Response to Reviewer 2 Comments

"Dear Reviewer, we appreciate the time you have taken to review our manuscript. We have addressed all your observations, which have helped improve the clarity and enrich the document. Additionally, we have included updated information regarding the use of bacterial cellulose as evidenced in scientific literature. Furthermore, we have enriched the document with the comments from the other reviewers. We kindly ask that you review our revised manuscript, and we appreciate any further feedback to enhance this review article."

Let us know if you'd like any other adjustments!

Comments 1: The first three chapters (the bibliographic study and its methodology, potential applications of BC) seemed promising, but the following part regarding the technologies is totally devoid of a systematic arrangement of the data, with many overlaps and repetitions, a flurry of reviews and punctual experimental articles, with imprecise citations, a very difficult text to follow.

I limit myself to only a few examples:
lines 244-252 mix the bioreactors with the producing strains, their genetic modification, and the composition of the culture media;
lines 245, 262, and 507 refer to wire mesh (tubes) [26], [20,22,24], citations without any relation to the content.
[10] is present in line 248 referring to active strains, but its place is only in line 369, referring to agro-industrial wastes as carbon sources;
[26] presents the author named R.R. et al, instead of Reshmy R. and the other authors;
[33] has nothing to look for in line 592, it refers to the agitator's configuration for production improvement.
You should make a major revision, grouping each subject separately: strains, their genetic improvement, culture media, fermentation technologies, and equipment, downstream processing, with the necessary attention to citations, mentioning separately the reviews and experimental papers, the latest having to be a majority.

Response 1
Agree. We have; accordingly, changed the distribution of the document in the section 4 to make it easier to follow
We revised the mentioned references, and made the following changes:

- **lines 244-252 mix the bioreactors with the producing strains, their genetic modification, and the composition of the culture media;**

These modifications to airlift reactors have the potential to increase the efficiency of industrial BC production, improving the quality of the final product and making it more suitable for specialized applications, such as biomaterials and medical products [31].
Airlift reactors are suitable for active bacterial strains, GMOs, and different carbon sources because of their efficiency in oxygen transfer, the absence of moving parts that can damage microorganisms, and their operational flexibility. In contrast, other types of reactors, such as stirred reactors, may present limitations in oxygen transfer and mechanical damage to cells [16].

- lines 245, 262, and 507 refer to wire mesh (tubes) [26], [20,22,24], citations without any relation to the content.

Various technologies have been developed to implement this immobilization, including the use of bacterial cellulose matrices, synthetic membranes, and other supports such as silicone and wire

mesh [25,44]

Additionally, advancements such as modified bioreactors, optimization of culture conditions, and a potential genetic modification of bacteria has been explored to further boost yields. These innovations aim to improve scalability and reproducibility in industrial applications [2,36]

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30. Reshmy, R.; Eapen, P.; Deepa, T.; Aravind, M.; Raveendran, S.; Binod, P.; Varjani, S.; Awasthi, M.K.; Pandey, A. Bacterial Nanocellulose: Engineering, Production, and Applications. Bioengineered 2021, 12, 11463–11483, doi:10.1080/21655979.2021.2009753.

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The production time of bacterial cellulose can be limited because it requires specific growing conditions, such as an adequate carbon and nitrogen source, optimal temperature and pH, and adequate agitation [25,33]. One of the main constraints in bacterial cellulose production is low yield and the need for large volumes of growth media [3].

We also follow your suggestion on grouping each subject separately, especially in secciton 4, for some instances it was impossible to separate somo subjects as the are linked in the same study

Comments 2: The figures are almost okay, only small editing corrections are necessary (e.g. immobilized bioreactor instead of "immovilized" reactor).

Response 2. Thank you for pointing this out, we have edit figure 5 so you can find the changes in line 363

Comments 3: The conclusions could be improved by systematizing and emphasizing actions to overcome the limitation of economic competitiveness, including the selection of appropriate applications.

Response 3. Thanks for the recommendation. After reviewing the conclusion we've decided to separate the conclusion as follows: Re-introduction to the main theme and problem, Challenges faced and main strategies to get over them, Detailed information about the main strategies, Closing paragraph with future perspectives

"Bacterial cellulose has garnered significant attention from the scientific and technological communities due to its versatility in applications such as tissue engineering, nanoelectronics, and beyond. Its biocompatibility, high porosity, and three-dimensional structure make it a promising material for biomedical use, particularly as a scaffold for microbial cells and biofilms. However,

realizing its full potential is accompanied by significant technical and environmental challenges. Slow and expensive production, the need for specific growing conditions, and the environmental impact of using natural resources present obstacles to large-scale adoption.

Overcoming the challenges in large-scale production and generating greater applications of bacterial cellulose requires an interdisciplinary approach. Strategies such as genetic modification and exploration of new applications are critical to improving efficiency and product quality. Another important strategy involves diversifying carbon sources, utilizing agro-industrial and organic waste could potentially reduce production costs and make the process more sustainable.

Innovation is crucial when addressing these challenges. Optimizing culture media and developing new purification technologies are key steps toward improving the production process and material quality. Furthermore, continuous research in the molecular biology field will help enhance the efficiency of bacterial cellulose production by introducing more efficient GMOs for bacterial cellulose production. Such innovations are essential to unlocking wider and more effective use of this biopolymer across various sectors.

Despite the current challenges, the future of bacterial pulp production and applications is promising. With sustained research focused on optimizing growing conditions, improving production efficiency, and addressing environmental concerns, the material has the potential to make a significant impact in medicine, technology, and beyond. The search for technical and environmental solutions and constant innovation is critical to making the most of this material and contributing to significant advances in fields ranging from medicine to technology."