AUTHORS RESPONSE TO REVIEWER COMMENTS

Comments from reviewers have been presented in **bold text**; and comments from reviewers #1 and #2 have been listed as C1.X and C2.X, respectively. As some comments persist from the last revisions, I have kept the same numbering listed by reviewers where possible for this – otherwise responses are labelled in ascending order. Where revisions have been made they are referred to using line numbers of the revised manuscript, and these changes have been highlighted in the revised manuscript using **bold red text**.

General Changes

In addition to changes based on reviewer recommendations, the following general changes have been made to the manuscript:

- Since the last revision, the work by Werling et al. on *AddBiomechanics* has been accepted in peer-reviewed form in *PLoS One*. The original *BioRxiv* pre-print reference has therefore been updated to the peer-reviewed manuscript version.

Reviewer #1

C1.8[a]: Figures 2 and 3 show the residual forces and torques that are applied to the pelvis. However, many other joints of the model are also actuated using a CoordinateActuator. These CoordinateActuators are used to compensate for muscles that are too weak and/or stiff to allow the model to track the measured kinematics. Many of the algorithms that are a part of OpenSim make use of CoordinateActuators so that it is possible to get a solution even if the model is poorly fit to the participant. The intention is that the analyst will then adjust the model until the CoordinateActutors are no longer needed.

Of the algorithms analyzed, these extra CoordinateActuators appear in:

1. RRA.
2. RRA3:
3. addBiomechanics: There are only joint torques reported in the results files of addBiomechanics. After briefly looking at the Werling et al. (2023) paper, I don't believe that muscle forces are solved for at all. As such addBiomechanics does not really have these extra forces, and can be excluded from the extra bit of reporting.
4. Moco: I was surprised to find CoordinateActuators in use with Moco, but CoordinateActuators also appear in Moco's setup file.

R1.8[a]: While coordinate actuators are often used to supplement muscles in muscle-driven simulations, this was not how they were used in this particular study. In the present study, all simulations were completely driven by joint torque actuators (i.e. coordinate actuators) to ensure an accurate comparison across approaches (i.e. RRA is fundamentally a joint torque actuator driven simulation, and hence the *MocoTrack* and other simulations were designed this way to replicate this). Similarly, *AddBiomechanics* inverse dynamics step where the residuals are reduced does not incorporate muscles. I have looked for opportunities to make it clear in each approach that joint torque actuators are being utlised within all approaches (see line 89, 91 and 131 in tracked version), particularly for *MocoTrack*.

Given this, the torque actuator values originally requested in relation to this comment are reported in the paper in summary form (i.e. group means) in Figure 5. It would be nice to report some variance or ranges around these data within the figure; however, as noted in the initial revisions for this paper – adjusting this figure to be legible required only mean data to be reported.

C1.9: **Please do reach out to Werling et al. for clarification - it's only an email. I think that your paper will be often read and cited. It would be really helpful moving forward if this detail was nailed down. I suspect that this will only result in a single sentence in the final manuscript. However, I have been surprised in the past by the CoP error that I've found when manually calibrating force plates. The fact that addBiomechanics adjusts ground forces is an important, but subtle point, that your future readers will appreciate.**

R1.9: After discussion with a member of the *AddBiomechanics* development team (Nick Bianco), the *AddBiomechanics* tool does in fact export the adjusted GRFs with the results (while also returning the original data with the **_raw* suffix). The initial confusion with these data is that they are returned in a nearly identical format (with some minor changes to data labelling), with some subjects data having minimal changes. Nonetheless, when reviewing these data across subjects it is clear that *AddBiomechanics* does adjust the ground reaction forces and torques, alongside the centre of pressure data in the outputs. To ensure this methodological process is clear to readers of this paper, a brief statement has been included in the methods of the revised manuscript (see line 161-162 in tracked version). A statement acknowledging that *AddBiomechanics* differs to the other approaches in its capacity to adjust the experimental ground reactions data has been included in the discussion section of the revised manuscript (see line 345-347 in tracked version):

"AddBiomechanics also differs to the other approaches examined in that minor adjustments to ground reactions and centre of pressure location are made."

alongside an individual participant example of where this has occurred (see Figure 7, line 356 in tracked version).

C1.12: **You can download Chand John's thesis from searchworks provided by Stanford's library. RRA is briefly mentioned in Appendix A.3. You probably should keep the web references and perhaps add the reference to Chand's thesis incase the web references dissappear and/or change. The choice is yours given how sparsely RRA is covered in Chand's thesis.**

R1.12: Thank you for the direct link to Chand's PhD thesis. The thesis does acknowledge a "New Approach: Residual Reduction Algorithm" in an appendix, and therefore it seems prudent to acknowledge this as the original source. I have therefore included a reference to Chand's thesis when introducing the RRA (see line 38 in tracked version).

Code

C1.15: Normally this information is put under a "#Dependencies" section.

R1.15: In addition to the comments in the README and analysis script about the OpenSim Geometry paths being present at C:\OpenSim 4.3 Geometry\, an additional comment on this has been included in the dependencies section of the archives top level README. Excerpt from the README:

Alongside the OpenSim Python dependency, the main runSimulations.py script assumes that OpenSim is installed at *C:\OpenSim 4.3* and that the associated Geometry folder that comes with installation contained within this (i.e. *C:\OpenSim 4.3\Geometry*). Users with this installed to a different location will need to adjust the *geomDir* variable in runSimulations.py. The code may still run without doing this, however constant prompt messages acknowledging an inability to find associated model geometry may be repeatedly displayed in the console while the code is running.

C1.17: That's great that you have a zipped version of the repository saved under Zenodo. However, the github repository you have is massive because you're storing the data in with the code. If you have the time for this project, please use the recommendations below to reduce the size of the repository. If you want to keep the existing history, then you'll need some skills with git (or help) to get this done. If you don't mind ditching the history then you can just start a new repository and organize it to support having a clear separation between the data and code.

R1.17: Thank you for the recommendations and I will definitely consider and implement in future projects. I wish to keep the dataset for this paper as an archived repository as originally planned for a couple of reasons. First, while it is plausible readers will find the associated GitHub repository (as you have found it yourself) – all mentions regarding data and code access in the paper refer to the SimTK page, which subsequently links to the Zenodo archive. Hence, this is the proposed main avenue for accessing the code and data – and the total archive size here (~600MB) is reasonable enough for readers to download. Second, I will potentially expand this GitHub repository to include other datasets in the future which will investigate residual reduction in other contexts (e.g. overground walking, sporting tasks) – therefore I feel it is best to direct readers of this paper to the archived repository, as long-term there may be additional aspects in this GitHub repository unrelated to this particular paper.

<u>Reviewer #2</u>

<u>C2.1:</u> **I am not intimately familiar with the AddBiomechanics tool, but based on my reading of the methods used in that tool it does not appear that it is capable of adjusting the ground reaction forces. If that is not the case, a comment to that effect in the manuscript could aid readers in understanding how each tool works.**

<u>R2.1:</u> Based on my reading of the *AddBiomechanics* materials, it appears that the various optimisation procedures work to ensure that the model outputs are consistent with the experimentally measured ground reactions – hence I would agree with this statement. This is a similar limitation to all of the tools examined outside of *MocoTrack* (i.e. RRA also cannot handle predicted changes to GRFs well), and has therefore been noted in the revised manuscript (see line 398-400 in tracked version):

"Including additional components in the MocoTrack cost function (e.g. tracking joint moments derived from inverse dynamics or using a foot-ground contact model to track and solve for external forces) could also assist in achieving smoother joint kinetic signals overall. This ability to alter the tools cost function and implement a foot-ground contact model to adjust ground reaction forces is a potentially useful aspect of MocoTrack not present in the other tools examined."

<u>C2.2:</u> **For what it is worth, I also agree with the author that adding optimization of a foot-ground contact model is out of scope for the current manuscript. Such an undertaking would certainly be interesting, but modeling foot-ground contact is challenging and would warrant its own investigation.**

<u>R2.2:</u> Thank you for this comment – and as a follow-up I am hoping to work on some other ideas in the near future that will help with estimating ground reactions in OpenSim that do not rely on a foot-ground contact model.

<u>C2.3:</u> **Am I correct that AddBiomechanics is using completely different algorithms from either RRA or Moco? That is, it is not just a user interface built on top of other existing OpenSim tools, correct? If so, an explicit statement to that effect might be helpful.**

<u>R2.3:</u> This assumption is correct – in that the scaling, inverse kinematics and inverse dynamics steps in *AddBiomechanics* differ to those of the core OpenSim tools. Amendments to the revised manuscript have tried to make this clear when introducing the tool (see line 149-150 in tracked version):

"AddBiomechanics [14] is an online application which provides automated processing of experimental marker and GRF data. It includes newly developed (i.e. different to the core OpenSim processes) processing steps, starting with model scaling and inverse kinematics…"

<u>C2.4:</u> **In line 91, specify that it is a "joint" actuator. Muscles are also actuators.**

<u>R2.4:</u> Statements at this point in the revised manuscript have been amended to make it clear that RRA uses joint torque actuators (see line 89 in tracked version):

"OpenSim's Residual Reduction Algorithm (RRA) completes a pair of joint torque actuator-driven tracking simulations to solve for the force and torque values that produce the desired motion while considering external ground reactions [8]. An objective function minimises both the weighted sum of joint actuator controls, and difference between model and desired joint coordinate accelerations [16]."

<u>C2.5:</u> **I am curious about the outliers in the AddBiomechanics results in Figure 2. It seems one trial was clearly different from all the others. Can you provide any explanation of what was different in that trial?**

<u>R2.5:</u> This is a good pick-up, as one particular subject's data contributed to these outliers – with the reason seeming to be the second optimisation aimed at driving residuals to zero failed in this subject. The potential for this to happen was highlighted in the methods related to the *AddBiomechanics* tool (see line 176 in tracked version), which provides a good opportunity to discuss and refer back to in the results (see line 209-210 in tracked version):

"The AddBiomechanics approach also subceeded this threshold for the majority of participants, with the exception of one or two cases where the primary reason for this appeared to be the second optimization failing (a noted potential limitation of the tool)."

<u>C2.6:</u> **Thank you for adding the pelvis kinematics in Figure 4, those are helpful in interpreting the results. One thing that stood out to me is the pelvis side translation results from MocoTrack, where the initial value is noticeably different from all other methods. This to me highlights an important distinction between MocoTrack and RRA (not sure about AddBiomechanics). RRA starts out exactly tracking the experimental kinematics, and can only "drift" from those kinematics as time progresses. In contrast, MocoTrack is free to vary the initial AND final conditions (assuming they have not been constraint to match the input data). I think this could be an interesting result to call out in the discussion.**

<u>R2.6:</u> This is another interesting point to pick up on, and provides some potential reasoning as to why the *MocoTrack* and *AddBiomechanics* approaches may be as good or better at reducing residuals (i.e. due to having more flexibility in altering initial kinematics). A discussion on this has been included in the revised manuscript (see line 328-338 in tracked version):

"While not consistently different across the entire gait cycle, the initial values for various joint coordinates (e.g. horizontal pelvis translations) differed between the MocoTrack and AddBiomechanics approaches to those from inverse kinematics and

the RRA/RRA3 results. This highlights an interesting difference between the modern residual reduction approaches versus the RRA. RRA begins by exactly tracking experimental kinematics and can only 'drift' from these as the simulation progresses, whereas this is not the case for the other approaches examined. Bounds or specific values on initial kinematics can be provided in MocoTrack, but this is not explicitly required. The flexibility in kinematic starting points may be a reason why the MocoTrack and AddBiomechanics approaches can perform as well or better in reducing residuals."

C2.7: Looking at the AddBiomechanics results in Figure 4, the excessive pelvis tilt and hip flexion in comparison to the other methods seem clearly related to the automated scaling and marker adjustment process. Anteriorly tilting the pelvis will directly cause increased hip flexion. Indeed, in the AddBiomechanics publication the authors state: "For example, the pelvis can be tilted slightly forward, with the markers at the front of the pelvis shifted upward, and if the angles of the hips and spine are appropriately adjusted then the markers will still closely match the target data." It seems this is what has happened here, and could potentially be corrected. It seems that the automated model scaling and marker adjustments are also a consideration for users of the tool. The AddBiomechanics tool claims to be easier to use because it automates more of the workflow, but it seems to be clearly introducing additional error into the results.

R2.7: This particular kinematic difference provides a useful point to discuss how underlying processes in the various approaches can influence the modelled kinematics, and therefore users likely need to understand these processes (and potential associated limitations) when using these tools. A discussion on this, with a particular reference to the anterior pelvic tilt results from *AddBiomechanics* has been included in the revised manuscript (see line 340-345 in tracked version):

"Some kinematic variations can be linked to the inherent design and processing steps within the examined approaches. For example, a greater anterior pelvic tilt was observed in the AddBiomechanics kinematics compared to all other approaches. This was likely due to a reported limitation of AddBiomechanics, where using only marker location data to scale body segments and register markers can result in a generalised anterior pelvic tilt [14]. An understanding of the processes and potential limitations involved in each approach will therefore allow users to appropriately interpret any modelled outputs (e.g. joint kinematics)."

C2.8: Throughout the manuscript, there are sentences of the form: "…, however …". I may be wrong about this, but I believe the correct structure would be a semicolon and comma "…; however, …" or a period and new sentence beginning with "However, …".

R2.8: I did some research on punctuation around the word *however* when used mid-sentence, and to reviewer 2's credit they are correct that the word should be followed by a comma and a semi-colon used at the end of the previous clause. Amendments to this end have been made throughout the manuscript – and made me realise how often I use the term *however*.

<u>**C2.9:**</u> **Introduction, line 23: should be "data are…"**

<u>R2.9:</u> This adjustment has been made in the revised manuscript (see line 23 in tracked version):

"*Kinematic data are typically collected via marker-based optical motion capture systems, …"*

<u>**C2.10:**</u> **Most instances of adding appropriate apostrophes to "participants" have been made, but there are a few that were missed (e.g., lines 113, 125)**

<u>R2.10:</u> The two suggested amendments have been made, alongside checking all other mentions of participants.

<u>**C2.11:**</u> **Line 271: should be "model's"**

<u>R2.11:</u> This adjustment has been made in the revised manuscript (see line 269 in tracked version):

"Minimising the residual forces and moments at a model's root segment is subsequently…"

<u>**C2.12:**</u> **Line 284: suggest to change from "remaining" to "RRA"**

<u>R2.12:</u> This adjustment has been made in the revised manuscript (see line 281-282 in tracked version):

"*… AddBiomechanics and MocoTrack approaches producing variable lower and upper body kinematics, respectively, versus the RRA approaches."*
