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November 11, 2019

JoVE 1 Alewife Center Suite 200 Cambridge MA 02140

Dear Editor,

Please find attached a revision of our manuscript titled "Step-by-step implementation of DeepBehavior: A deep learning toolbox for automated behavior analysis" for consideration for publication in an appropriate JoVE journal, preferably JoVE Behavior or Neuroscience.

We have made all the recommended changes and please see our point-by-point responses to Editorial and Reviewer comments below.

Thank you for your consideration.

Sincerely,

Ahmet Arac, M.D. Assistant Professor Department of Neurology UCLA Los Angeles, CA

RESPONSES:

Editorial comments:

Changes to be made by the Author(s):

1. Please take this opportunity to thoroughly proofread the manuscript to ensure that there are no spelling or grammar issues. The JoVE editor will not copy-edit your manuscript and any errors in the submitted revision may be present in the published version.

Response: We have revised the manuscript accordingly.

2. Please revise the title to be more concise and avoid punctuations.

Response: We have now shortened the title and made it more concise.

3. Please remove all commercial language from your manuscript and use generic terms instead. All commercial products should be sufficiently referenced in the Table of Materials and Reagents.

For example: NVIDIA, CUDA versions, CUDNN, etc.

Response: We have revised it accordingly.

- 4. All steps in the protocol should be a numbered action step. Please adjust the numbering of the Protocol to follow the JoVE Instructions for Authors. For example, 1 should be followed by 1.1 and then 1.1.1 and 1.1.2 if necessary. Please refrain from using bullets or dashes. Response: We have numbered the sections accordingly.
- 5. Please ensure that all text in the protocol section is written in the imperative tense as if telling someone how to do the technique in a step wise manner from beginning to the end (e.g., "Do this," "Ensure that," etc.). The actions should be described in the imperative tense in complete sentences wherever possible. Avoid usage of phrases such as "could be," "should be," and "would be" throughout the Protocol. Any text that cannot be written in the imperative tense may be added as a "Note."

Response: We have ensured to use imperative tense.

6. The Protocol should be made up almost entirely of discrete steps without large paragraphs of text between sections. Please simplify the Protocol so that individual steps contain only 2-3 actions per step.

Response: We have made the steps more discrete.

7. Please revise the protocol text to avoid the use of any personal pronouns in the protocol (e.g., "we", "you", "our" etc.).

Response: We have removed the personal pronouns.

8. Please add more details to your protocol steps. Please ensure you answer the "how" question, i.e., how is the step performed?

Response: We have added additional details to make it clearer.

9. All software steps must be explained explicitly. Please include GUIs, button clicks in the softwares, command lines etc.

Response: We have included and revised Figure-4 for this.

10. Please make the protocol subheadings as installations, pretraining preparations, data collection (how are the human and animal data collected, which behavior/s is/are recorded, how many videos are made), validating the framework, configuring the experiment, executing the experiment, data collection, data analysis, etc. So, the protocol should show how you perform your experiment in a step wise manner providing all specific actions in detail. Please do not generalize. Maybe take the examples described in the result section and build up the whole protocol on it.

Response: As this manuscript is focused on the analysis of behavior imaging data (rather than the acquisition), we have made each step very clear.

- 11. 2: is tensorbox open access? If not, please use generic term. Please reword 2.1 to show what is being done and how? e.g., set up tensor box by clicking xxxx or running the command xxxx Response: We have made it clear. Yes, tensorbox is open access.
- 12. 2.1.1: How do you ensure?

Response: We have provided links to our github account.

- 13. Lines 111 onwards: Are these command lines or button clicks? Please be explicit. Response: We have clarified these.
- 14. There is a 10-page limit for the Protocol, but there is a 2.75-page limit for filmable content. Please highlight 2.75 pages or less of the Protocol (including headings and spacing) that identifies the essential steps of the protocol for the video, i.e., the steps that should be visualized to tell the most cohesive story of the Protocol.

Response: We have highlighted the appropriate sections.

- 15. In the representative result section, please include the conclusion drawn from your protocol. Response: We have provided this.
- 16. Please obtain explicit copyright permission to reuse any figures from a previous publication. Explicit permission can be expressed in the form of a letter from the editor or a link to the editorial policy that allows re-prints. Please upload this information as a .doc or .docx file to your Editorial Manager account. The Figure must be cited appropriately in the Figure Legend, i.e. "This figure has been modified from [citation]."

Response: The corresponding author of this manuscript is also the corresponding author of the other paper and we have obtained permission to adapt the figures. We have also checked with the other journal (Frontiers Systems Neuroscience) for copyright issues and confirmed that there are no issues.

- 17. As we are a methods journal, please revise the Discussion to explicitly cover the following in detail in 3-6 paragraphs with citations:
- a) Critical steps within the protocol
- b) Any modifications and troubleshooting of the technique
- c) Any limitations of the technique
- d) The significance with respect to existing methods
- e) Any future applications of the technique

Response: We have modified accordingly.

Reviewers' comments:

Reviewer #1:

The authors present the unique observation that traditional behavior analyses can take a superficial approach to otherwise rich behavioral data sets. To address this shortcoming, the

authors propose the DeepBehavior toolbox. Step-by-step instructions to implement the DeepBehavior learning algorithms are included. While the authors cite their 2019 paper (Arac et al., 2019) which provides detailed examples of DeepBehavior's applications in both clinical and preclinical populations, the current paper would be strengthened by briefly emphasizing how DeepBehavior is distinct from typical behavioral analyses methods. This can be accomplished by succinctly comparing and contrasting applications and outputs of DeepBehavior toolbox with more typical behavioral analyses approaches. Additionally, implementation of the DeepBehavior toolbox requires a Linux operating system and working knowledge of Python. This is a limitation of the toolbox and should be stated early in the paper.

The authors provide detailed installation and implementation instructions and also comment on errors which may occur when using the toolbox, A notable strength of the toolbox proposed here, are the three different neural architectures and descriptions of when to use each. Importantly, DeepBehavior can be used to analyze both clinical and preclinical behavioral data and the paper would be strengthen by explicitly stating this early.

The authors should consider defining all acronyms the first time they are used to make the paper more user friendly for a diverse audience. However, the paper is well written and overall presents an exciting and novel methodology with a diverse range of applications and utility. Response: We thank the reviewer for these comments. We have emphasized how this method is distinct from other typical behavior analysis methods, and also addressed the linux/python concern.

Reviewer #2:

Manuscript Summary:

The authors provide detailed step-by-step instructions with visualizations of our recent methodology, DeepBehavior, utilizing deep learning algorithms. The proposed method uses deep learning frameworks built with convolutional neural networks to rapidly process and analyze behavioral videos. The paper is of scientific and original nature, related to a step-by-step user guide for implementation of DeepBehavior: A deep learning toolbox for automated behavior analysis. These methods provide robust, automated, and precise ways to quantify behavioral tasks.

Minor Concerns: For a better clarification, please edit your paper as follows: Enlarge the Introduction with current results reported in the world and Europe, - References to expand the results of European authors registered in SCOPUS / WoS such as: Advanced Robotic Grasping System Using Deep Learning and Trends in Simulation and Planning of Manufacturing Companies. Unify font in tables. Correct English grammar in this paper.

Please, edit the paper according to previous comments and after minor changes I recommend the paper to be published.

Response: We thank the reviewer for these comments. We have now revised the manuscript with recommended expansions, grammar corrections and appropriate references.