Touch-induced Mechanical Strain in Somatosensory Neurons is Independent of Extracellular Matrix Mutations in C. elegans

Adam Nekimken, Beth Pruitt, and Miriam Goodman

Corresponding author(s): Miriam Goodman, Stanford University

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Editor-in-Chief: Matthew Welch

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. The original formatting of letters and referee reports may not be reflected in this compilation.)
Dear Professor Goodman:
Thank you very much for your submission to MBoC's special issue on 'Forces on/in cells'. Two expert reviewers have examined your submission and are overall positive. We hope you can submit a responsive revision, with changes to the text and figures that address the various concerns in both reviews about mechanical strain. It is the type of topic that is highly relevant to this special issue.
Regards,
- dennis.

Dear Dr. Goodman:

The review of your manuscript, referenced above, is now complete. The Monitoring Editor has decided that your manuscript is not acceptable for publication at this time, but may be deemed acceptable after specific revisions are made. Any specific areas to be addressed are outlined in the reviewer comments included below.

A reminder: Please do not contact the Monitoring Editor directly regarding your manuscript. If you have any questions regarding the review process or the decision, please contact the MBoC Editorial Office (mboc@ascb.org).

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Thank you for submitting your manuscript to Molecular Biology of the Cell. We look forward to receiving your revised paper.

Sincerely,

Eric Baker
Journal Production Manager
MBoC Editorial Office
mbc@ascb.org
"Touch induces local mechanical strain in C. elegans sensory neurons" by Nekimken et al. uses a microfluidic device to apply small deformations to worms and microscopy to measure longitudinal strain in neurons using labelled mitochondria as natural fiducial markers. The authors claim this is first in vivo measurement of touch-induced deformation in mechanosensory neurons. Given that the transformation of an external mechanical stimulus to neural deformation is critical for a detailed understanding of touch, this represents an important first step for the field. The authors further show that disrupting ECM attachment to neurons has no detectable effect on neuron strain in their system using several mutants, even though the mutants do show defects in touch sensation. Overall the paper is clearly presented.

There are two aspects of the paper that the authors should clarify in my opinion.

In a previously published model, the authors predicted a strain of 0.12 given the magnitude of indentation they performed but observed a strain of 0.03. If I understand their argument correctly, their method only gives a lower bound on the strain because the mitochondria are sparse and they assume the strain is constant in between the markers. If there the strain is not constant between the markers there will be some regions of higher strain than the estimate. That makes sense, but the discrepancy seems quite large. Would it be possible to take the model-predicted strains and, using the observed mitochondrial positions, estimate the strain using their method? This would help in understanding whether the discrepancy is due to limited resolution or due to a difference between the real worm mechanics and the model. If it's the latter, this would be a further useful result from the paper that might point towards future model refinements.

Figures 2B and 4B show the dependence of strain on neural displacement. The authors observe an increase in strain with displacement (not surprising in and of itself) but looking at the scatter in the data, I wonder if the observed dependence is statistically significant. Do the authors have an expectation for this dependence, perhaps from their previously published model or from a geometric argument? This would give more confidence that the measurement is working as expected. Is it a concern that the fit intercept is not 0 strain at 0 displacement? Alternatively, if the fits are constrained to go through the origin, is the fit much worse?

Minor comments:
-bottom of page 2: 'used to' -> 'used it to'
-top of page 3, the sentence ending in 'distributed along their sensory' is missing a word or two at the end.
-page 3: 'devices trap' -> 'device's trap'
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-page 9: 'dont' -> 'don't' or 'do not'
-the first sentence of the Figure 4 caption is missing a word after mechanical

Reviewer #2 (Remarks to the Author):

"Touch induces local mechanical strain in C. elegans sensory neurons" by Nekimken et al. uses a microfluidic device to apply small deformations to worms and microscopy to measure longitudinal strain in neurons using labelled mitochondria as natural fiducial markers. The authors claim this is first in vivo measurement of touch-induced deformation in mechanosensory neurons. Given that the transformation of an external mechanical stimulus to neural deformation is critical for a detailed understanding of touch, this represents an important first step for the field. The authors further show that disrupting ECM attachment to neurons has no detectable effect on neuron strain in their system using several mutants, even though the mutants do show defects in touch sensation. Overall the paper is clearly presented.

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Figures 2B and 4B show the dependence of strain on neural displacement. The authors observe an increase in strain with displacement (not surprising in and of itself) but looking at the scatter in the data, I wonder if the observed dependence is statistically significant. Do the authors have an expectation for this dependence, perhaps from their previously published model or from a geometric argument? This would give more confidence that the measurement is working as expected. Is it a concern that the fit intercept is not 0 strain at 0 displacement? Alternatively, if the fits are constrained to go through the origin, is the fit much worse?

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-the first sentence of the Figure 4 caption is missing a word after mechanical
The authors use imaging methods to assess the strain on C. elegans mechanosensory neurons during touch stimuli from a microfluidic device. They show that touch stimuli sufficient to active the touch neurons is associated with approximately a 3% strain at maximum. Measurement of strains in mutants affecting links between the ECM and TRNs did not show any differences, suggesting that a fully intact ECM is not necessary for mechanosensation.

This is an interesting manuscript and some of the results are novel. However, I have some concerns that should be addressed.

- The treatment of strain in the manuscript is overly simplistic and at times confusing. First, many mechanosensory systems detect shear strain, not normal strain as quantified here. Moreover, normal strain in a 3-dimensional material with a local deformation cannot be sensibly reduced to a single number as done in the manuscript. If a material is incompressible, which is likely true to a good approximation, then for each direction in which the strain is positive there must be one or more directions along which the normal strain is negative, and directions in which it is zero. In a complex structure like a living organism, the direction would be expected to fluctuate from location to location. Indeed this is consistent with the strain moving above and below zero in Fig 1D, 2A, and elsewhere.

Given the authors' extensive work on modeling C. elegans body dynamics during deformation, I would expect a more sophisticated analysis of the geometry of the strain field. In Sec 3.1 it is stated that "Due to the nature of our measurement, we were only able to measure one-dimensional strain along the length of the TRN". But since the authors acquired a confocal z stack to image mitochondria in 3 dimensions, and there are 6 cells expressing the transgene, I don't see why strain can only be measured in one direction. In fact, the authors have already measured displacement in the direction of the stimulus (perpendicular to the body axis), as shown in Fig. 1b.

- It would be useful to see not just the strain but the direction of displacement of each fluorescent object during the stimulus. This would shed some light into the strain field.

- I am not convinced that the distance between mitochondria is a good representative of strain in a neurite. For example, some fibers exhibit a tortuous shape under compression. They are not really under compression/extension in the simplistic way suggested here but instead alter their extension via local bending. Showing micrographs of deformed and undeformed worms with a cytoplasmic GFP label in mechanosensory cells would help show how strain occurs in the touch neurons.

- It is touted as a major result of the paper that "we showed for the first time that local indentation of the body of a worm leads to local strain in its TRNs", and this is also reflected in the title. However, this is a completely expected result. I can't think of any scenario in which local indentation of the body would NOT lead to strain in the TRNs, which are only a few microns away from the cuticle. I would suggest the finding that TRN strain is not changed of ECM mutants is a much more significant finding.

- I don't see much relevance of this work to the topic of this journal.

Minor comments:
- In experiments measuring the strain in TRNs, it is not clear how the touch stimulus amplitude was set, and therefore what the 3.1% strain result really means. Is this the threshold for TRN activation? If so, what were the temporal properties of the deformation?

- Section 2.4: "While some mechanical coupling is by definition required to move the TRNs from their juvenile position, it is unknown what actually applies the force to move the neuron." This sentence seems to ignore the strong possibility that TRNs move themselves by cell migration.

- Section 3.5: It may be correct that TRN response to a high-velocity stimulus is greater than to a low-velocity stimulus, but I don't know what is meant by "TRNs are activated mostly by high-velocity stimuli".

- Section 5.3: The viscosity of iodixanol at this concentration will be likely about 20 times greater than that of water or saline. This may be much lower than that of other compounds tested, but I would not call it "only slightly higher" than saline. It would be helpful to be more specific here.

- Fig. 1a. This does not look anything like a Max projection of mitochondria in the TRN of a worm. It looks like a bright field image of a worm in a microfluidic. Scale bar is not defined.

- Fig. 1b. What exactly is being shown in panel B, labeled "Motion of mitochondria induced by mechanical stimulus"? Is it an image of the mitochondrial tag? If so, how does it show motion as indicated by the caption? The color scheme is very odd for a fluorescence micrograph. What is the length of the scale bar? I would suggest showing the stimulated and unstimulated puncta on the same image so that we can see how the cell is deforming. Illustration of the strain field via arrows would also be helpful.

- Fig 1c. Why is the displacement in the direction of actuation being shown? Wouldn't the longitudinal displacement be more relevant to this experiment?

- Spelling errors: "longitundinal" should be "longitudinal" in Fig. 1. Sec 3.3. "differtiate" should be "differentiate"

- Fig 2. (a) is this for a single trial? If so please also show data averaged over all worms tested. If not, please indicate number of trials and number of worms. (b) "neuronal displacement" is not accurate. This is displacement of the fluorescent tagged mitochondrion, not the neuron as a whole or its cell body. Since strain is calculated for displacements up to 100 microns, why does panel (b) show only displacements between 4 and 8 microns? Or does "displacements" mean something different in this context?

(c) It's a bit confusing to compare wild-type vs. "control", since wild-type (N2) is actually serving at the control in this experiment. It is better expressed as comparing N2 vs. jsls1073 worms, or wild-type vs. transgenic worms

Fig. 3. Are these individual trials? If not, how many worms were assayed for each plot with how many trials each? How are the shaded error regions defined?
We thank the reviewers for their feedback and evaluation of our manuscript and, especially, for the opportunity to build upon this feedback to improve the presentation of our findings and our research. Both reviewers agreed that this study included the first in vivo measurements of touch-induced strain of the TRNs and noted the unexpected result that disrupting ECM attachment did not appear to affect touch-induced mechanical strain in the TRNs. In revising the manuscript we sought to improve the clarity of writing and of data presentation, inspired by comments and questions from both reviewers. In this spirit, all of the figures have been revised, the introduction has been edited to provide the reader with more information about the prior state of knowledge and key knowledge gaps relevant to this research, and both the results and discussion have been edited to be more concise. We hope that the reviewers and editors agree that these revisions improve the quality of the manuscript. Regrettably, we have not been able to collect any new data for this revised submission and hope that the reviewers and editor understand that the suspension of normal research operations made this goal unattainable.

Reviewer #1 (Remarks to the Author):

There are two aspects of the paper that the authors should clarify in my opinion.

1. In a previously published model, the authors predicted a strain of 0.12 given the magnitude of indentation they performed but observed a strain of 0.03. If I understand their argument correctly, their method only gives a lower bound on the strain because the mitochondria are sparse and they assume the strain is constant in between the markers. If there the strain is not constant between the markers there will be some regions of higher strain than the estimate. That makes sense, but the discrepancy seems quite large. Would it be possible to take the model-predicted strains and, using the observed mitochondrial positions, estimate the strain using their method? This would help in understanding whether the discrepancy is due to limited resolution or due to a difference between the real worm mechanics and the model. If it’s the latter, this would be a further useful result from the paper that might point towards future model refinements.

The reviewer seems to be puzzled by the discrepancy between the measured strain (0.03) and the previously predicted strain (0.12) and suggests that the limitations of the current measurement method are not sufficient to explain the four-fold discrepancy. We agree that there are other factors—namely that the model we published late in 2019 (Sanzeni, et al., eLife, 2019; Katta, et al., J Gen Physiol, 2019) was applied to a very different mechanical loading regime than what occurs in the microfluidic-based pneumatic stimulator used in this manuscript. Specifically, the previous loading regime involved indentation with a stiff sphere that was either 10µm in diameter (Sanzeni, et al., 2019) or 20µm in diameter (Katta, et al., 209). The current loading regime is a flexible PDMS membrane that is 50 µm long and has the largest deformation at its center. These differences in the geometry of the mechanical loading regime make it inappropriate to apply the previous, finite-element model to the present data. We would need to revise the model to accommodate the new loading regime, an effort that we believe is outside the scope of the present study. There is another factor that may account for the discrepancy: the present measurements are at steady-state and the model computations were able to address dynamic changes in strain.

To clarify these points for the reader, we revised the text as follows:

- RESULTS, p. 6, line 132-146, we discuss the technical limitations preventing us from detecting shear or bending strain.
DISCUSSION, p. 10, line 254-266, we discuss the discrepancy between the measured strain and predicted/theoretical strain.

Figures 2B and 4B show the dependence of strain on neural displacement. The authors observe an increase in strain with displacement (not surprising in and of itself) but looking at the scatter in the data, I wonder if the observed dependence is statistically significant. Do the authors have an expectation for this dependence, perhaps from their previously published model or from a geometric argument? This would give more confidence that the measurement is working as expected. Is it a concern that the fit intercept is not 0 strain at 0 displacement? Alternatively, if the fits are constrained to go through the origin, is the fit much worse?

As you point out, we would expect larger displacements to result in larger strains, but with the noise in our measurement, this relationship is not statistically significant. We’ve added a note about the weak dependence of strain on deformation in our measurements (p. 7, lines 166-177). Additionally, we noted that we did not explore a wide range of TRN deformation distances (p. 6, 175). Because of the noise in the data and the fact that we selected worms with a TRN that visibly deforms due to actuation, none of our data has deformations less than 3 μm. We also removed the corresponding plot with data from the mutants, since it is not central to our argument.

Minor comments:
- bottom of page 2: 'used to' -> 'used it to'
- top of page 3, the sentence ending in 'distributed along their sensory' is missing a word or two at the end.
- page 3: 'devices trap' -> 'device's trap'
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- page 9: 'don't' -> 'don't' or 'do not'
- the first sentence of the Figure 4 caption is missing a word after mechanical

Thank you for noting these errors. We’ve made all of the corrections or updated the text containing these errors.

Reviewer #2 (Remarks to the Author):

- The treatment of strain in the manuscript is overly simplistic and at times confusing. First, many mechanosensory systems detect shear strain, not normal strain as quantified here. The reviewer is, of course, correct that many systems detect shear strain (e.g. in fluid flow across blood vessel walls). In this system, however, normal loads are converted into longitudinal strain based on the mechanics of the worm body (Eastwood et al., 2015; Sanzeni et al., 2019; Katta et al, 2019). The general mechanics model is drawn from Landau and Lifshitz and has been applied to biology in other contexts, for instance modeling how microtubules respond to indentation of their cylindrical walls with an increase in strain along the length of the cylinder (e.g. de Pablo, et al, 2003, Phys Rev Lett). To clarify things for the reader, we revised the text as follows:
• RESULTS, p. 6, line 132-146, we discuss the technical limitations preventing us from detecting shear or bending strain.

Moreover, normal strain in a 3-dimensional material with a local deformation cannot be sensibly reduced to a single number as done in the manuscript.

We thank the reviewer for prompting us to think more carefully about our assumptions. The experimental method we deployed here has limited spatial resolution and is not well-suited to detect strains in other dimensions. Our prior modeling studies also support the view that this particular system is compatible with a simplification to a one-dimensional longitudinal strain. In particular, the models indicate that indentation generates a strain field that is larger in the y dimension (along the long axis of the worm's cylindrical body) than it is in other dimensions (see Fig. 1, Sanzeni et al., 2019;).

![Diagram](image)

Also, the TRN is very thin relative to the worm’s body (300 nm vs. 50µm in diameter) and positioned within 200nm of the skin surface and can be viewed as a line passing through the strain field at the surface. Finally, the TRNs have very straight axons and do not meander. Taken together, these features suggest that the strain is generated primarily along the long axis of the body and the axon and that the size and morphology of the TRN make it reasonable to consider a one-dimensional longitudinal strain. Still, we sought to improve our communication to the reader regarding the rationale for considering only longitudinal strain and for discussing why this method is not suitable for three-dimensional strain in the Results section.

Given the authors' extensive work on modeling C. elegans body dynamics during deformation, I would expect a more sophisticated analysis of the geometry of the strain field. In Sec 3.1 it is stated that “Due to the nature of our measurement, we were only able to measure one-dimensional strain along the length of the TRN”. But since the authors acquired a confocal z stack to image mitochondria in 3 dimensions, and there are 6 cells expressing the transgene, I don't see why strain can only be measured in one direction. In fact, the authors have already measured displacement in the direction of the stimulus (perpendicular to the body axis), as shown in Fig. 1b. The field of view of our measurement limits us to imaging one TRN at a time, so we cannot take full advantage of the six TRNs expressing the transgene. While we do have measurements of displacement in 3 dimensions for one TRN, the initial distance between mitochondria in the direction of the stimulus (x) and optical axis (z) directions is close to zero, so calculating strain in those dimensions by dividing the
displacement by the initial distance leads to large non-sensical values. The diameter of the TRNs (200-300 nm) is also roughly the same as the theoretical resolution of the microscope we used (254 nm), so we cannot distinguish deformations within the cross-section of the neuron, only along its length. We’ve noted this in the manuscript and added a plot of the displacements in x, y, and z for control animals. Further, we’ve clarified that we’ve measured “longitudinal strain” by using this term throughout the paper.

- It would be useful to see not just the strain but the direction of displacement of each fluorescent object during the stimulus. This would shed some light into the strain field. We added a plot to Figure 2 showing the displacements in the x, y, and z directions as a function of distance from the center of the actuator.

- I am not convinced that the distance between mitochondria is a good representative of strain in a neurite. For example, some fibers exhibit a tortuous shape under compression. They are not really under compression/extension in the simplistic way suggested here but instead alter their extension via local bending. Showing micrographs of deformed and undeformed worms with a cytoplasmic GFP label in mechanosensory cells would help show how strain occurs in the touch neurons. The TRNs in the worm are unusually straight, even as the worm crawls (Krieg et al., eLife, 2017). Additionally, our results indicate that the TRN is in tension on average, so a tortuous buckling shape would be unlikely. Although we would have liked to include additional images of GFP-tagged neurons during deformation in the ‘poking chip’, we were unable to collect these data before our university reduced research operations on March 17, 2020.

- It is touted as a major result of the paper that “we showed for the first time that local indentation of the body of a worm leads to local strain in its TRNs”, and this is also reflected in the title. However, this is a completely expected result. I can't think of any scenario in which local indentation of the body would NOT lead to strain in the TRNs, which are only a few microns away from the cuticle. I would suggest the finding that TRN strain is not changed of ECM mutants is a much more significant finding. While this result is expected, it was not previously shown with experimental evidence. One goal of the paper was to provide this experimental evidence. An alternate hypothesis is that the TRNs are anchored at the cell body and slide with respect to the cuticle of the worm in response to mechanical stimuli. As experimentalists, we seek to test conceptual or theoretical ideas and sometimes we find what we expected (touch induces strain) and sometimes we make new discoveries (TRN attachment and ECM proteins are not essential for touch-induced strain). This manuscript has a bit of both types of findings.

Minor comments:

- In experiments measuring the strain in TRNs, it is not clear how the touch stimulus amplitude was set, and therefore what the 3.1% strain result really means. Is this the threshold for TRN activation? If so, what were the temporal properties of the deformation?

With our device, we do not have a way to directly measure the stimulus amplitude, but instead rely on applying a controlled pressure to the actuator and assume the stimulus is reasonably consistent. In our Methods section, we note that we applied 300 kPa of pressure to the actuator for each stimulus event. In previous experiments, a 10 Hz sinusoid between 200 kPa and 350 kPa was sufficient to activate the TRNs. Our imaging method was too slow to resolve varying stimuli, so we used a 300 kPa step stimulus and started acquiring each image stack after the stimulus settled.
Section 2.4: "While some mechanical coupling is by definition required to move the TRNs from their juvenile position, it is unknown what actually applies the force to move the neuron." This sentence seems to ignore the strong possibility that TRNs move themselves by cell migration. This sentence was intended to show the gap in our knowledge of how the forces responsible for moving the TRNs from their juvenile position. As part of our restructuring of the material introducing the ECM mutants, we have rephrased this to say "In him-4 and in mec-1(e1738) mutants analyzed here, the ALM and PLM neurons are displaced from their normal body position near the lateral midlines and are not properly embedded in the epidermis (Emtage et al., 2004; Vogel and Hedgecock, 2001). This effect is inferred to arise from a defective TRN-ECM attachment (Vogel and Hedgecock, 2001)."

Section 3.5: It may be correct that TRN response to a high-velocity stimulus is greater than to a low-velocity stimulus, but I don't know what is meant by "TRNs are activated mostly by high-velocity stimuli". We've clarified this sentence to say "wild-type C. elegans TRNs are preferentially activated mostly by high-velocity stimuli" and included references to the literature upon which this claim is based (Eastwood et al., 2015; Katta et al., 2019; Nekimken et al., 2017a; Suzuki et al., 2003).

Section 5.3: The viscosity of iodixanol at this concentration will be likely about 20 times greater than of water or saline. This may be much lower than that of other compounds tested, but I would not call it "only slightly higher" than saline. It would be helpful to be more specific here. We've changed our description of the mixture to clarify that its viscosity is closer to that of saline compared to the glycerin and halocarbon oil we tested. We did not make measurements of the mixture's viscosity, of any of these compounds, but only rejected glycerin and halocarbon oil because their viscosity was too high to be functional in our device.

Fig. 1a. This does not look anything like a Max projection of mitochondria in the TRN of a worm. It looks like a bright field image of a worm in a microfluidic. Scale bar is not defined. The image was mis-labeled. Panel A is a brightfield image. The label has been corrected and the scale bar defined appropriately.

Fig. 1b. What exactly is being shown in panel B, labeled "Motion of mitochondria induced by mechanical stimulus"? Is it an image of the mitochondrial tag? If so, how does it show motion as indicated by the caption? The color scheme is very odd for a fluorescence micrograph. What is the length of the scale bar? I would suggest showing the stimulated and unstimulated puncta on the same image so that we can see how the cell is deforming. Illustration of the strain field via arrows would also be helpful. We have changed the color scheme in the micrograph to a more traditional and colorblind-friendly green/magenta overlay and added the scale bar length. We have also clarified in the caption that this is an image of the mitochondria before and after the stimulus is applied.

Fig 1c. Why is the displacement in the direction of actuation being shown? Wouldn't the longitudinal displacement be more relevant to this experiment? The displacement in the direction of actuation is shown to give readers a better idea of the shape of the deformation profile. Displacements in other directions are now shown in Figure 2B.

Spelling errors: "longitundinal" should be "longitudinal" in Fig. 1.
Sec 3.3. "differtiate" should be "differentiate"
Sec 2.4.2 "mecanosensory" should be "mechanosensory"
We've corrected these spelling errors.

- Fig 2. (a) is this for a single trial? If so please also show data averaged over all worms tested. If not, please indicate number of trials and number of worms. (b) "neuronal displacement" is not accurate. This is displacement of the fluorescent tagged mitochondrion, not the neuron as a whole or its cell body. Since strain is calculated for displacements up to 100 microns, why does panel (b) show only displacements between 4 and 8 microns? Or does "displacements" mean something different in this context?

The x-axis on this plot was “Dist from actuator (um)”, which is easy to confuse with displacement. We’ve update all similar axis labels to simply say “distance, y (um)”.

(c) It’s a bit confusing to compare wild-type vs. "control", since wild-type (N2) is actually serving at the control in this experiment. It is better expressed as comparing N2 vs. jsIs1073 worms, or wild-type vs. transgenic worms.

We’ve changed our terminology to clarify as suggested.

Fig. 3. Are these individual trials? If not, how many worms were assayed for each plot with how many trials each? How are the shaded error regions defined?

We’ve updated the figure to indicate the number of trials averaged in each plot and noted the number of worms tested in the figure legends.
RE: Manuscript #E20-01-0049R
TITLE: "Touch Induces Local and Longitudinal Mechanical Strain in the Sensory Dendrites of C. elegans Somatosensory Neurons"

Dear Dr. Goodman:

I found your rebuttal to be reasonably responsive, with perhaps one exception.

Reviewer #2's last major point concerns significance of the work and the title. Please edit your title accordingly, such as: "Touch Induces Mechanical Strain in Somatosensory Neurons Independent of Extracellular Matrix Mutations in C. elegans"

Secondly, I believe it will benefit the reviewers and future readers to understand the handling of your revised submission if you allow MBoC to publish the complete review history of your manuscript. This will include decision letters (which includes reviewer comments to the author) as well as the author's rebuttal comments for all versions of the manuscript.

Thank you for submitting to the special 'Forces' issue of MBoC.

Sincerely,
Dennis Discher
Monitoring Editor
Molecular Biology of the Cell

Dear Dr. Goodman,

The review of your manuscript, referenced above, is now complete. The Monitoring Editor has decided that your manuscript requires minor revisions before it can be published in Molecular Biology of the Cell, as described in the Monitoring Editor's decision letter above and the reviewer comments (if any) below.

A reminder: Please do not contact the Monitoring Editor directly regarding your manuscript. If you have any questions regarding the review process or the decision, please contact the MBoC Editorial Office (mboc@ascb.org).

When submitting your revision include a rebuttal letter that details, point-by-point, how the Monitoring Editor's and reviewers' comments have been addressed. (The file type for this letter must be "rebuttal letter"; do not include your response to the Monitoring Editor and reviewers in a "cover letter.") Please bear in mind that your rebuttal letter will be published with your paper if it is accepted, unless you have opted out of publishing the review history.

Authors are allowed 180 days to submit a revision. If this time period is inadequate, please contact us immediately at mboc@ascb.org.
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Authors of Articles and Brief Communications whose manuscripts have returned for minor revision ("revise only") are encouraged to create a short video abstract to accompany their article when it is published. These video abstracts, known as Science Sketches, are up to 2 minutes long and will be published on YouTube and then embedded in the article abstract. Science Sketch Editors on the MBoC Editorial Board will provide guidance as you prepare your video. Information about how to prepare and submit a video abstract is available at www.molbiolcell.org/science-sketches. Please contact mboc@ascb.org if you are interested in creating a Science Sketch.

Thank you for submitting your manuscript to Molecular Biology of the Cell. Please do not hesitate to contact this office if you have any questions.

Sincerely,

Eric Baker
Journal Production Manager
MBoC Editorial Office
mbc@ascb.org
We thank the editor for his feedback and rapid response to our revised manuscript. According to the suggestions, we have revised the title (as indicated below) and verified that our analysis code is available in a publicly accessible repository.

“Touch-induced Mechanical Strain in Somatosensory Neurons is Independent of Extracellular Matrix Mutations in *C. elegans*”
RE: Manuscript #E20-01-0049RR
TITLE: "Touch-induced Mechanical Strain in Somatosensory Neurons is Independent of Extracellular Matrix Mutations in C. elegans"

Dear Dr. Goodman:

I am pleased to accept your manuscript for publication in Molecular Biology of the Cell.

Sincerely,
Dennis Discher
Monitoring Editor
Molecular Biology of the Cell

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