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Peer Review File

# Solution-Processable and Photo-Curable System for Low-cost and Scalable Transient Electronics

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**This file contains all reviewer reports in order by version, followed by all author rebuttals in order by version.**

Version 0:

Reviewer comments:

Reviewer #1

(Remarks to the Author)
Summary of the manuscript: The submitted manuscript describes a simple approach to realizing low-cost transient electronics by presenting solution processable and photo-curable material systems. The authors have innovated insulating, semiconducting, and conductive materials and performed detailed characterization of all three. Given the growing interest in bioelectronics as well as transient electronics, the presented research is timely. Although detailed characterization of the functional properties of the developed materials has been performed, additional characterization of these properties as the materials "age/degrade" in biological conditions is required to corroborate the initial claims.

Major comments:
1. The authors claim that the developed materials are biodegradable and biocompatible. This is confirmed by immunohistochemistry and blood chemistry analysis. What about the cytotoxicity of the materials? This can be confirmed following the protocol and metrics described in ISO 10993.
2. The degradability of the materials and devices is presented at high pH of 13 (Figure 1.e). What are the kinetics of degradation of the conductive materials under neutral pH? Figures 2.d, 2.h and S6 present this information for insulating and semiconducting materials. Similar characterization for the conducting materials will be helpful. This is also help quantify the expected lifespan of the devices under physiological conditions?
3. Is there a difference between structural degradation rate and the functional degradation rate of the devices? To be more specific- do the devices "fail" in their function at a faster rate than structural degradation?
4. PEDOT:PSS is used as a building block of the conductive materials in these bioelectronics; however, it is not known to be inherently biodegradable. Therefore, can the authors comment on the structure of PEDOT:PSS after the substrate materials degrade? Experimentally, analysis of the eluent solution can be performed as determine the structure of PEDOT:PSS when the conductive materials are exposed to simulated biological conditions for long-periods.
5. Please present the data in Figures 3.b, 3.c, 3.e, and 3.n as mean ± error, if possible.
6. For bidirectional bioelectronics and neural interfaces, it is important to characterize both the electrochemical impedance as well as the stimulation capacity. In this work, the electrode impedance has been characterized for as fabricated devices, however characterization of the stimulation capacity should also be included. For reference, see- https://www.annualreviews.org/content/journals/10.1146/annurev.bioeng.10.061807.160518
7. How does the electrochemical impedance and electrical conductance of the conducive materials in the bioelectronics change over time? Since the electrodes are biodegradable and are expected to starting degrading when exposed to biological systems, does their impedance also increase? Does that affect the recording capabilities and the signal quality?

Minor comments:
1. Low-cost and economic feasibility are presented as key properties of the suggested materials and processes. In the supplementary information, a subjective analysis of the cost of the materials and processes is presented. The authors are suggested to include a quantitative cost-comparison of the materials and processes. I acknowledge that costs vary across regions and vendors, therefore either a range can be provided or an estimate using the actual cost of materials and processes utilized in this work.
2. Do the devices and the materials following a linear heating trend at elevated temperatures?
3. Line 56: Please remove "that" from "… which offers that a…"
4. Figure S23, please provide details on the error bars and the n value of the characterization.

Reviewer #2

(Remarks to the Author)
The manuscript by Han et al., demonstrates the development of a solution processable and photo-patternable electronic material that can be utilized as substrates, semiconductors and conductors for building simple cost-effective and scalable fabrication of soft, stretchable and transient electronics. The authors presented massive results from their in vivo animal tests demonstrating the diagnostic and therapeutic capabilities of the transient system in the central organs such as the brain and heart; however, several items must be refined to ensure scientific structure and enhance the work's potential.
Major Concerns
1. Firstly, I suggest changing the tone of the writing style. In the current style, everything all goes as description of figures, one by one.. "Figure 1a illustrates" ... ", "Figure 2a elucidates"... etc – it all reads like description of the figures. I suggest the authors to structure their manuscript based on the story, and have the figures support the story, and not the other way around... When describing figure by figure, this massive work actually reads like a review and it is not clear which part the authors have made, how does it compare to the state-of-the-art (especially considering that there are ~10 different combinations of the materials).
2. To continue on the previous point, it would be essential to show a comprehensive comparison table for materials and devices made in this work compared (noteworthy) to other transient electronic devices (state-of-the-art).
3. The manuscript significantly lacks discussion, especially in terms of fabrication processes, device performance, and their applications. This would help showiing significance.
4. All figures are very busy, showing that a lot has been done, but it might be better to emphasize certain elements of the work, and remove secondary analysis into supplementary. I would suggest the authors to re-evaluate, together with working on the "discussion" section of the paper - what is deemed most novel element of the paper - and craft the figures accordingly.
5. I would also suggest the authors to add the figures in-line with the text and not at the end (it is very difficult to review in such a way).
6. The manuscript lacks details on how electrophysiology data can be affected based on charging strains. Please add systematic recordings ECG/EMG and impedance spectra at 0 %, 10 %, 20 %, and 30 % strain to assess whether stretching degrades the SNR, increases noise, or shifts impedance magnitude/phase.
7. Figure 3j, the EMG data does not show clear differences in consistent morphology during hand close and open. If you high-pass (perhaps 20 Hz), rectify, envelope and increase trial count so that hand-open vs hand-close bursts show consistent, statistically comparable waveform features.
8. Figure 4c and 4d are not sufficient, and need to represent the data in terms of frequency or show SNR differences. Might be helpful to quantify signal fidelity across the 8-week implant with frequency-domain metrics rather than time-domain traces alone.
9. Figure 4g reports spike count and amplitude reductions after stimulation, but the time window used to define a valid cycle and count spikes is missing. Kindly, specify definition of the valid analysis window, Spike-detection algorithm (threshold, normalization etc.), and Exact segment duration used for counts.
10. In Figure 4j, stimulation is specified as 5 V pulses of 100 μs duration, but the delivered current is not reported. Because tissue impedance can vary both between electrodes and over time, the actual stimulation current and the effective stimulation intensity may fluctuate too across trials. The authors should clarify whether they used a constant current source or monitored and regulated the current on each pulse to ensure consistent interpretation of the observed heart-rate and QRS-amplitude changes.
11. Figure S21 is not sufficiently processed to understand the significant Stimulation related spike event. Please apply band-pass filtering or wavelet denoising, then overlay averaged baseline vs post-stimulation spike waveforms to clearly show amplitude changes.
12. Figure S22 is somewhat unclear. The differences in the data should be better justified using spectrograms or power spectra, with clearly defined frequency ranges for motion artifacts, noise, average signals, and post-stimulation high-frequency activity. The suppression of epileptic spikes is generally more interpretable in the frequency domain than in the time domain.

Minor Concerns:
1. In figure S19 – please discuss whether ~30 kΩ at 1 kHz is compatible with low-noise in vivo recordings and suggest strategies to lower impedance for use.

Reviewer #3

(Remarks to the Author)
I co-reviewed this manuscript with one of the reviewers who provided the listed reports. This is part of the Nature Communications initiative to facilitate training in peer review and to provide appropriate recognition for Early Career Researchers who co-review manuscripts.

Version 1:

Reviewer comments:

Reviewer #1

(Remarks to the Author)
The authors acknowledge that PEDOT:PSS remains chemically stable under physiological conditions in their response to

original comment #2. This would then negate the claims presented in the paper regarding biodegradable and biocompatible electronics since PEDOT:PSS is not biodegradable. The authors should revise the claims such that they are well corroborated by experimental results.

Reviewer #2

(Remarks to the Author)
The reviewers addressed all of the previously raised comments. Happy to recommend publication of the manuscript as is at this stage.

Reviewer #3

(Remarks to the Author)
I co-reviewed this manuscript with one of the reviewers who provided the listed reports. This is part of the Nature Communications initiative to facilitate training in peer review and to provide appropriate recognition for Early Career Researchers who co-review manuscripts.