Photoreceptor physiology and evolution: Cellular and molecular basis of rod and cone phototransduction

Trevor D Lamb
DOI: 10.1113/JP282058

Corresponding author(s): Trevor Lamb (trevor.lamb@anu.edu.au)

The following individual(s) involved in review of this submission have agreed to reveal their identity: Rick H Cote (Referee #2)

Review Timeline:

| Event                  | Date      |
|------------------------|-----------|
| Submission Date        | 06-Dec-2021|
| Editorial Decision     | 14-Feb-2022|
| Revision Received      | 12-Mar-2022|
| Accepted               | 29-Mar-2022|

Senior Editor: Ian Forsythe
Reviewing Editor: Omar Mahroo

Transaction Report:

(Note: With the exception of the correction of typographical or spelling errors that could be a source of ambiguity, letters and reports are not edited. Depending on transfer agreements, referee reports obtained elsewhere may or may not be included in this compilation. Referee reports are anonymous unless the Referee chooses to sign their reports.)
Dear Dr Lamb,

Re: JP-SR-2021-282058 "Photoreceptor physiology: Cellular and molecular basis of rod and cone phototransduction" by Trevor D Lamb

Thank you for submitting your invited Review-Symposium to The Journal of Physiology. It has been assessed by a Reviewing Editor and by 2 expert referees and I am pleased to tell you that it is considered to be acceptable for publication following satisfactory revision.

Please advise your co-authors of this decision as soon as possible.

The reports are copied at the end of this email. Please address all of the points and incorporate all requested revisions, or explain in your Response to Referees why a change has not been made.

NEW POLICY: In order to improve the transparency of its peer review process The Journal of Physiology publishes online as supporting information the peer review history of all articles accepted for publication. Readers will have access to decision letters, including all Editors' comments and referee reports, for each version of the manuscript and any author responses to peer review comments. Referees can decide whether or not they wish to be named on the peer review history document.

I hope you will find the comments helpful and have no difficulty in revising your manuscript within 4 weeks.

Your revised manuscript should be submitted online using the links in Author Tasks Link Not Available. This link is to the Corresponding Author's own account, if this will cause any problems when submitting the revised version please contact us.

The image files from the previous version are retained on the system. Please ensure you replace or remove any files that have been revised. Your revised submission should include:

- A Word file of the complete text (including figure legends any Tables);
- An Abstract Figure (with legend in the Article file)
- Each figure as a separate, high quality, file;
- A full Response to Referees;
- A copy of the manuscript with the changes highlighted.
- Author profile. A short biography (no more than 100 words for one author or 150 words in total for two authors) and a portrait photograph of the two leading authors on the paper. These should be uploaded, clearly labelled, with the manuscript submission. Any standard image format for the photograph is acceptable, but the resolution should be at least 300 dpi and preferably more.

You may also upload:

- A 'Cover Art' file for consideration as the Issue's cover image;
- Appropriate Supporting Information (Video, audio or data set https://jp.msubmit.net/cgi-bin/main.plex?form_type=display_requirements#supp).

To create your 'Response to Referees' copy all the reports, including any comments from the Reviewing Editor into a Word, or similar, file and respond to each point in colour or CAPITALS and upload this when you submit your revision.

I look forward to receiving your revised submission.

If you have any queries please reply to this email and staff will be happy to assist.

Yours sincerely,

Ian D. Forsythe
Deputy Editor-in-Chief
The Journal of Physiology
https://jp.msubmit.net
http://jp.physoc.org
The Physiological Society
Hodgkin Huxley House
30 Farringdon Lane
London, EC1R 3AW
UK
http://www.physoc.org
http://journals.physoc.org
REQUIRED ITEMS:

-Please include an Abstract Figure. The Abstract Figure is a piece of artwork designed to give readers an immediate understanding of the Review Article and should summarise the main conclusions. If possible, the image should be easily 'readable' from left to right or top to bottom. It should show the physiological relevance of the Review so readers can assess the importance and content of the article. Abstract Figures should not merely recapitulate other figures in the Review. Please try to keep the diagram as simple as possible and without superfluous information that may distract from the main conclusion of the Review. Abstract Figures must be provided by authors no later than the revised manuscript stage and should be uploaded as a separate file during online submission labelled as File Type 'Abstract Figure'. Please ensure that you include the figure legend in the main article file. All Abstract Figures will be sent to a professional illustrator for redrawing and you may be asked to approve the redrawn figure before your paper is accepted.

-Your MS must include a complete "Additional information section" with the following 4 headings and content:

Competing Interests: A statement regarding competing interests. If there are no competing interests, a statement to this effect must be included. All authors should disclose any conflict of interest in accordance with journal policy.

Author contributions: Each author should take responsibility for a particular section of the study and have contributed to writing the paper. Acquisition of funding, administrative support or the collection of data alone does not justify authorship; these contributions to the study should be listed in the Acknowledgements. Additional information such as 'X and Y have contributed equally to this work' may be added as a footnote on the title page.

It must be stated that all authors approved the final version of the manuscript and that all persons designated as authors qualify for authorship, and all those who qualify for authorship are listed.

Funding: Authors must indicate all sources of funding, including grant numbers. If authors have not received funding, this must be stated.

It is the responsibility of authors funded by RCUK to adhere to their policy regarding funding sources and underlying research material. The policy requires funding information to be included within the acknowledgement section of a paper. Guidance on how to acknowledge funding information is provided by the Research Information Network. The policy also requires all research papers, if applicable, to include a statement on how any underlying research materials, such as data, samples or models, can be accessed. However, the policy does not require that the data must be made open. If there are considered to be good or compelling reasons to protect access to the data, for example commercial confidentiality or legitimate sensitivities around data derived from potentially identifiable human participants, these should be included in the statement.

Acknowledgements: Acknowledgements should be the minimum consistent with courtesy. The wording of acknowledgements of scientific assistance or advice must have been seen and approved by the persons concerned. This section should not include details of funding.

-Please upload separate high quality figure files via the submission form.

-Author profile(s) must be uploaded via the submission form. Authors should submit a short biography (no more than 100 words for one author or 150 words in total for two authors) and a portrait photograph of the two leading authors on the paper. These should be uploaded, clearly labelled, with the manuscript submission. Any standard image format for the photograph is acceptable, but the resolution should be at least 300 dpi and preferably more. A group photograph of all authors is also acceptable, providing the biography for the whole group does not exceed 150 words.

EDITOR COMMENTS

Reviewing Editor:

This is a very clearly written review, synthesising key data, providing wide-ranging insights, and, perhaps uniquely, combining a detailed description of the molecular basis for rod and cone phototransduction, its kinetics and the evolutionary origin of the main molecular players. I think this will be of great interest to readers in the fields of retinal physiology, visual neuroscience, sensory transduction and others. The reviewers, who are highly positive in their reviews, have highlighted some areas where the manuscript might be improved and/or made more accessible (as well as typographical errors). We would be grateful if the author might consider making minor revisions in light of these. Some of Reviewer 2's comments are very pertinent, but the detail requested is probably beyond the scope of the length of a symposium review, and so do not need to be acted on in full.
Senior Editor:

Dear Trevor, thank you for a fascinating Review. In addition to the minor issues raised by the referees, and to increase the appeal of your article to the widest audience, please re-write your abstract along the following lines. It should contain more factual information about the findings of your literature review and mention key insights. Avoid letting the abstract be a simple outline of the review topics, instead give your readers the condensed information and come to a clear conclusion in the last sentence. Avoid saying more work needs to be done as the conclusion (in the abstract) it is always true, but lacks a hook to attract a reader from pubmed to your JP article. Thanks again, this article should be well cited.

-----------------

REFEREE COMMENTS

Referee #1:

This review entitled "Photoreceptor physiology: Cellular and molecular basis of rod and cone phototransduction" by Trevor Lamb describes the molecular mechanisms of phototransduction in rod and cone photoreceptors, kinetic models linking phototransduction mechanisms to photoreceptor response kinetics and the evolutionary origin of rod and cone photoreceptors. Overall, this is a beautifully written and clear review, which is a delight to read both in its scientific depth as well as its style. I have only a few comments related mainly to deepening the presentation in a few important places, where the reader would need a bit more tools to understand the contents profoundly.

Comments:

Page 4: The 50-fold difference in kinetics between amphibian rods and vertebrate rods is mentioned to be due to differences in outer segment volume and temperature. It would be really nice to explain this to the reader in more depth by briefly explaining which parameters of the amplification constant are sensitive to temperature and to the outer segment volume and how. E.g. correlating the temperature effects to the diffusion speed of proteins and their impact on the speed of phototransduction could be helpful for the reader (see Calvert et al. Nature 2001). Similarly brief explanation for the connection between photoreceptor volume and response kinetics would be very useful.

Page 5: "Difference in cone phototransduction parameters". It would be very nice to expand a bit the discussion on how the speed of vision related to light adaptation. Now it is not obvious to the reader how light-adapted humans can reach extremely high flicker fusion frequency. It would be useful to expand this appropriately to the reader and give insights about how light adaptation connects to the kinetics parameters of photoresponses.

Page 7: Currently there are contradicting numbers in the literature for the number of transducing molecules activated by a single rhodopsin - some of which the author points out. The author sides now with particular estimates but it would be useful for the reader to understand where the discrepancy arises (if possible. Is the difference in analysis methods, different recording conditions or what?

Minor:

Fig 3 is missing panel labels (A, B & C)

Referee #2:

See attached file.

END OF COMMENTS

Confidential Review

06-Dec-2021
Summary:

This manuscript presents a wide-ranging view of our current understanding about the cellular and molecular mechanisms underlying the first steps in vision, and how rods and cones have evolved to respond to photopic and scotopic levels of illumination. The level and clarity of the presentation is outstanding for a wide audience of researchers in sensory transduction.

Major points:

1. Given the current debate in the literature about the rate and extent of transducin activation by each photoactivated rhodopsin, Section 2.6 would benefit from a fuller discussion of the various estimates of the in vivo rate of transducin activation that are based on measurements of the single photon response (where the number of R* is precisely known) compared with dim and bright flash response estimates. While the biochemical literature on this topic is extensive, most in vitro studies are conducted under conditions that are non-physiological (e.g., protein concentrations orders of magnitude lower than found in the outer segment).

2. The review would be strengthened if there was a greater connectedness between molecular mechanisms of phototransduction (Section 2) and the evolution of rod and cone isoforms of the central proteins involved in visual transduction (Section 3). Specifically, a review of the electrophysiological properties of rods and cones throughout vertebrate evolution would help connect these two sections. Since Korenbrot’s 2012 review on this topic, there have been significant advances in our understanding of species differences in rod and cone physiology that could be mentioned (e.g., Morshedian and Fain, 2017 on lamprey phototransduction).

3. The dates discussed at the beginning of Section 3 regarding the evolution of metazoans and deuterostomes are much older than in recent analyses based on genome scale data, which estimate the origin of Bilateria (the split between deuterostomes and protostomes) by at least 700 Mya, and deuterostomes and chordates must be more recent than that. In the text, 700 Mya is given for the origins of deuterostomes, but this is probably more like 600 Mya [dos Reis et al. (2015) Current Biol. 25, 2939-2950; Dohrmann and Worheide (2017) Scientific Reports 7, 3599]. The timing given for the proto-vertebrate ancestor (600-500 Mya) is more consistent with recent work. Citations for the assertions made in Section 3.1 about the general features of vertebrate evolution are recommended to support the dates for speciation events.

4. An additional Section 3.6 that evaluates the evaluation of rod and cone isoforms for their functional relevance is suggested. Of the genes described in Fig. 7, which ones are candidates contributing to the differences in excitation, inactivation, and dark and light adaptation of rods and cones? In Section 2.4, the author suggests that the levels of RGS9 may account for faster cone photoresponse recovery and points out limitations in biochemical studies of cone phototransduction. However, the evolutionary analysis of rod and cone isoforms could also be evaluated for the functional implications of some phototransduction proteins having different isoforms while others do not.

Secondary points:

1. Fig. 2 has a minor inconsistency in that it depicts rod PDE6 (i.e., α and β subunits) whereas cone PDE6 is a homodimer. Otherwise, the figure accurately represents the activation components shared by rods and cones.

2. Fig. 3. It is suggested to remove the units for time on the x-axis on Fig. 3, since the photoresponse kinetics vary for rods and cones as well as for different species. The three panels in Fig. 3 are missing labels A, B, and C.

3. Sections 2.2 and 2.3 should specify in the section title that the rod photoresponse is being analyzed.
4. Section 2.4 addresses how cone photoresponses differ from rod photoresponses. It is suggested to mention either here or in Section 1 the extent to which anatomical differences in the rod and cone outer segment may affect the photoresponse independently of the mentioned biochemical differences.

5. At the end of Section 2.6, a concluding statement is needed to provide possible explanations for the 4-8-fold difference in the calculated number of G* molecules activated per rhodopsin in Lamb and Kraft (2020) compared with the two other cited studies.

6. In Figure 8A, time trees with extant taxa on them usually extend the branches to the present time on the right. As Figure 8A is now, it appears as though the animal taxa indicated are all extinct because their branches don’t make it to the present.

7. In general, the manuscript lacks citations in several areas that support the statements made. Perhaps this is a feature of a Symposium Review, since the author has published a number of comprehensive, well-cited review articles on the topics covered here?

Minor issues:

p.4, l.2: continuous, not “continues”

p.4, 2nd line after Fig.4 insert: Figure 4B, not 3B

p.4, sentence starting with “Eqn (2)...”: suggested change “...as the product of three parameters (vE**, βE**, and n).”

p.5, termination of rod transducin/PDE activity should mention of RGS9 acting in concert with PDEγ to accelerate the GTPase activity of transducin. RGS9 is introduced in the following section on cone phototransduction, but it is also important for inactivation of the rod photoresponse.

p.5, l.17: The nomenclature for the guanylate cyclases found in rod and cone photoreceptors can be confusing since the gene name differ in different species (see Pflugers Arch. review by Dizhoor and Peshenko, 2021). Rather than refer to GC-E (a pseudogene in humans) it might be preferable to refer to GUCY2D and GUCY2F by their HGNC names, as is done later in the article.

p.5, last sentence: capitalize “Because...”

p.7, l. 9: “…expression level of PDE6...”

p.7, Section 3, last sentence of first paragraph: consider simplifying the sentence structure to avoid confusion, for example: “…while the 7 protein subunits that make up the RGS9 complex and the two guanylyl cyclases and their GCAPs are encoded by common genes in the two classes of photoreceptors (Fig. 7).”

p. 9 Section 3.3, first sentence: Fig. 9A shows only 4 paralogons not 6, and 15 phototransduction genes, not 14.

p. 10, last line: subunits, not “sub-units”

Figure legends: In some instances, the legends for the figures do not indicate the source of the illustrations that have been previously published. For Fig. 9, please add the color definitions used (as described in the main text). In Fig. 10, the meaning of the green color should be mentioned.
Responses to Editor and Referee comments

Reviewing Editor:
This is a very clearly written review, synthesising key data, providing wide-ranging insights, and, perhaps uniquely, combining a detailed description of the molecular basis for rod and cone phototransduction, its kinetics and the evolutionary origin of the main molecular players. I think this will be of great interest to readers in the fields of retinal physiology, visual neuroscience, sensory transduction and others. The reviewers, who are highly positive in their reviews, have highlighted some areas where the manuscript might be improved and/or made more accessible (as well as typographical errors). We would be grateful if the author might consider making minor revisions in light of these. Some of Reviewer 2's comments are very pertinent, but the detail requested is probably beyond the scope of the length of a symposium review, and so do not need to be acted on in full.

Thank you. I have made revisions to deal with all of Reviewer #1’s comments and also with all but two of Reviewer #2’s.

In light of the first sentence above, and similar comments by both Reviewers, and in order to better reflect the content, I have added “and evolution” to the title of the review.

Senior Editor:
Dear Trevor, thank you for a fascinating Review. In addition to the minor issues raised by the referees, and to increase the appeal of your article to the widest audience, please rewrite your abstract along the following lines. It should contain more factual information about the findings of your literature review and mention key insights. Avoid letting the abstract be a simple outline of the review topics, instead give your readers the condensed information and come to a clear conclusion in the last sentence. Avoid saying more work needs to be done as the conclusion (in the abstract) it is always true, but lacks a hook to attract a reader from pubmed to your JP article. Thanks again, this article should be well cited.

Thank you. I have rewritten the second half of the Abstract along these lines.

REFEREE COMMENTS

Referee #1:
This review entitled "Photoreceptor physiology: Cellular and molecular basis of rod and cone phototransduction" by Trevor Lamb describes the molecular mechanisms of phototransduction in rod and cone photoreceptors, kinetic models linking phototransduction mechanisms to photoreceptor response kinetics and the evolutionary origin of rod and cone photoreceptors. Overall, this is a beautifully written and clear review, which is a delight to read both in its scientific depth as well as its style. I have only a few comments related mainly to deepening the presentation in a few important places, where the reader would need a bit more tools to understand the contents profoundly.

Thank you.

Comments:
Page 4: The 50-fold difference in kinetics between amphibian rods and vertebrate rods is mentioned to be due to differences in outer segment volume and temperature. It would be really nice to explain this to the reader in more depth by briefly explaining which parameters of the amplification constant are sensitive to temperature and to the outer segment volume and how. E.g. correlating the temperature effects to the diffusion speed of proteins and their impact on the speed of phototransduction could be helpful for the reader (see Calvert et al. Nature 2001). Similarly brief explanation for the connection between photoreceptor volume and response kinetics would be very useful.
Explanations of both have now been expanded in penultimate paragraph of page 4, and the reference has been added.
Page 5: "Difference in cone phototransduction parameters". It would be very nice to expand a bit the discussion on how the speed of vision related to light adaptation. Now it is not obvious to the reader how light-adapted humans can reach extremely high flicker fusion frequency. It would be useful to expand this appropriately to the reader and give insights about how light adaptation connects to the kinetics parameters of photoresponses.
The paragraph (now on page 6) has been completely rewritten.
Page 7: Currently there are contradicting numbers in the literature for the number of transducing molecules activated by a single rhodopsin - some of which the author points out. The author sides now with particular estimates but it would be useful for the reader to understand where the discrepancy arises (if possible. Is the difference in analysis methods, different recording conditions or what?
The material at the bottom of page 7 and top of page 8 has been substantially rewritten.
Minor:
Fig 3 is missing panel labels (A, B & C) Labels added.

Referee #2:
Summary:
This manuscript presents a wide-ranging view of our current understanding about the cellular and molecular mechanisms underlying the first steps in vision, and how rods and cones have evolved to respond to photopic and scotopic levels of illumination. The level and clarity of the presentation is outstanding for a wide audience of researchers in sensory transduction.
Thank you.
Major points:
1. Given the current debate in the literature about the rate and extent of transducin activation by each photoactivated rhodopsin, Section 2.6 would benefit from a fuller discussion of the various estimates of the in vivo rate of transducin activation that are based on measurements of the single photon response (where the number of R* is precisely known) compared with dim and bright flash response estimates. While the biochemical literature on this topic is extensive, most in vitro studies are conducted under conditions that are non-physiological (e.g., protein concentrations orders of magnitude lower than found in the outer segment).
The material at the bottom of page 7 and top of page 8 has been substantially rewritten.
2. The review would be strengthened if there was a greater connectedness between molecular mechanisms of phototransduction (Section 2) and the evolution of rod and cone isoforms of the central proteins involved in visual transduction (Section 3). Specifically, a review of the electrophysiological properties of rods and cones throughout vertebrate evolution would help connect these two sections. Since Korenbrot’s 2012 review on this topic, there have been significant advances in our understanding of species differences in rod and cone physiology that could be mentioned (e.g., Morshedian and Fain, 2017 on lamprey phototransduction).
The material now at the top of page 12 has been substantially rewritten, and three references have been added.
3. The dates discussed at the beginning of Section 3 regarding the evolution of metazoans and deuterostomes are much older than in recent analyses based on genome scale data, which estimate the origin of Bilateria (the split between deuterostomes and protostomes) by at least 700 Mya, and deuterostomes and chordates must be more recent than that. In the text, 700 Mya is given for the origins of deuterostomes, but this is probably more like 600 Mya [dos Reis et al. (2015) Current Biol. 25, 2939-2950; Dohrmann and Worheide (2017) Scientific Reports 7, 3599]. The timing given for the proto-vertebrate ancestor (600-500 Mya) is more consistent with recent work. Citations for the assertions made in Section 3.1 about the general features of vertebrate evolution are recommended to support the dates for speciation events.
The timings >450 Mya have been adjusted, in Figure 8A and in the text, and the suggested references added.

4. An additional Section 3.6 that evaluates the evaluation of rod and cone isoforms for their functional relevance is suggested. Of the genes described in Fig. 7, which ones are candidates contributing to the differences in excitation, inactivation, and dark and light adaptation of rods and cones? In Section 2.4, the author suggests that the levels of RGS9 may account for faster cone photoresponse recovery and points out limitations in biochemical studies of cone phototransduction. However, the evolutionary analysis of rod and cone isoforms could also be evaluated for the functional implications of some phototransduction proteins having different isoforms while others do not.

Thank you, but I feel that an additional Section of this nature would make the review too long.

Secondary points:

1. Fig. 2 has a minor inconsistency in that it depicts rod PDE6 (i.e., α and β subunits) whereas cone PDE6 is a homodimer. Otherwise, the figure accurately represents the activation components shared by rods and cones.

Note added to Figure caption.

2. Fig. 3. It is suggested to remove the units for time on the x-axis on Fig. 3, since the photoresponse kinetics vary for rods and cones as well as for different species.

Note added that the time scale applies to mammalian rods.

The three panels in Fig. 3 are missing labels A, B, and C. Labels added.

3. Sections 2.2 and 2.3 should specify in the section title that the rod photoresponse is being analyzed. Section titles changed to specify “rod”.

4. Section 2.4 addresses how cone photoresponses differ from rod photoresponses. It is suggested to mention either here or in Section 1 the extent to which anatomical differences in the rod and cone outer segment may affect the photoresponse independently of the mentioned biochemical differences.

Explanation now expanded in penultimate paragraph of page 4 (Section 2.2).

5. At the end of Section 2.6, a concluding statement is needed to provide possible explanations for the 4-8-fold difference in the calculated number of G* molecules activated per rhodopsin in Lamb and Kraft (2020) compared with the two other cited studies.

The material at the bottom of page 7 and top of page 8 has been substantially rewritten.

6. In Figure 8A, time trees with extant taxa on them usually extend the branches to the present time on the right. As Figure 8A is now, it appears as though the animal taxa indicated are all extinct because their branches don’t make it to the present.

Sentence added to Figure 8 caption to state that line endings do not represent extinctions.

7. In general, the manuscript lacks citations in several areas that support the statements made. Perhaps this is a feature of a Symposium Review, since the author has published a number of comprehensive, well-cited review articles on the topics covered here?

In an attempt to make the review more readable to those outside the immediate field, the use of citations is deliberately less extensive than it would be in a specialist review article.

Minor issues:

p.4, l.2: continuous, not “continues” Corrected.

p.4, 2nd line after Fig.4 insert: Figure 4B, not 3B Corrected.

p.4, sentence starting with “Eqn (2)…”: suggested change “…as the product of three parameters (\(vE^{**}, \beta E^{**}, \) and \(n\)).” Done.

p.5, termination of rod transducin/PDE activity should mention of RGS9 acting in concert with PDEγ to accelerate the GTPase activity of transducin. RGS9 is introduced in the following section on cone phototransduction, but it is also important for inactivation of the rod photoresponse. Done.

p.5, l.17: The nomenclature for the guanylate cyclases found in rod and cone photoreceptors can be confusing since the gene name differ in different species (see Pflugers Arch. review by Dizhoor and Peshenko, 2021). Rather than refer to GC-E (a pseudogene in humans) it might be
preferable to refer to GUCY2D and GUCY2F by their HGNC names, as is done later in the article. In fact GC-E is the protein encoded by the gene *GUCY2D* (which is named confusingly in human). The names of the encoding genes have been added.

p.5, last sentence: capitalize “Because…” Corrected.

p.7, l. 9: “…expression level of PDE6…” Corrected.

p.7, Section 3, last sentence of first paragraph: consider simplifying the sentence structure to avoid confusion, for example: “…while the 7 protein subunits that make up the RGS9 complex and the two guanylyl cyclases and their GCAPs are encoded by common genes in the two classes of photoreceptors (Fig. 7).” Sentence rewritten.

p.9 Section 3.3, first sentence: Fig. 9A shows only 4 paralogons not 6, and 15 phototransduction genes, not 14. The sentence correctly states that four paralogons are shown. “15” corrected.

p.10, last line: subunits, not “sub-units” Done.

Figure legends: In some instances, the legends for the figures do not indicate the source of the illustrations that have been previously published. Added to captions for Figures 2 and 6.

For Fig. 9, please add the color definitions used (as described in the main text). Added.

In Fig. 10, the meaning of the green color should be mentioned. Added.
Dear Professor Lamb,

Re: JP-SR-2022-282058R1 "Photoreceptor physiology and evolution: Cellular and molecular basis of rod and cone phototransduction" by Trevor D Lamb

I am pleased to tell you that your Symposium Review article has been accepted for publication in The Journal of Physiology, subject to any modifications to the text that may be required by the Journal Office to conform to House rules.

NEW POLICY: In order to improve the transparency of its peer review process The Journal of Physiology publishes online as supporting information the peer review history of all articles accepted for publication. Readers will have access to decision letters, including all Editors' comments and referee reports, for each version of the manuscript and any author responses to peer review comments. Referees can decide whether or not they wish to be named on the peer review history document.

The last Word version of the paper submitted will be used by the Production Editors to prepare your proof. When this is ready you will receive an email containing a link to Wiley's Online Proofing System. The proof should be checked and corrected as quickly as possible.

All queries at proof stage should be sent to tjp@wiley.com

The accepted version of the manuscript is the version that will be published online until the copy edited and typeset version is available. Authors should note that it is too late at this point to offer corrections prior to proofing. Major corrections at proof stage, such as changes to figures, will be referred to the Reviewing Editor for approval before they can be incorporated. Only minor changes, such as to style and consistency, should be made at proof stage. Changes that need to be made after proof stage will usually require a formal correction notice.

Are you on Twitter? Once your paper is online, why not share your achievement with your followers. Please tag The Journal (@jphysiol) in any tweets and we will share your accepted paper with our 22,000+ followers!

Yours sincerely,

Ian D. Forsythe
Deputy Editor-in-Chief
The Journal of Physiology
https://jp.msubmit.net
http://jp.physoc.org
The Physiological Society
Hodgkin Huxley House
30 Farringdon Lane
London, EC1R 3AW
UK
http://www.physoc.org
http://journals.physoc.org

-------------------
Comments:

Reviewing Editor:

The author has revised according to reviewer comments, and this excellent review is, to me, acceptable for publication.

Senior Editor:

Congratulations on a really interesting article!

-------------------

REFEREE COMMENTS:
Referee #1:

This really nice review has further improved during the revision. All my previous points were addressed. This is a great read. Congratulations to the author.

Referee #2:

The author has thoroughly and appropriately addressed all of the reviewers’ comments.

* IMPORTANT NOTICE ABOUT OPEN ACCESS *

Information about Open Access policies can be found here https://physoc.onlinelibrary.wiley.com/hub/access-policies

To assist authors whose funding agencies mandate public access to published research findings sooner than 12 months after publication The Journal of Physiology allows authors to pay an open access (OA) fee to have their papers made freely available immediately on publication.

You will receive an email from Wiley with details on how to register or log-in to Wiley Authors Services where you will be able to place an OnlineOpen order.

You can check if you funder or institution has a Wiley Open Access Account here https://authorservices.wiley.com/author-resources/Journal-Authors/licensing-and-open-access/open-access/author-compliance-tool.html

Your article will be made Open Access upon publication, or as soon as payment is received.

If you wish to put your paper on an OA website such as PMC or UKPMC or your institutional repository within 12 months of publication you must pay the open access fee, which covers the cost of publication.

OnlineOpen articles are deposited in PubMed Central (PMC) and PMC mirror sites. Authors of OnlineOpen articles are permitted to post the final, published PDF of their article on a website, institutional repository, or other free public server, immediately on publication.

Note to NIH-funded authors: The Journal of Physiology is published on PMC 12 months after publication, NIH-funded authors DO NOT NEED to pay to publish and DO NOT NEED to post their accepted papers on PMC.