

**Reviewer Recommendation and Comments for Manuscript Number ABME-D-16-00586****Mechanics reveals the biological trigger in wrinkly fingers**

Original Submission  
Cormac Flynn **Reviewer 1**

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**Recommendation:** Major Revision

**Transfer Authorization**

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**Response**

Yes

If this submission is transferred to another publication, do we have your consent to include your original review?

Yes

**Custom Review Question(s)**

Is this paper significant enough to merit publication in the Annals of Biomedical Engineering? A study may be well-executed and "solid," but does it present significant, impactful research? Keep in mind that only 25% of papers submitted are accepted for publication.

**Response**

Yes

Have the authors provided a Conflict of Disclosure statement describing potential relationships, both financial and personal, that might affect the conduct or interpretation of the work?

Yes

If the work involves human subjects, has the work has been performed with approval by the appropriate ethical committees (e.g. Institutional Review Board, IRB) related to the institution(s) in which it was performed? If "yes", does a statement regarding approval appear in the Methods section of the manuscript?

N/A

If the work involves vertebrate animals, is there evidence that the work was approved by and performed in accordance with the guidelines of the institution(s) where it was performed (e.g. Institutional Animal Use and Care Committee, IACUC)? If "yes", does a statement regarding approval appear in the Methods section of the manuscript?

N/A

If the work involves human embryonic stem cells, has the procurement and research been performed with approval by the appropriate ethical committees (e.g. Embryonic Stem Cell Research Oversight committee, ESCRO), related to the institution(s) in which it was performed? If "yes", does a statement regarding approval and accordance appear in the Methods section of the manuscript?

N/A

If the work makes use of cells or tissues obtained by the authors by means other than commercial sale, have they been obtained by means approved by the appropriate ethical committees (e.g. IRB) related to the institution(s) in which it was performed? If "yes", does a statement regarding approval and accordance appear in the Methods section of the manuscript?

N/A

Is the research in this article newsworthy (does it merit a promotional media story)? If so, please give a quotable description or explanation.

no

**Reviewer Blind Comments to Author:**

Mechanics reveals the biological trigger in wrinkly fingers

**Summary**

The authors present a finite element model to investigate the mechanics of finger skin wrinkling. A neo-Hookean law represented the soft tissue layers with material parameters from the literature used. A growth model based on previous work is used to simulate swelling and contraction of the layers. They simulate three situations - 1. swelling of the epidermis; 2. contraction of the dermis; 3. swelling of epidermis and contraction of dermis combined. Key results include: 1. epidermal expansions of 10% required for wrinkling to occur; 2. dermal contractions of 20% required for wrinkling to occur; 3. When both expansion and contraction occur simultaneously then lower levels are required than if they occurred individually; 4. Comparing with observations of patients whose fingers do not wrinkle and whose dermis is incapable of contraction, the authors conclude that expansion of the epidermis should be less than 10%.

The manuscript is well presented but I would suggest a proof-read by a native English speaker. I have several specific comments that need to be addressed in addition to spelling and grammar issues. These are detailed below.

**Specific comments**

- Line 9, Page 2: In the Abstract, what does 10% expansion or 20% contraction mean? Is it based on volume change?
- Line 9, Page 2: "Therefore, the upper layers can not exceed this expansion level in order to not contradict in vivo observations". At this point it is not clear to the reader what the in vivo observations are. It would be helpful to detail them briefly.
- Line 9, Page 3: "... to allow for a better grip, faster and more easily, on ...". This phrase needs to be reworded to be grammatically correct.
- Line 17, Page 3: "... allow water to flow away of the finger as ...". "of" needs to be "from".
- Line 29, Page 3: It is the external and stiffer layer in the epidermis." This sentence does not make sense.
- Line 32, Page 3: "... which make the epidermis to swell." should read "... which makes the epidermis swell."
- Line 54, Page 3: "hypodermic" should be "hypodermis".
- Line 59, Page 3: "set" should be "sets".
- Line 24, Page 4: "18, 19 studied ..." The author names should be given here.
- Lines-46-49: "... and among them, and as far as we know any have analyzed the coupling effect of the contraction and expansion mechanisms" should be reworded ", and as far as we know none analyze the coupling effect of the contraction and expansion mechanisms" or similar.
- Line 54, Page 4: "referenced" should be "referenced".
- Line 31, Page 5: "in what extend" should be "to what extent"
- Equation (2): C needs to be defined here. It is later on.

14. Lines 45-58, Page 9: It would be helpful to have a diagram illustrating the finite element model - even a simplified representation of the model
15. Lines 39-54, Page 10: Can the authors provide further details on the adaptive time stepping? Initial step size, maximum, minimum step size?
16. Line 56, Page 10: "As the only boundary condition in the problem ..."; a second boundary condition is described on the following page so it is not the only one.
17. Line 56, Page 10 - Line 16, Page 11: How realistic are the boundary conditions? Is there no relative movement of tissue at the bone/tissue interface.
18. Lines 35-37, Page 11: The two instances of "... associated to ..." should read "... associated with ...".
19. Line 52, Page 11: "... a exploration ..." should be "... an exploration ...".
20. Figures 3 and 4: The subscripts "epi" and "dermis" should be added to correspond to the caption parameters
21. Lines 57-59, Page 13: "... the wrinkles clearly appeared even though the individual counterparts were almost imperceptible." Can the authors clarify this sentence? What are the individual counterparts? Are you referring to cases where contraction and expansion were simulated separately?
22. Figure 5: The presentation is a little confusing. I suggest putting the swelling and contraction in brackets underneath each sub-figure as is done in the caption for A, B, and C. If this is done then the caption can be shortened. Similar comments apply to Figure 6.
23. Lines 41-42, Page 15: "unperceptible" should be "imperceptible".
24. Lines 49-51, Page 15: "... not as determining as the expansion of the epidermis." I suggest rewording this phrase. Perhaps "... less effective than expansion of the epidermis".
25. Swelling and expansion are used to describe the change to the epidermis. I suggest using a consistent term.
26. Line 56, Page 15: in vivo should not be hyphenated
27. Line 59, Page 15: "stablished" should be "established". There are a few instances of this.
28. Line 27, Page 17: "?shrink?" and "?swell?" - presumably there is a formatting error here and there should be quotes in place of the ?
29. Line 30, Page 17: The author name should be before 46.
30. Line 57, Page 17: There is a question mark after the no. 7 reference.
31. Line 21, Page 18: "... alone was ..." should be "... alone were".
32. Line 24, Page 18: "... level have ..." should be "... level has ...".
33. Lines 31-34, Page 18: "it would imply that the vasculature is made of 50% of the tissue volume and that it would be entirely collapsed inward." What is the % volume of the vasculature?
34. Lines 54, Page 18: "require" should be "required"
35. Line 39, Page 19: "... the low variability on these factors support this approach." Can the authors provide references to support this statement?
36. The formatting of the references is not consistent. For example, [29, 33, 37]
37. Comparing Figure 4 and Figure 5: Should the fourth sub-figure in Figure 4 be the same as the middle sub-figure in Figure 5? They don't look the same even though they have the same level of contraction. Can the authors clarify?
38. What effect does the geometry have on the results? Does the size of the finger have an effect?
39. The neo-Hookean model chosen to represent the soft tissue is isotropic. Skin is an anisotropic material and exhibits a non-linear stress strain curve. What is the effect of your simplifications on the results? This limitation needs to be addressed in the discussion.
40. Skin is in tension on the human body. Tension fields have a significant effect on the formation of wrinkles. You have ignored this in your model. What influence does this have on your results? This limitation also needs to be addressed in the discussion.

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#### Reviewer Confidential Comments to Editor:

##### COMMENTS TO THE EDITOR:

Is any question raised of violation of WHO/CIOMS  
 "International Guiding Principles for Research Involving Animals and Human Beings"?  
 Yes  
 No

Please write a brief statement regarding the nature and significance of the contribution made by the paper and any other confidential comments to the Editor. If it does not make a significant contribution, please say so here:  
 The paper is an interesting one and the results are reasonably well presented (asides from comments raised above). My main concern are the simplifications made representing the soft tissue with a neo-Hookean model and ignoring the in vivo tension. The latter, in particular, would have an effect on the results. The authors need to address these limitations.

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