nature portfolio

Peer Review File

One-pot Fabrication of High-strength Janus Hydrogel for Wet Tissue Hemostasis and Intestinal/Intrauterine Anti-adhesion

Corresponding Author: Professor Keke Wu

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)
This work presents a novel method for preparing Janus hydrogels with high-strength and remarkable bilateral asymmetric adhesion via a streamlined one-pot synthesis. Remarkably, this entire process can be accomplished in under 5 minutes. This Janus hydrogel functions effectively as an emergency patch to achieve hemostasis and sealing for various organs. Meanwhile, in rat models with intestinal and endometrial tissue damage, the Janus hydrogel exhibited robust unilateral adhesion to the injured intestinal and endometrial tissues, significantly facilitating wound healing and markedly reducing postoperative adhesions. This study offers a viable and practical design for the next generation of biological adhesives, underscoring its immense potential as a substitute for internal wound repair sutures. This work contains high scientific novelty as it for developing Janus hydrogels with high mechanical strength through simple, efficient, and cost-effective methods. I here recommend the publication of this work in Nature Communications after some revision. Detailed comments are provided below.
1.In the comparison of adhesion strength (Fig. 2L), the author is encouraged to provide more comparative data with different commercial gels or adhesives for further highlight the advantages of this Janus hydrogel.
2. Why choose sodium lignosulfonate as the anionic surfactant for regulation? Could other anionic surfactants also be used as regulatory molecules for the bilateral asymmetric adhesion? If so, what are the advantages of choosing sodium lignosulfonate? Please explain.
3. The preparation of Janus hydrogel involved the use of acrylic acid and acrylamide, both of which are toxic monomers. Using them in in vivo experiments may pose potential threats. How did the author avoid their effects? And provide relevant experimental evidence to prove it.
4. In the in vivo intestinal injury model, based on previous research, the authors scored the degree of intestinal adhesion. To enhance the rigor of the animal experiments and the readability of the text, the authors need to draw on and construct the adhesion scoring standard specific to this study and add it to the supporting information, rather than simply citing it directly.
5. In the swelling experiment (Figure 3L), why did the swelling ratios of hydrogels containing different amounts of sodium lignosulfonate show differences after 168 hours? Please explain the possible reasons for this phenomenon and describe them in the text.
6. The author uses sodium lignosulfonate as a regulatory molecule, whose primary functions are to emulsify hydrophobic molecules and drive the formation of heterogeneous structures. This indicates that it does not undergo covalent cross-linking within the hydrogel, which may lead to its loss over time during application. Could this potentially result in the disruption of the hydrophobic layer's structure? The author needs to verify this through experiments and provide an analysis.
7. In the cell compatibility experiment (Figure S8-S10), it was observed that sodium lignosulfonate at a high concentration (3% w/v) had a certain impact on cell proliferation. Please explain this phenomenon and supplement the explanation into the text.
8. Explain how immunohistochemistry (e.g., PCNA) and immunofluorescence (e.g., TNF-α, TGF-β1) were quantified and to what the expression was normalized (e.g., DAPI-positive cells, area); clarify what "71% expression" (e.g., PCNA) represents.
9. Statistical analysis: Were the homogeneity and normality of the data analyzed? If so, indicate the tests performed.
10. The sample size in vivo experiment (n=3) was below the commonly accepted standard (typically n≥6). Were repeated trials conducted, or is there a plan to increase the sample size in subsequent studies?
11. A comprehensive review of the manuscript is recommended to ensure linguistic accuracy and phraseological consistency throughout the text, which would enhance the overall clarity of scholarly communication.
12. In Scheme 1A, the naming of the hydrogel (SLAA hydrogel) is inconsistent with that in the text (SLAA Janus hydrogel). Please make revisions to ensure uniformity.

13. In Figure 7C, the author needs to use arrows or dashed lines to distinguish between normal tissue and adhesive tissue to enhance readers' understanding of the image.
14. Method section: for crucial experiments such as the modeling of animal experiments, relevant literature should be cited to provide support. Additionally, the description of the experimental methods should be as detailed as possible to enhance the reproducibility.

Reviewer #2

(Remarks to the Author)
This manuscript describes an original and interesting hydrogel system, termed "Janus", as promising alternatives to traditional sutures for internal wound closure and management. The hydrogel is well characterized, using various in-vitro relevant tests and animal studies.
Although a lot of study has been performed, it appears that the manuscript in its current form is not suitable for publication in Nature Communications for the following reasons:
1. It only describes the results, without discussing them. The "discussion" section is actually a summary of the results, rather than a discussion. Therefore, thorough understanding of the science that stands behind the technology is missing. I.e., it has only applicability value, without any scientific value.
2. The manuscript contains many Figures, and each one includes several sections. The Figures are small and not clear, which makes the manuscript hard to read and understand.
Based on this opinion, it appears that this manuscript may be more suitable for publication in one of the Biomaterials Journals, with applicative nature, rather than in Nature Communications.

Version 1:

Reviewer comments:

Reviewer #1

(Remarks to the Author)
The authors have fully revised the manuscript according to the suggestions. I suggest accepting the current version.

Dear Editor,

We would like to express our sincere gratitude for your comments concerning our manuscript entitled "***One-pot Fabrication of High-strength Janus Hydrogel for Wet Tissues Rapid Hemostasis and Intestinal/Intrauterine Anti-adhesion*****" (Manuscript No. NCOMMS-25-103478A)**" and for giving us the valuable opportunity to make revisions. The comments are valuable and constructive for improving our manuscript. We have looked into your comments carefully and made some changes accordingly. Revised parts were marked in red in the 'Revised Manuscript with Track Changes' file and the 'Supplementary Material' file. Responses to address the concerns of the two reviewers are outlined below:

Response to the reviewers' comments:

Reviewer #1 (Remarks to the Author):

This work presents a novel method for preparing Janus hydrogels with high-strength and remarkable bilateral asymmetric adhesion via a streamlined one-pot synthesis. Remarkably, this entire process can be accomplished in under 5 minutes. This Janus hydrogel functions effectively as an emergency patch to achieve hemostasis and sealing for various organs. Meanwhile, in rat models with intestinal and endometrial tissue damage, the Janus hydrogel exhibited robust unilateral adhesion to the injured intestinal and endometrial tissues, significantly facilitating wound healing and markedly reducing postoperative adhesions. This study

offers a viable and practical design for the next generation of biological adhesives, underscoring its immense potential as a substitute for internal wound repair sutures. This work contains high scientific novelty as it for developing Janus hydrogels with high mechanical strength through simple, efficient, and cost-effective methods. I here recommend the publication of this work in Nature Communications after some revision. Detailed comments are provided below.

Response: We sincerely appreciate your positive appraisal and valuable feedback on our manuscript. Based on your constructive suggestions, careful revisions were made to the manuscript point by point. We hope that the revisions meet your expectations and adequately address all concerns.

Comment 1: In the comparison of adhesion strength (Fig. 3L), the author is encouraged to provide more comparative data with different commercial gels or adhesives for further highlight the advantages of this Janus hydrogel.

Response: Thank you sincerely for your recommendations. To further demonstrate the excellent adhesive performance of SLAA Janus hydrogel and make a comprehensive comparison with other commercial gels or adhesives, we tested the adhesion strength of three new commercial adhesives (Tegaderm^{TM}, Dermafuse^{TM}, and Dermabond^{TM}) and compared them with SLAA Janus hydrogel. As shown in **Fig R1**, it could be found that the burst pressure of Tegaderm^{TM} (~76 mmHg), Dermafuse^{TM} (~79 mmHg), and Dermabond^{TM} (~91 mmHg) were significantly lower than the

maximum burst pressure of SLAA Janus hydrogel (~286 mmHg). The results further highlight the advantages of this Janus hydrogel over current commercial gels or adhesives. The related descriptions were shown and highlighted in the “Asymmetric adhesion properties” subsection of the “Results” section of the 'Revised Manuscript with Track Changes' file. And the related figure revision was also shown in **Fig. 3L** in the 'Revised Manuscript with Track Changes' file.

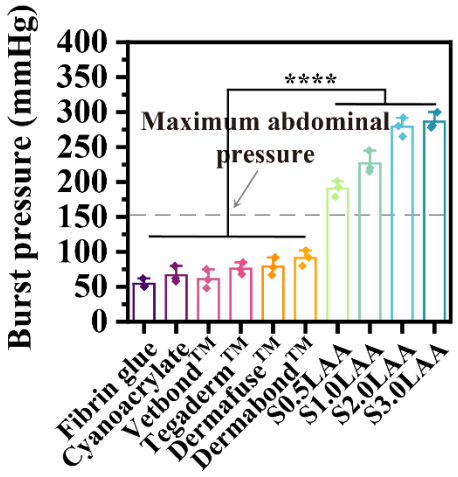

Fig. R1. Comparison of burst pressure of SLAA Janus hydrogels to some commercial bio-adhesives.

Comment 2: Why choose sodium lignosulfonate as the anionic surfactant for regulation? Could other anionic surfactants also be used as regulatory molecules for the bilateral asymmetric adhesion? If so, what are the advantages of choosing sodium lignosulfonate? Please explain.

Response: Sodium lignosulfonate (SL) is a sulfonate derived from lignin via sulfonation modification. Compared with other anionic surfactants, it is a by-product of the papermaking industry, characterized by its abundant sources and low cost. Utilizing it as a high-value-added material

contributes to the reduction of resource waste and environmental pressures, aligning with the principles of a circular economy. Meanwhile, SL has attracted growing interest in biomedical-related fields such as bioimaging, drug delivery, and functional material construction in recent years, owing to its cost-effectiveness, environmental friendliness, superior dispersibility, and high stability. For instance, Ni et al. developed a lignin hydrogel with favorable stretchable, compressible and antifreeze properties, which is suitable for advanced bionic hand control (***Advanced Functional Materials, 2025, 35: 2416916***). Huang et al. designed a mixed hyaluronic acid hydrogel composite material via biosynthetic lignin dehydrogenation polymer for cartilage repair (***Advanced Composites and Hybrid Materials, 2023, 6, 180***). These findings suggest that SL holds promise for the development of advanced functional hydrogels. Based on the above reasons, we chose sodium lignosulfonate as the anionic surfactant to participate in the preparation of the hydrogel and to carry out the regulation.

Comment 3: The preparation of Janus hydrogel involved the use of acrylic acid and acrylamide, both of which are toxic monomers. Using them in in vivo experiments may pose potential threats. How did the author avoid their effects? And provide relevant experimental evidence to prove it.

Response: During the formation of hydrogels, acrylic acid and acrylamide monomers will polymerize into polyacrylic acid and polyacrylamide. Their chemical properties are stable and they are not absorbed by organisms. It

has been confirmed that they have no biological toxicity (***Journal of the American Chemical Society, 2018, 140(30): 9466-9477***). In order to remove the residual reagents (including acrylic acid and acrylamide) inside the hydrogel, the hydrogels were thoroughly purified by immersing it in the deionized water (500 mL for 2 h and repeated 6 times) to remove the residual reagents inside the hydrogel. And the purified Janus hydrogel was obtained until reaching the original weight by putting it in the hood at RT. After purification, the hydrogel was immersed in deionized water for 24 h, and the absorption of acrylic acid and acrylamide in the extract was detected by ultraviolet spectrophotometer. As shown in **Fig. R2**, no acrylic acid or acrylamide monomers were detected in the extract, indicating that these monomers had been completely removed from the hydrogel during purification-ensuring they would not interfere with hydrogel performance during application. Besides, as displayed in the subcutaneous implantation experiment (**Figs. 5D-5H**), the implantation of hydrogel did not cause inflammatory infiltration, necrosis or suppuration in healthy skin tissue or lesions in important organs within 21 days. The result further demonstrated favorable biocompatibility of the hydrogel *in vivo*. The related descriptions were shown and highlighted in "*In vitro* anti-adhesion and bio-compatibility properties" and "Preparation and characterization of SLAA Janus hydrogels" subsection of the "Results" section and **Supplementary Fig. 1** in Supplementary Material of the 'Revised Manuscript with Track

Changes' file.

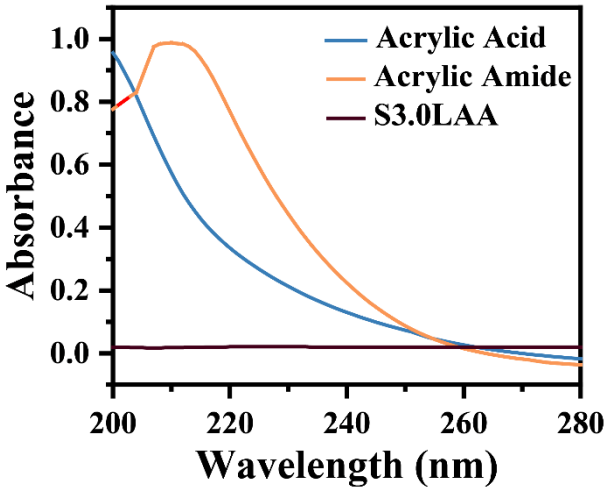

Fig. R2. UV-vis spectra of acrylic acid, acrylic amide and S3.0LAA.

Comment 4: In the in vivo intestinal injury model, based on previous research, the authors scored the degree of intestinal adhesion. To enhance the rigor of the animal experiments and the readability of the text, the authors need to draw on and construct the adhesion scoring standard specific to this study and add it to the supporting information, rather than simply citing it directly.

Response: Thank you for your suggestions. To further enhance the rigor of the animal experiments and the readability of the text, we referred to the reference (***Advanced Functional Materials, 2025, 34(21): 2314402***) and construct the adhesion scoring standard specific to this work. As shown in **Fig. R3**, fourteen days after intestinal injury, rats were euthanized, and the level of abdominal adhesions was evaluated. A standardized adhesion scoring system using a double-blind method was applied where: score 0, no adhesion; score 1, one thin filmy adhesion; score 2, more than one thin

adhesion; score 3, thick adhesion with plantar attachment or more than one thick adhesion with a focal point; score 4, very thick vascularized adhesion or more than one plantar adhesion. The related descriptions were shown and highlighted in "*In vivo* intestinal injury sealing and tissue anti-adhesion" subsection of the "Results" section and **Supplementary Fig. 17** in Supplementary Material of the 'Revised Manuscript with Track Changes' file.

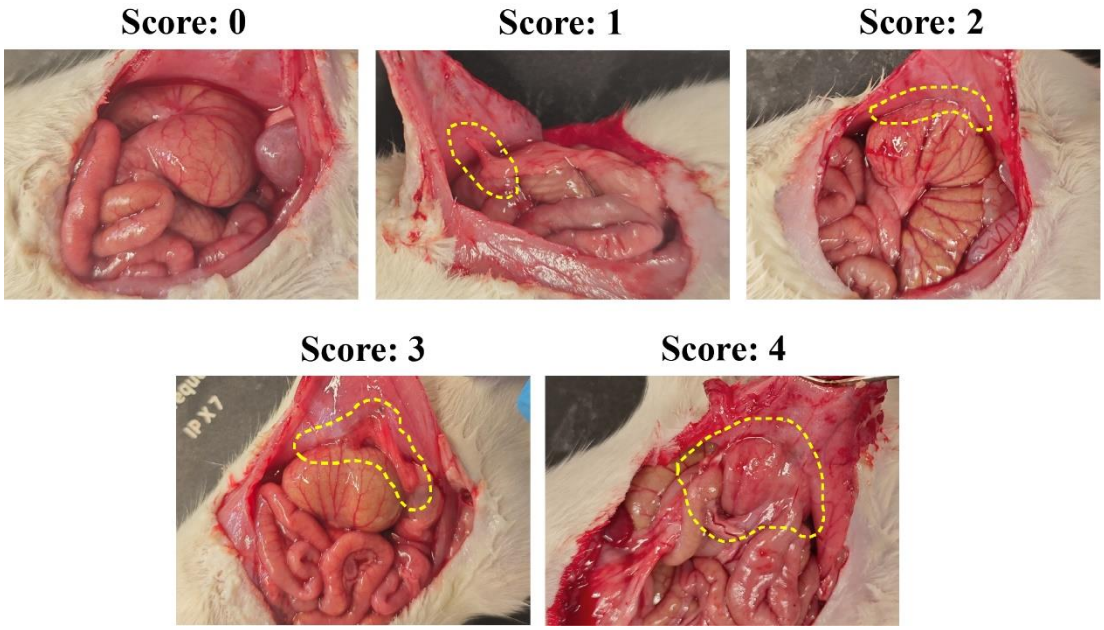

Fig. R3. The standard scoring system was used to evaluate the degree of adhesion.

Comment 5: In the swelling experiment (Figure 4L), why did the swelling ratios of hydrogels containing different amounts of sodium lignosulfonate show differences after 168 hours? Please explain the possible reasons for this phenomenon and describe them in the text.

Response: As shown in **Fig. 4L**, with increasing sodium lignosulfonate (SL) content, the equilibrium swelling ratios of hydrogel increased from ~19% (S0.5LAA) to ~24% (S3.0LAA) after 168 hours. It indicated that the

equilibrium swelling ratios was positively correlated with the content of SL. The possible reasons for this phenomenon might be as follows: SL drives directional enrichment of carboxyl groups within the hydrogel, forming a heterogeneous structure at the top and bottom. With increasing SL, this asymmetry became increasingly evident. The increase of SL intensifies the formation of this asymmetrical structure, thereby weakening the uniformity of the hydrogel network and causing an uneven distribution of internal stress. The uneven internal stress will make the hydrogel more susceptible to water molecule penetration and swelling (***Nature Reviews Materials*, *2024, 9(6): 380-398***). Therefore, the change in SL content to some extent affects the swelling rate of the hydrogel. The related descriptions were shown and highlighted in fourth paragraph of the "Discussion" section of the 'Revised Manuscript with Track Changes' file.

Comment 6: The author uses sodium lignosulfonate as a regulatory molecule, whose primary functions are to emulsify hydrophobic molecules and drive the formation of heterogeneous structures. This indicates that it does not undergo covalent cross-linking within the hydrogel, which may lead to its loss over time during application. Could this potentially result in the disruption of the hydrophobic layer's structure? The author needs to verify this through experiments and provide an analysis.

Response: Thank you for your insightful suggestion. To demonstrated whether the hydrophobic layer's structure of Janus hydrogels was reserved

during application. We characterized the Janus structure of S3.0LAA Janus hydrogel which were used in the animal experiments (rat intestinal injury model) in this study (**Fig. 7**) and collected after the experiments were finished. As shown in **Fig. R4**, SEM images suggested that the top of the hydrogel still presented a distinct porous network structure compared to the bottom, with no significant changes from before use, revealing that the hydrophobic layer structure of the hydrogel was not damaged. Additionally, the surface contact angles (SCA) of the top and bottom of the hydrogel were measured, with values of 100.3° and 55.7°, respectively. This indicated that the top of the hydrogel still exhibited hydrophobic properties compared to the hydrophilic bottom structure. Hence, both the findings in SEM images and SCA test illustrated that the hydrophobic layer's structure of Janus hydrogels were not be disrupted during application. The reason for this phenomenon could be that the hydrophobic molecules, lauryl methacrylate (LMA), emulsified by sodium lignosulfonate, and the hydrophilic molecules, acrylamide and acrylic acid, underwent covalent cross-linking under the initiation of the initiator. This enabled the hydrophobic property at the top of the hydrogel to be maintained even when a portion of the sodium lignosulfonate was lost. The related descriptions were shown and highlighted in “In vivo intestinal injury sealing and tissue anti-adhesion” subsection of the “Results” section and **Supplementary Fig. 18** in Supplementary Material of the 'Revised

Manuscript with Track Changes' file.

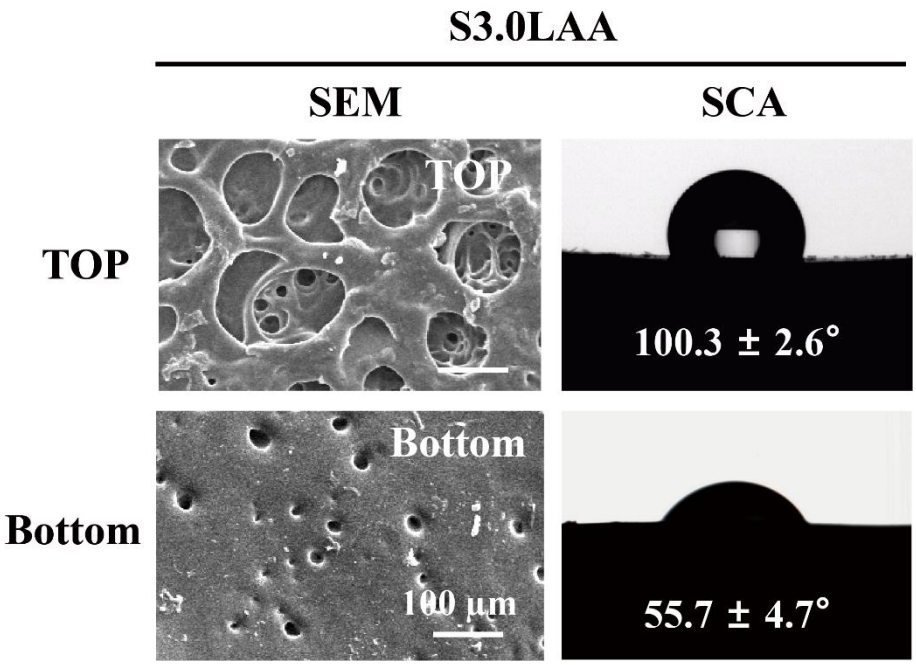

Fig. R4. SEM images and SCA test of S3.0LAA Janus hydrogel.

Comment 7: In the cell compatibility experiment (Figure S9-S11), it was observed that sodium lignosulfonate at a high concentration (3% w/v) had a certain impact on cell proliferation. Please explain this phenomenon and supplement the explanation into the text.

Response: Thank you for your question. In the cell compatibility experiments (**Supplementary Figs. 9-11**), we found that when the mass volume fraction of sodium lignosulfonate was within the range of 0.5% to 2.0%, the cell viability was comparable to that of the blank control group, which further verified that it had favorable cytocompatibility. When the mass volume fraction was raised to 3.0%, a slight decline in cell viability was observed. This might be attributed to the fact that as an anionic surfactant, it would increase the ion content (sodium ions and sulfonate anions) in the solution upon dissolution, creating a high osmotic pressure

environment that could lead to an imbalance of water inside and outside the cells, thereby disrupting normal metabolic activities. This dehydration stress can inhibit cell proliferation, manifesting as a decrease in proliferation rate or cell cycle arrest (***Nature Communications, 2020, 11, 1732***). The related descriptions were shown and highlighted in the fifth paragraph of the “Results” section of the 'Revised Manuscript with Track Changes' file.

Comment 8: Explain how immunohistochemistry (e.g., PCNA) and immunofluorescence (e.g., TNF-α, TGF-β1) were quantified and to what the expression was normalized (e.g., DAPI-positive cells, area); clarify what "71% expression" (e.g., PCNA) represents.

Response: We used Image J software to conduct the semi-quantitative analysis of immunohistochemistry and immunofluorescence. For immunofluorescence (e.g., TNF-α, TGF-β1), the mean fluorescence intensity (MFI) of the positive area corresponding to the fluorescence channel for each marker was analyzed and compared between groups. For immunohistochemistry (e.g., PCNA), the average optical density (AOD) values of the positive areas of the markers were analyzed and compared between groups. The corresponding description: “*For semi-quantitative analysis, ImageJ software was employed to process the data. For the results of immunofluorescence staining, the mean fluorescence intensity (MFI) within the positive regions corresponding to the fluorescence*

channel of each specific marker was meticulously measured and compared across experimental groups. Similarly, for immunohistochemical staining outcomes, a comparable analysis was conducted by calculating and comparing the average optical density (AOD) values of the positive areas corresponding to the markers among different groups." was added and highlighted in "Rat IUA model construction" subsection of the "Methods" section of the 'Revised Manuscript with Track Changes' file. "71% expression" (e.g., PCNA) represented the relative average optical density expression level of PCNA, the clarification was added and highlighted in "Rat IUA model construction" subsection of te "Methods" section of the 'Revised Manuscript with Track Changes' file.

Comment 9: Statistical analysis: Were the homogeneity and normality of the data analyzed? If so, indicate the tests performed.

Response: In the Statistical analysis section, we did not conduct homogeneity and normality tests on the data.

Comment 10: The sample size in vivo experiment (n=3) was below the commonly accepted standard (typically n≥6). Were repeated trials conducted, or is there a plan to increase the sample size in subsequent studies?

Response: Thank you for your valuable advice. Before conducting the *in vivo* animal experiments, we carried out relevant pre-experiments, including the construction and observation of rat intestinal and intrauterine

injury models. After becoming familiar with the experimental procedures, we officially launched the animal experiments. Therefore, we did not set a larger sample size for each group in the formal experimental stage. To address the issue of insufficient sample size (n=3), we will increase the sample size of *in vivo* experiments in our subsequent research plan to meet the generally accepted standard (n≥6), thereby further enhancing the statistical power of the research results.

Comment 11: A comprehensive review of the manuscript is recommended to ensure linguistic accuracy and phraseological consistency throughout the text, which would enhance the overall clarity of scholarly communication.

Response: The manuscript has undergone thorough revision, including grammatical corrections, stylistic adjustments, and terminology refinement. All modifications are highlighted in the revised version for clarity. We believe these improvements will enhance the readability and accuracy of our work.

Comment 12: In Figure 1A, the naming of the hydrogel (SLAA hydrogel) is inconsistent with that in the text (SLAA Janus hydrogel). Please make revisions to ensure uniformity.

Response: We have revised the naming of the hydrogel in Figure 1A from "SLAA Hydrogel" to be consistent with that used in the text ("SLAA Janus hydrogel"), and displayed in the following **Fig R5**. The related revision

was shown in **Figure 1** in the 'Revised Manuscript with Track Changes' file.

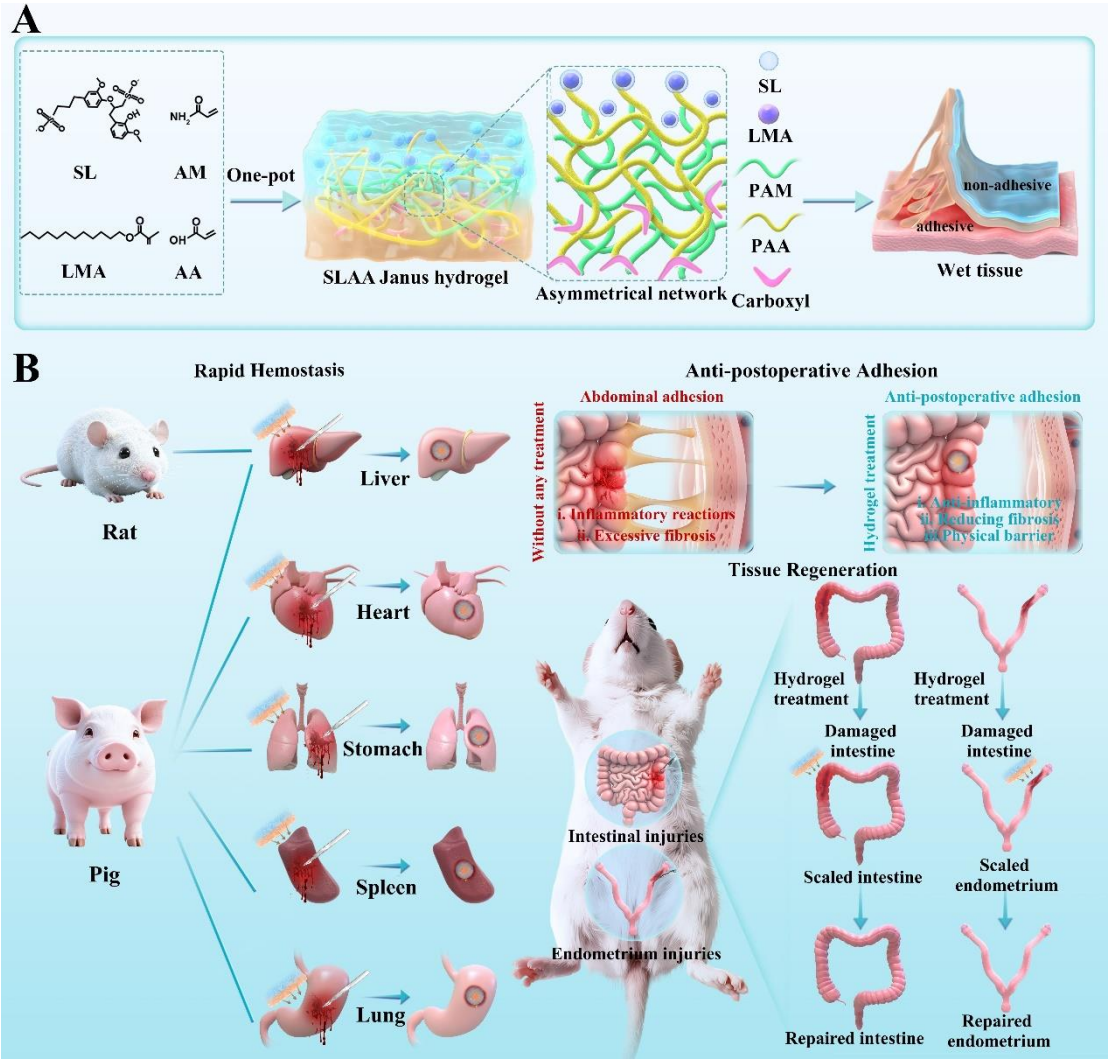

Fig. R5. Preparation and application of SLAA Janus hydrogels.

Comment 13: In Figure 8C, the author needs to use arrows or dashed lines to distinguish between normal tissue and adhesive tissue to enhance readers' understanding of the image.

Response: To enhance the visual differentiation between normal and adhesive tissues in **Fig. 8C** and thereby improve readers' understanding of the image, we demarcated the boundary between normal tissue and adhesive tissue with dashed black lines in representative H&E-stained

uterine sections at 14 days post-treatment, also used arrows to specifically indicate the adherent tissue regions (**Fig R6**). The related revision was shown in **Fig. 8C** in the 'Revised Manuscript with Track Changes' file.

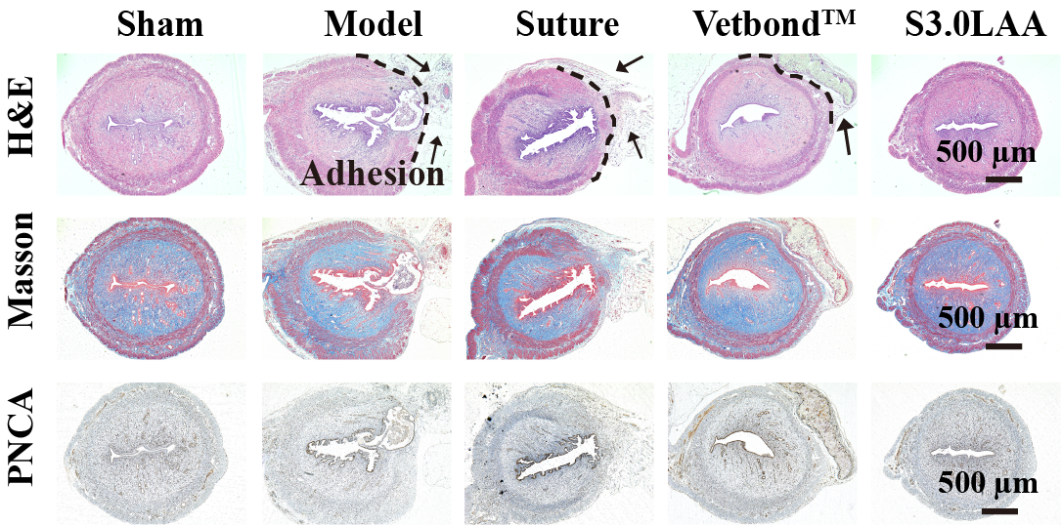

Fig. R6. Representative H&E, Masson and immunohistochemical PNCA staining images of uteri at 14 days post-treatment.

Comment 14: Method section: for crucial experiments such as the modeling of animal experiments, relevant literature should be cited to provide support. Additionally, the description of the experimental methods should be as detailed as possible to enhance the reproducibility.

Response: Thank you for your suggestion. In the method section, we have cited relevant literature for crucial experiments (including cell experiments, hemostasis tests, rat intestinal injury modeling, and IUA model construction). We also provide a more detailed description of the experimental details to enhance readers' understanding and the reproducibility of the experiment. For instance, for the *In vivo* hemostasis test, the related descriptions: "*First, the rats were anesthetized by intraperitoneal injection of 1% sodium pentobarbital (40 mg/kg), and then*

the liver was exposed by incision of the abdomen. A needle punch created a 3-mm-diameter wound. Meanwhile, the filter paper was positioned beneath the liver. The SLAA Janus hydrogels adhered to the wound, the bleeding volume was calculated by weighing the filter paper. Untreated wounds were used as Blank controls. Gauze and commercially available glue (Vetbond TM) were used as positive controls. On the 3rd and 7th days after surgery, H&E staining, Masson's trichrome staining, and immunofluorescence staining for CD45 were performed on liver tissue." has been revision to: "*First, rats were anesthetized via intraperitoneal injection of 1% sodium pentobarbital at a dose of 40 mg/kg. Following anesthesia, a midline abdominal incision was made to expose the liver. A 3-mm-diameter wound was then created on the liver surface using a sterile needle punch. To collect and quantify blood loss, filter paper was carefully placed beneath the liver. The SLAA Janus hydrogel was promptly applied to the wound site to achieve hemostasis, and the bleeding volume was subsequently determined by weighing the blood-soaked filter paper. Untreated wounds served as blank controls for comparison. For positive controls, standard gauze and a commercially available tissue adhesive (VetbondTM) were applied to separate wounds using the same procedure. On the 3rd and 7th days after surgery, H&E staining, Masson's trichrome staining, and immunofluorescence staining for CD45 were performed on liver tissue.*" The related descriptions were shown and highlighted in the

“Methods” section of the 'Revised Manuscript with Track Changes' file.

Reviewer #2 (Remarks to the Author):

This manuscript describes an original and interesting hydrogel system, termed "Janus", as promising alternatives to traditional sutures for internal wound closure and management. The hydrogel is well characterized, using various in-vitro relevant tests and animal studies. Although a lot of study has been performed, it appears that the manuscript in its current form is not suitable for publication in Nature Communications for the following reasons:

Response: Thank you very much for your appraisal of our manuscript, which are helpful for us to improve the quality of our work. Based on your suggestions, careful revisions were made, and we hope that you will be satisfied with the revised version. In this study, we innovatively utilized sodium lignosulfonate to induce the heterogeneous aggregation of carboxyl groups to construct a novel high-strength Janus hydrogel. In addition to studying its potential application value, we also verified and explored its internal formation and regulation mechanism through a series of physicochemical property characterizations and simulation calculations, providing a feasible and practical design strategy for the next generation of bio-adhesives. We believe this work constitutes a significant advancement in the field of Janus hydrogel-based bio-adhesives, demonstrating both innovative material design and functional versatility. The study's interdisciplinary nature-spanning life sciences, health sciences, and

engineering-aligns with Nature Communications's scope as a premier multidisciplinary journal that publishes original research across a broad spectrum of scientific disciplines. This alignment ensures the work will engage a diverse readership while contributing to the frontier of bio-adhesive technology.

Comment 1: It only describes the results, without discussing them. The "discussion" section is actually a summary of the results, rather than a discussion. Therefore, thorough understanding of the science that stands behind the technology is missing. I.e., it has only applicability value, without any scientific value.

Response: Thank you for your valuable feedback. In the original manuscript, the results section and the discussion section were merged and labeled as "Results", whereas the "Discussion" section was, in fact, a summary of the results. This may lead to certain misinterpretations by readers during the reading process. To address this issue, we reorganized the text content, separating the content that belongs to the "Results" section from the "Discussion" section that discusses the results. Meanwhile, in the "Discussion" section, we carried out a more in-depth analysis and discussion of each chapter of the research, particularly focusing on important phenomena and core data, thereby further highlighting the scientific value of the study. The related descriptions were shown and highlighted in the “Discussion” section of the 'Revised Manuscript with

Track Changes' file.

Comment 2: The manuscript contains many Figures, and each one includes several sections. The Figures are small and not clear, which makes the manuscript hard to read and understand.

Response: Thank you for your valuable feedback. To further enhance the reading and comprehension of the manuscript, we have maximized the size of the images and fonts in all figures (**Figs. 1-8**) as much as possible, and increased their pixel resolution to improve clarity and visual intuitiveness. For illustration, we take the original and modified versions of **Fig. 4** as an example, presented below.

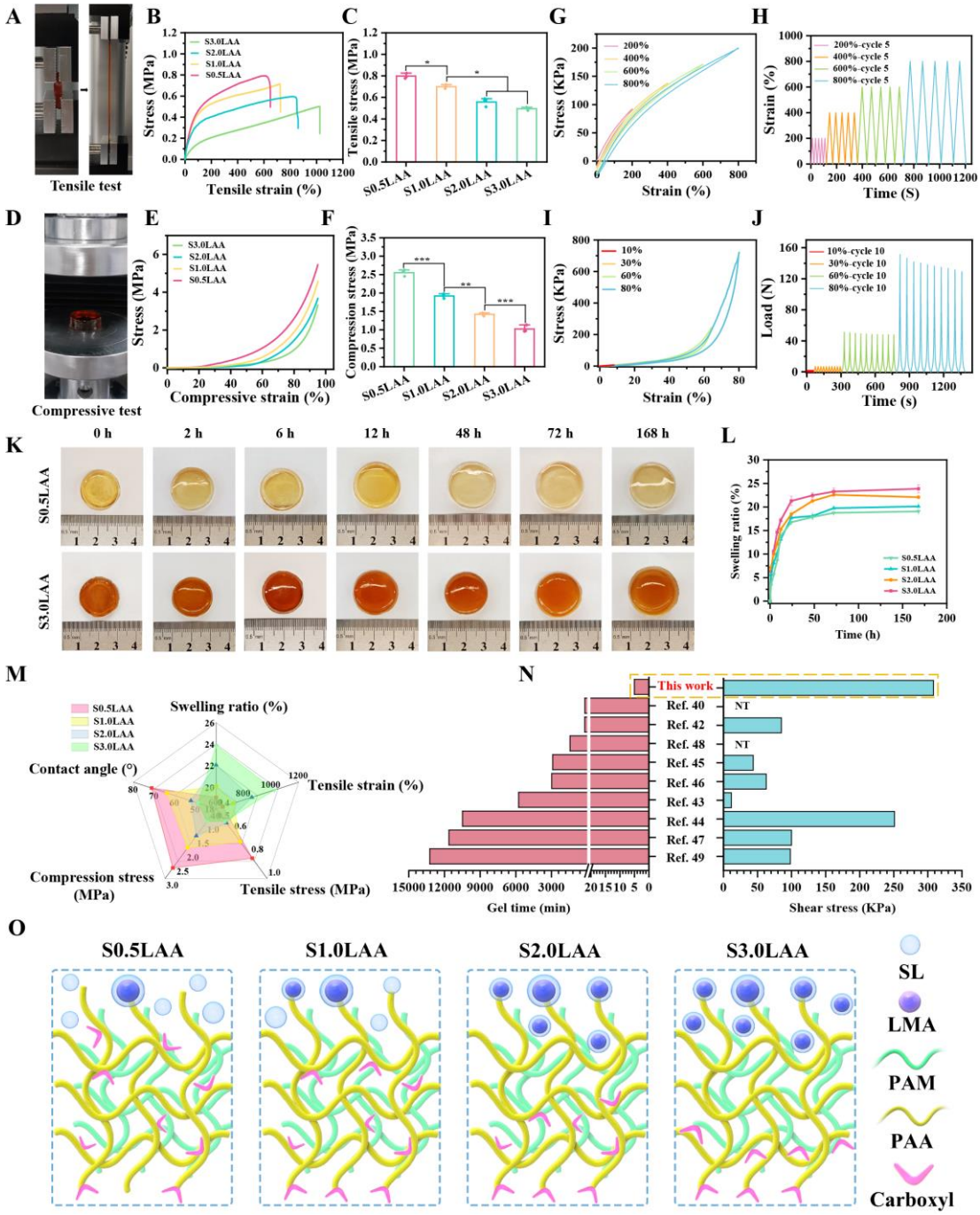

Fig. 4 (original version)

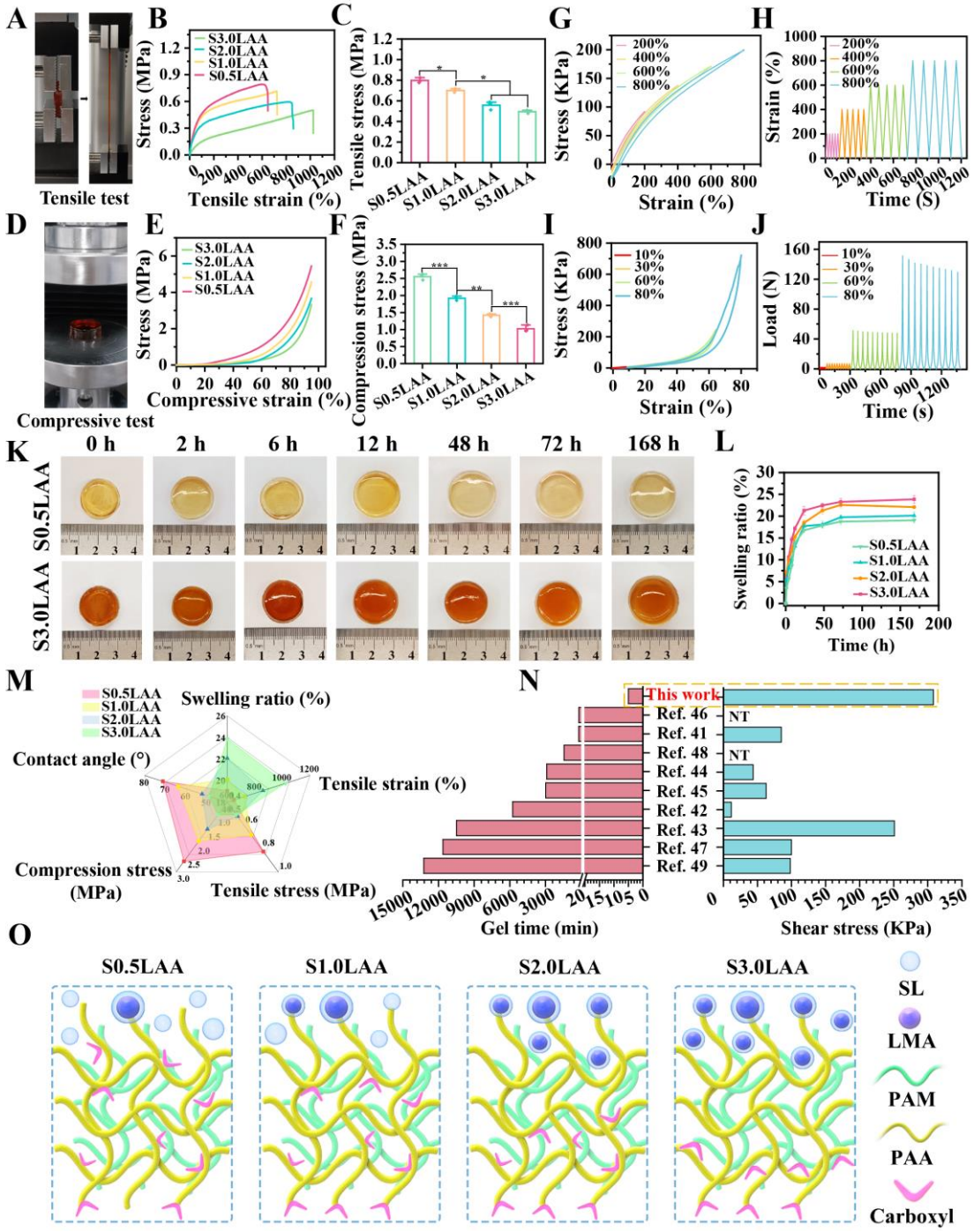

Fig. 4 (modified version)

Besides, we also upload each high-definition Figure separately as supporting information for reference. The related revision was shown in all Figures (**Figs. 1-8**) in the manuscript in the 'Revised Manuscript with Track Changes' file.

Dear Editor,

We would like to express our sincere gratitude for your comments concerning our manuscript entitled "***One-pot Fabrication of High-strength Janus Hydrogel for Wet Tissues Rapid Hemostasis and Intestinal/Intrauterine Anti-adhesion*****" (Manuscript No. NCOMMS-25-103478A)**" and for giving us the valuable opportunity to make revisions. The comments are valuable and constructive for improving our manuscript. We have looked into your comments carefully and made some changes accordingly. Revised parts were marked in red in the 'Revised Manuscript with Track Changes' file and the 'Supplementary Material' file.

Response to the reviewers' comments:

Reviewer #1 (Remarks to the Author):

The authors have fully revised the manuscript according to the suggestions. I suggest accepting the current version.

Response: Thank you for your positive evaluation and for confirming that the revisions meet your expectations. We are pleased that the current version is satisfactory and appreciate your recommendation to accept the manuscript. We value your insightful comments, which have been instrumental in refining our work.