by their education – give them a chance to correct!
- Consider: Is impact a reason to decline a manuscript for this journal? (Science versus PLOS ONE)
How to Write a Peer Review – what do other Scientists suggest?

- A paper review should be a clear, efficient persuasive argument directed at (1) the editor, who will be making a decision on the paper, and (2) the authors. Start the review with a brief paragraph that clearly indicates your judgement regarding the fate of the manuscript. If you recommend rejection, mention another journal where it might be appropriate and/or indicate what would be needed to make it publishable (e.g., different analyses, two more years of data, a proper experiment, etc.). Follow the summary paragraph with an elaboration of each general criticism (typically 2-5 points in my reviews). Make these first two sections easy for the editor to understand, evaluate, and briefly paraphrase. Follow this with detailed comments that are more minor and which typically reference particular lines or paragraphs. Clearly label these sections: overview, major concerns, minor concerns.

Matt Ayres, Professor of Biological Sciences, Dartmouth College (adapted from)
How much time to spend on a review?

- Enough to meet your responsibilities and no more, unless you altruistically choose to try to help the authors. I may do more than I need to if I see that the author is a junior scientist, is not a native speaker of English, or is from a country or institution that is under-represented in the literature. I may also do more than I need to if I think the paper has great potential but is not quite there yet or if it seems like the data really should be published but the manuscript has to be fixed first.

- Do a good job with your reviews but do not spend too much time. I try to do reviews with 3 to 4 hours of work (but usually with four separate bouts of work - the first to read it, the second to study it again and outline my response, the third to actually write the review, and the fourth to read it again for tone and content before submitting it.) I spend the most time on papers that I recommend publishing (to convince myself that I am not admitting junk science) and when I am trying to be helpful to authors.

Matt Ayres, Professor of Biological Sciences, Dartmouth College (adapted from)
Conflicts of Interest and Confidentiality

- Conflicts of interest (COI) for reviewing papers are not usually very explicit and the norms seem to be less stringent than, for example, reviewing proposals for the National Science Foundation. Try to avoid reviews from people who are at the same institution, are identified in the acknowledgements, have co-authored papers with the authors, or had a student or mentor relationship with one or more authors.

- Editors cannot always tell if there is a COI, so the potential reviewer has a responsibility to decline if there is a conflict of interest. However, knowing an author (and liking or disliking them) cannot be grounds for declining a review because the world is small and qualified reviewers will frequently know the authors. My view is that being a sometime competitor or cooperator with one or more of the authors also cannot be an automatic conflict of interest for the same reason (but it provides reason for careful consideration).

Matt Ayres, Professor of Biological Sciences, Dartmouth College (adapted from)
When to Accept or Decline Requests to Review?

- Decline any reviews for which you would not be qualified, but do not underestimate your qualifications – there will usually be parts of any good manuscript where your expertise is limited.

- Decline any reviews that you cannot complete within the approximate time frame that the journal expects. You have a responsibility to write as many reviews as reviews that you receive (e.g., review 2-3 papers for every paper of yours that gets evaluated by two reviewers plus an editor).

- If you decline to review a paper, do it promptly and try to suggest one or two other people who could be qualified. Feel free to tell mentors or senior colleagues with related interests to think of you as a potential reviewer to suggest when they get a paper that they do not have time to review. Note that many editors will welcome suggestions for qualified grad students to review papers, especially if it comes from an advisor who offers to work with their student on the review.

Matt Ayres, Professor of Biological Sciences, Dartmouth College (adapted from)
Peer review is at the heart of the processes of not just medical journals but of all of science. It is the method by which grants are allocated, papers published, academics promoted, and Nobel prizes won. Yet it is hard to define. It has until recently been unstudied. And its defects are easier to identify than its attributes. Yet it shows no sign of going away. Famously, it is compared with democracy: a system full of problems but the least worst we have.

**CONCLUSION**

So peer review is a flawed process, full of easily identified defects with little evidence that it works. Nevertheless, it is likely to remain central to science and journals because there is no obvious alternative, and scientists and editors have a continuing belief in peer review. How odd that science should be rooted in belief.
Does Peer Review Work?

Journals using the following classic system. The editor looks at the title of the paper and sends it to two friends whom the editor thinks know something about the subject. If both advise publication the editor sends it to the printers. If both advise against publication the editor rejects the paper. If the reviewers disagree the editor sends it to a third reviewer and does whatever he or she advises. This pastiche—which is not far from systems I have seen used—is little better than tossing a coin, because the level of agreement between reviewers on whether a paper should be published is little better than you’d expect by chance.¹

That is why Robbie Fox, the great 20th century editor of the *Lancet*, who was no admirer of peer review, wondered whether anybody would notice if he were to swap the piles marked ‘publish’ and ‘reject’. He also joked that the *Lancet* had a system of throwing a pile of papers down the stairs and publishing those that reached the bottom. When I was editor of the *BMJ* I was challenged by two of the cleverest researchers in Britain to publish an issue of the journal comprised only of papers that had failed peer review and see if anybody noticed. I wrote back ‘How do you know I haven’t already done it?’²

Peer review might also be useful for detecting errors or fraud. At the *BMJ* we did several studies where we inserted major errors into papers that we then sent to many reviewers.³,⁴ Nobody ever spotted all of the errors. Some reviewers did not spot any, and most reviewers spotted only about a quarter. Peer review sometimes picks up fraud by chance, but generally it is not a reliable method for detecting fraud because it works on trust. A major question, which I will return to, is whether peer review and journals should cease to work on trust.
People have a great many fantasies about peer review, and one of the most powerful is that it is a highly objective, reliable, and consistent process. I regularly received letters from authors who were upset that the BMJ rejected their paper and then published what they thought to be a much inferior paper on the same subject. Always they saw something underhand. They found it hard to accept that peer review is a subjective and, therefore, inconsistent process. But it is probably unreasonable to expect it to be objective and consistent.

If I ask people to rank painters like Titian, Tintoretto, Bellini, Carpaccio, and Veronese, I would never expect them to come up with the same order. A scientific study submitted to a medical journal may not be as complex a work as a Tintoretto altarpiece, but it is complex. Inevitably people will take different views on its strengths, weaknesses, and importance.

Sometimes the inconsistency can be laughable. Here is an example of two reviewers commenting on the same papers.

Reviewer A: ‘I found this paper an extremely muddled paper with a large number of deficits’

Reviewer B: ‘It is written in a clear style and would be understood by any reader’.

This—perhaps inevitable—inconsistency can make peer review something of a lottery. You submit a study to a journal. It enters a system that is effectively a black box, and then a more or less sensible answer comes out at the other end. The black box is like the roulette wheel, and the prizes and the losses can be big. For an academic, publication in a major journal like Nature or Cell is to win the jackpot.
Peer Review is Biased

The evidence on whether there is bias in peer review against certain sorts of authors is conflicting, but there is strong evidence of bias against women in the process of awarding grants. The most famous piece of evidence on bias against authors comes from a study by DP Peters and SJ Ceci. They took 12 studies that came from prestigious institutions that had already been published in psychology journals. They retyped the papers, made minor changes to the titles, abstracts, and introductions but changed the authors’ names and institutions. They invented institutions with names like the Tri-Valley Center for Human Potential. The papers were then resubmitted to the journals that had first published them. In only three cases did the journals realize that they had already published the paper, and eight of the remaining nine were rejected—not because of lack of originality but because of poor quality. Peters and Ceci concluded that this was evidence of bias against authors from less prestigious institutions.

The editorial peer review process has been strongly biased against ‘negative studies’, i.e. studies that find an intervention does not work. It is also clear that authors often do not even bother to write up such studies. This matters because it biases the information base of medicine. It is easy to see why journals would be biased against negative studies. Journalistic values come into play. Who wants to read that a new treatment does not work? That’s boring.

We became very conscious of this bias at the BMJ; we always tried to concentrate not on the results of a study we were considering but on the question it was asking. If the question is important and the answer valid, then it must not matter whether the answer is positive or negative. I fear, however, that bias is not so easily abolished and persists.
Peer Review is Easily Abused and Ideas for Improving Peer Review

There are several ways to abuse the process of peer review. You can steal ideas and present them as your own, or produce an unjustly harsh review to block or at least slow down the publication of the ideas of a competitor. These have all happened. Drummond Rennie tells the story of a paper he sent, when deputy editor of the New England Journal of Medicine, for review to Vijay Soman. Having produced a critical review of the paper, Soman copied some of the paragraphs and submitted it to another journal, the American Journal of Medicine. This journal, by coincidence, sent it for review to the boss of the author of the plagiarized paper. She realized that she had been plagiarized and objected strongly. She threatened to denounce Soman but was advised against it. Eventually, however, Soman was discovered to have invented data and patients, and left the country. Rennie learnt a lesson that he never subsequently forgot but which medical authorities seem reluctant to accept: those who behave dishonestly in one way are likely to do so in other ways as well.

have been tested experimentally. The options include: standardizing procedures; opening up the process; blinding reviewers to the identity of authors; reviewing protocols; training reviewers; being more rigorous in selecting and deselected reviewers; using electronic review; rewarding reviewers; providing detailed feedback to reviewers; using more checklists; or creating professional review agencies. It might be, however, that the best response would be to adopt a very quick and light form of peer review—and then let the broader world critique the paper or even perhaps rank it in the way that Amazon asks users to rank books and CDs.
Ideas for Improvement of Peer Review

The next important step was hearing the results of a randomized trial that showed that blinding reviewers to the identity of authors improved the quality of reviews (as measured by a validated instrument). This trial, which was conducted by Bob McNutt, A T Evans, and Bob and Suzanne Fletcher, was important not only for its results but because it provided an experimental design for investigating peer review. Studies where you intervene and experiment allow more confident conclusions than studies where you observe without intervening.

This trial was repeated on a larger scale by the BMJ and by a group in the USA who conducted the study in many different journals. Neither study found that blinding reviewers improved the quality of reviews. These studies also showed that such blinding is difficult to achieve (because many studies include internal clues on authorship), and that reviewers could identify the authors in about a quarter to a third of cases. But even when the results were analysed by looking at only those cases where blinding was successful there was no evidence of improved quality of the review.

Our randomized trial of training reviewers had three arms: one group got nothing; one group had a day’s face-to-face training plus a CD-rom of the training; and the third group got just the CD-rom. The overall result was that training made little difference. The groups that had training did show some evidence of improvement relative to those who had no training, but we did not think that the difference was big enough to be meaningful. We cannot conclude from this that longer or better training would not be helpful. A problem with our study was that most of the reviewers had been reviewing for a long time. ‘Old dogs cannot be taught new tricks’, but the possibility remains that younger ones could.