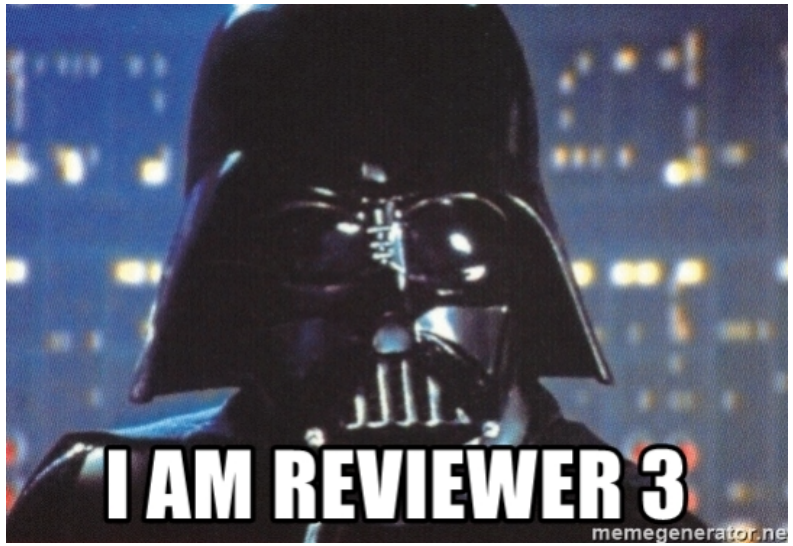
Navigating peer review



December 28, 2020

What is ‘peer-review’?

- ‘The process of subjecting a scholarly work to the scrutiny of others who are experts in the field’.
- In science, this means that the (written) opinion of at least two scientists active in the field is sought.
  - Decision to publish the work (or fund the research) is made by an editor with consideration of these opinions

Integrative Biology

Peer Review Process

First hurdle: the handling Editor

- Editor will skim read your paper (title, cover letter, abstract, first and last sections of intro and discussion, figures)
- Options: desk rejection or peer review
- Editor is evaluating: impact, interest to readers of the journal, potential citations, general quality
- Most good journals desk reject the vast majority of new submissions
- If your paper goes out for peer review, celebrate!

Reviewer choice

- Editor usually makes a list of 6-8 potential reviewers
  - Usually about half from your suggestions (and even then, they'll be careful to look for conflicts)
  - Won't necessarily avoid the reviewers you ask them to avoid!
  - Will use your reference list, internet search etc. to identify potential reviewers
    - Tip – they will probably know the famous people in your field (and they are probably busy). Try to suggest less well-known people you think would do a good job.
  - May ask editorial board members for advice
- Finding reviewers is hard!
  - Editors will occasionally reject a paper if they cannot find reviewers (may indicate journal's audience isn't interested).

Reviews returned to Editor

- Handling editor reads reviews and re-reads manuscript
- Handling editor crafts decision letter
- In large journals, this decision letter will go to Editor-in-Chief who will usually sign off or may add to decision letter (variable input)
- Journal sends decision letter to corresponding author

Components of a decision letter

- Editor and handling editor's summary of manuscript and reviews
- Decision (accept, revise, reject)
- Reviews from 2-4 peers
- Timeline for revisions (often 3 or 6 months)

Interpreting a Decision Letter

- Options:
  - Accept as is (never happens on first round)
  - Minor revisions (this is cause for celebration!)
  - Major revisions
  - Reject-Resubmit
  - Reject (*revise* and submit elsewhere)
- 'Major Revisions' and 'Reject-Resubmit'
  - The line between major and minor revisions is subjective, don't be discouraged
  - Some journals keep their turnaround time statistics low by automatically rejecting everything on first submission (even if it's just minor revisions needed).
  - The 'new' submission will be hopefully be reviewed (and accepted) quickly = fast advertised 'time-to-decision' for the journal!

Responding to the reviewers

- Give it time!
- Always treat the reviewers respectfully (they are volunteers, and we can assume they want to make the paper better)
  - Ultimately, the reviewer is your friend.
  - If something isn't clear, or they didn't understand it, that's your fault, not theirs.
  - ALWAYS change the small things, unless it drastically shifts meaning
  - Balance between response to reviewers and change in the text
  - Be honest. Sometimes the flaw really is fatal.
  - Sometimes removing something is the best approach
  - Don't be defensive or take pot-shots at reviewers

  Discussion: What is the best way to handle unfriendly or off-base reviews?

Structure of a response to reviewer's document

- Cover letter to editor
  - Thank editors and reviewers for their time and support
  - Restate importance and novelty of work
  - Describe main changes, with reference to editor's summary
- Detailed response to EVERY SINGLE reviewer comment
  - Include line and page numbers, quotes from revised manuscript as appropriate
  - Upbeat, grateful, and non-defensive tone
  - Be tactful in pointing out reviewer errors
  - ***Do not*** use this document to convince the editor that the reviewers are wrong or unfriendly

Principle: This letter is for the editor, who by this point is your number one advocate and champion

Take-away points on responding to reviews

- The acceptance is yours to lose if you are invited to resubmit
- Put in the same effort as writing the manuscript
  - No sloppy errors, typos, or incorrect line references, professional formatting
  - Differentiate reviewer comment and response clearly
- Every point should be thoughtfully and RESPECTFULLY addressed – reviewers are your colleagues
- Quote changes in text with line numbers
- Summarize main changes in letter to editor

Principle – make it as easy as possible for the editor to evaluate the changes!

YOU can be a reviewer!

- Practice by doing mock peer reviews of colleagues' work before they submit it
- Once you've published a good paper in a journal as corresponding author, you are probably 'on the list'
- Present at international meetings, introduce yourself to editors there
- If you interact with a journal or editor regularly, email the (Associate) Editor and volunteer your services.
  - Be sure to give a clear indication of your expertise.
  - Include a CV
- Tell your advisor that you would like mentored experience in reviewing
- Reviewing is a great way to improve your own writing and to learn about new and exciting science
- If you are a good reviewer, you will get a lot of requests. Be prepared to say 'no'!

How to review a paper efficiently

- Read it first, and think about it for a few days
- Then read it critically, making notes.
- Key things to cover:
  - Do I understand it all? What don't I understand?
  - Is the context in the introduction and discussion appropriate?
  - Is the question interesting? Is it clearly stated? Do the authors actually answer it?
  - Are the methods appropriately described? Are they easy to follow? Are they appropriate?
  - Are the results complete? Interesting? Are the values/results consistent?
  - Are the conclusions supported by the data?
- Is there anything the authors can do to make this ms even better?
- Remember: you are making a recommendation, not a decision.

Components of a submitted review

- Comments for the editor
  - A general assessment, and perhaps an explanation for why you made the recommendation you did
  - Identify any 'must do's
  - Identify any ethical or methodological problems that should kill the paper (fatal flaws)
  - Your decision recommendation with justification (do not put this in author's section!)
- Comments for the Author
  - A general assessment of the ms, including summary of main conclusion, impact and novelty, interest to readers of the journal, and summary of main issues that need to be addressed (ideally with assessment of how critical they are to the conclusions)
  - Expanded description of main concerns and suggestions
  - Specific comments: line by line analysis of any minor comments

Example reviews and responses (some are edited for anonymity)

This is a nice little manuscript that demonstrates (contrary to popular opinion) that Yeti can be freeze-tolerant (at least those in mid-winter). The authors demonstrate that most Yeti* survive freezing, at least briefly. In mid-winter, the Yeti* can survive down to -20C for one hour. The authors also demonstrate that there is a mid-winter peak in osmolality and glycerol levels, as well as a concomittant decrease in water content and supercooling point. It is unfortunate that it was not possible to measure these parameters in the summer for a comparison, but apparently this species was difficult to find, and the trends are apparent and statistically significant.*

In the abstract, the authors state that: "All late-winter Yeti survived being frozen for 24h at -9°C; 50% survived one week." I cannot find the data in the manuscript that shows that survival after one week at -9C.*

We thank the reviewer for their positive comments. Indeed, measuring cold tolerance during the summer would probably be irrelevant (as well as nearly impossible!) because of their life cycle, we are glad the referee appreciates this.
Regarding the survival for one week frozen at -9°C, this experiment is in the methods (paragraph beginning line 104), and the results are presented (in the text only) on line 128:
"All *Yeti** in April and March survived being frozen at -8.6°C or -9.0 ±0.7°C for 24h, and 8/12 of March-collected *Yeti** survived frozen for one week at -9.0°C"
We are sorry the reviewer missed this in the text, but there isn't much we can do to present the data in any different way, so we have left it as is.

*organism name changed

The simultaneous use of months and terms such as "autumn", "winter", and "spring" is confusing. I recommend either axing the above terms or adding a statement defining the terms within the context of your study (for example: Autumn refers to those Yeti that were field-collected during October and November, winter refers to those Yeti* collected between December and January, etc…).*

We apologise for the confusion about months and seasons. For the majority of the methods and results, we specify by month, and we then generalise these to season in the discussion. As the referee suggests, we now specify which months belong to which seasons at two key points:
Line 88 in the Methods, we specify:
"We cooled Yeti* from 4°C (winter - January, February, March) or 20°C (spring - April, May and autumn - November) to 0°C at 1.0°C·min^{-1}, and 0.5°C·min^{-1} (or 0.25 °C ·min^{-1} before July 2016) thereafter."
And line 141 at the beginning of the Discussion:
"…but by midwinter (January and February), *Abominabilis** sp. can survive at least one week …"

Might also be good to discuss limitations, given your sample size (for example, it is likely difficult to detect changes in glycerol concentrations with such large SEMs).

Because our key conclusions are qualitative (whether or not the Yeti* survived freezing), we don't expend a great deal of space on the nitty-gritty of the limitations of sample size. We agree that this is a bit egregious in the case of the glycerol (which does have a large variance… although we still detect some differences). We now address this in the discussion, and take the opportunity to also provide some context for the observation that even a comparison with higher statistical power wouldn't affect the biological relevance, by comparing the 15 mM increase to other species (line 180):
"Although our small sample sizes (and consequently high variance) mean that we probably lack statistical power to detect small differences in [glycerol], the magnitude of the change from summer to winter (~15 mM) is substantially lower than the large changes observed in other Yeti*; for example, the freeze-avoidant *A. snowmanii** accumulates c. 0.5 M glycerol."

72) Add "lower" to say: "lower temperature at which 50% of individuals…"
Done

73) Change "We placed Yeti individually…" to "We individually placed Yeti*..."*
This wording was deliberate. 'We placed *Yeti** individually' implies that they were in their own tubes; 'we individually placed *Yeti**' talks only about how we placed them, not explicitly how many per vial. No change.

74) Seems tricky to get a TC in contact with a Yeti! Nice work!*
Thanks!

78) I find this section confusing. Perhaps say something like: "We cooled Yeti from 4 °C (if collected between Jan and March) or 20 °C (if collected between April and November) to 0 °C at 1 °C/min.*
We've modified this sentence. It now reads (line 98):
"We began cooling at 21°C (for March measurements), 15°C (November), or 4°C (January …"

79) As written it sounds like you cooled the Yeti twice; once at 1 °C/min and then re-warmed them and cooled the same Yeti* again at 0.5 °C/min. Is this correct? If so, perhaps explain how you controlled for cold hardening between runs.*
We definitely only cooled them once! We've changed this to read (line 101)
"…or to 0°C at 1°C·min^{-1}, and 0.5°C·min^{-1} thereafter…", which is hopefully clearer.

*organism name changed

Editor's summary – highlights key points to respond to

"We have now received two reviews of your manuscript "Cold-adaptation increases rates of nutrient flow and metabolic plasticity during cold exposure in Drosophila melanogaster" Both of the reviewers have raised some valid concerns.

Reviewer 1 raises the important point that selection for chill coma recovery time may actually result in changes in other traits (vigilance or righting propensity) rather than cold tolerance, and points out that it would be valuable to know if the different lines also differ in other cold tolerance traits such as survival or CTmin and/or to demonstrate that there is no difference in spontaneous activity. I agree with this concern, and suggest that you add such data (or cite appropriate studies of the same selection lines) to reassure the reader that there are genuine differences in cold tolerance among selection lines.

I also agree with reviewer 2 that you need to consider changes in body mass of selected lines, or at least reassure the reader that changes in mass do not confound your conclusions."

These are critical and MUST be addressed thoughtfully

“Dear Dr. Costa, Dr. White, and reviewers,

Thank you for your constructive comments, and the opportunity to revise the manuscript. The comments have guided us in making changes that we feel have improved the manuscript considerably, and we hope you agree. We believe that this work is of broad general significance to biologists because it addresses fundamental mechanisms underpinning life history evolution in response to stress. Cold is a ubiquitous feature of temperate environments and strongly drives ecology and evolution, and this work suggests that cold adaptation may invoke resource-based trade-offs that reduce the ability to invest in other life history traits, through raised metabolic costs of cold hardiness. This work is novel in revealing for the first time the differences in nutrient flux that underpin the metabolic costs of cold hardiness, and suggesting the nature of benefits that cold hardy flies may experience. Experiments examining metabolic flux in live animals are still relatively rare due to the difficulty of these techniques, particularly in small animals like flies, and this is the first information on metabolic flux in live animals during a stress exposure. The power of this study lies in combining innovative biochemical techniques for measuring metabolic flux *in vivo*, with an artificial selection experiment in a model organism (*Drosophila melanogaster*), allowing us to rapidly generate divergent, genetically based, and ecologically relevant cold hardiness phenotypes. Thus we have brought together cutting edge techniques in biochemistry and evolutionary biology to answer an important ecological question, namely how do extreme low temperatures shape patterns of nutrient allocation in ectotherms. We now highlight these areas of novelty and broad interest in the abstract, introduction, and conclusions.

The reviewers were concerned about the potential for mass differences between lines. While this manuscript was in revision, a related piece of work was published that presented an extensive study of metabolic rates, growth rates, and body size differences among the lines also used in this paper. The related manuscript shows that there are no mass differences among lines at their normal rearing temperature (used in the current study), and that the mass-scaling of metabolic rate does not differ among lines. We are thus confident that mass differences among lines do not contribute to the elevated nutrient flux rates, as we describe in our response to the reviewer's comment. The metabolic rate results from the related manuscript are concordant with our observations in the current manuscript, and the current manuscript extends these findings to the biochemical level showing the alterations to metabolic flux that underpin the whole-organism metabolic rates. We have updated the introduction and discussion to include the related manuscript.

The other major concern raised about our manuscript was that the differences in the chill coma recovery phenotype may results from differences in activity levels or motivation to stand among lines. We agree that differences in activity may contribute to the fast-recovery phenotype, in fact we argue that these differences in activity are likely to part of the phenotype selected for during latitudinal adaptation in the wild. However, we demonstrate through additional experiments that the differences in recovery times among lines persist when flies are continually pestered during recovery, presumably providing ample motivation to wake up as soon as they are able and thus eliminating the reviewer's concern about us artificially selecting for motivation to behave at all rather than an ecologically reasonable chill coma recovery phenotype.

We also substantially rearranged the methods to make the rationale and flow of experiments more clear. We think this is a big improvement and thank the reviewers for the useful suggestions.

Sincerely,

Caroline Williams, on behalf of the authors"

Reviewer comment:

"While chill coma recovery time has been shown to differ along latitudinal gradients etc. it is also a controversial measure of cold tolerance. Chill coma recovery time consists of two processes a) the physiological ability to regain posture, and b) the "psychological" drive to regain posture. The consequence of this is that flies can often stand before they actually do stand (because they just haven found the "motivation"). For this reason selection for chill coma recovery time could simply be selection for increased vigilance?"

Author response:

"Chill coma recovery time varies clinally along environmental temperature gradients consistent with local adaptation (e.g. David et al. 2003), and thus appears to be a target of natural selection. The association between fast recovery from chill coma and high metabolic rates was found both in the artificial selection lines described in the current manuscript, and also in an independent set of lines (the Drosophila melanogaster genetic reference panel), suggesting that this association is not an artifact of the artificial selection process (Williams et al. in press Integrative and Comparative Biology). We now point this out on L444-446:

"We also found increased metabolic rates were associated with faster chill coma recovery in naturally occurring fly genotypes (Williams et al. 2016), further supporting the generality of this phenomenon."

Author response continued…

"The physiological and behavioral (i.e. motivation) aspects of chill coma recovery time are difficult to separate, and to some degree the relative contributions of these two aspects are beyond the scope of this paper and do not impact the conclusions. However, a few lines of evidence suggest that the differences in chill coma recovery time between the lines have a physiological basis:

1. Divergence in the cold-induced plasticity of all the metabolic traits measured suggests that the responses are functionally related to cold. If differential responses of cold-selected flies were unrelated to cold hardiness but originated solely from differences in activity levels, we would expect reaction norms to be parallel and only the intercept to change.
2. To remove the role of motivation in determining standing time, we repeated our chill coma recovery assays while continuously disturbing the flies by tapping their petri dish every 15s during recovery, to increase the motivation to stand if flies were physiologically able. The first replicate population had unfortunately become compromised in the intervening time between submitting this manuscript and receiving these reviews and could not be re-assayed, so we were only able to assess replicate population 2. Within replicate population 2, the recovery times were similar to those previously measured in undisturbed flies (cold hardy: 9.36 ± 0.34 min (mean ± SEM), range 7.23-12.47, n=19 flies; cold-susceptible: 17.53 ± 1.4 min, range 13.04-30.19, n=8 flies), suggesting that the difference in recovery times is not due to differences in motivation to stand and be active, but the ability to stand and be active. To repeat the assays on all lines would require re-ordering the lines – we are willing to do this if the reviewers and editor deem it necessary, but we do not think that the results will change. "

