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EVALUATION REPORT FOR THE PhD THESIS OF M.Sc. MARIA CELESTE TIRELLI: POSITIVE REVIEW WITH PROPOSAL FOR HONORS

Scientific Board
Institute of Physical Chemistry
Polish Academy of Sciences

To whom it may concern

Dear colleagues,

first of all, I would like to thank you for your kind consideration. Acting as external reviewer for the **PhD thesis of M.Sc. Maria Celeste Tirelli**, entitled “**Microfluidic assisted 3D printing of functionally graded biomaterials**” and performed under the supervision of **Dr. hab. Marco Costantini**, is a great honor for me after years of collaboration with many colleagues from the Polish Academy of Sciences.

I have studied the complete version of the PhD thesis document with great interest, as it addresses relevant and previously unsolved research challenges in connection with a variety of research fields including: additive manufacturing, biofabrication, biomaterials, chemistry and microfluidics, which puts forward the multidisciplinary nature of the research performed. The main objective, which has been achieved with outstanding results, is engineering spherical-based porous metamaterials in a cost-effective manner with controlled architecture across multiple length scales. These hierarchical bio-metamaterials are of great relevance for adequately mimicking the multi-scale features of human tissues, as required for progressively approaching successful high-fidelity and high-performance solutions in tissue engineering, regenerative medicine and biofabrication.

The PhD thesis starts with a systematic overview of porous biomaterials and provides a justified rationale for aiming at designing and manufacturing truly spatially controlled, multi-scale and functionally graded biomaterials for a variety of applications, mainly in the biomedical field. It also provides a review of additive manufacturing approaches for achieving diverse porous biomaterials and highlights the use of microfluidic-assisted manufacturing methods for reaching the required levels of geometrical control, the desired gradients and the pursued multi-scale. The introduction is beautifully written and provides a grasping introduction to the topic, while also providing an overview of the well-planned structure of the whole PhD thesis.

Subsequently, the PhD thesis presents the research results in three main chapters, each of them providing a brief introduction to the specific challenges towards the global objective, methodically presenting the materials and methods employed, illustrated with a variety of diagrams, images and photographs from the experimental results for enhanced reproducibility, detailing and discussing the achieved results and main challenges, and discussing the advances as compared with the state-of-the-art.

These three main chapters provide the following remarkable outcomes:

- Microfluidic chips integrated with extrusion systems enable the creation of emulsions with tunable droplet size and dispersed phase volume fraction. These droplets serve as sacrificial templates for pore formation, yielding highly controllable pore architectures, which are validated printing by porous hydrogel constructs with controlled pore-size distributions, spatially modulated porosity, and both discontinuous and continuous density gradients. The precision achieved, architectural control and quality of results goes beyond the state-of-the-art, when verifying the extensive literature cited, and constitutes the first key result of the PhD thesis.
- Beyond the more classical soft hydrogel systems, the second key result of the work translates these design principles to ceramic-based materials for the fabrication of mechanically robust porous scaffolds, which are indeed required for load-bearing applications in tissue engineering, regenerative medicine and biofabrication. To this end, a systematic investigation of processing parameters and formulations compatible with sintering processes is performed and exemplified by a collection of scaffolds with truly biomimetic and biomechanical performance.
- Based on the above key results, a higher degree of geometrical and material diversity is achieved by systematically fostering topological gradients in multi-material constructs, whose experimental validation is the third key result of the PhD thesis. Indeed, considering that human tissues are multi-material, multi-scale and functionally graded, a universal solution for tissue engineering would require the possibility of processing multiple materials, at different scales and with controlled gradients. This is achieved by microfluidic micromixing, which proves a versatile tool/process for advancing tissue engineering.

Among the most interesting aspects shared by the three key results of the PhD thesis, it is very relevant to highlight that the presented strategies are highly reproducible, modular and industrially scalable. In my view, apart from the scientific relevance of the study, its technological component and the possibility of leading to novel industrial processes for massively impacting the areas of tissue engineering, regenerative medicine and biofabrication, is praiseworthy.

In this respect, taking into account the industrial potential beyond the biomedical field, I would have expected a broader reflection on the future research directions and proposals. The future work proposed in page 150 is limited to a couple of paragraphs, but I personally believe that the PhD thesis can lead to a huge variety of solutions for materials science and technology and to industrial applications in several areas. If possible, I would like the PhD candidate to discuss with a bit more detail those possible applications beyond healthcare during the defense.

Finally, it is also necessary to highlight a variety of scientific dissemination and communication outputs, including 7 international journal publications in high-impact journals and 3 public presentations in relevant international events linked to biofabrication, biomaterials and microfluidics, which again puts forward the multidisciplinary and impactful research performed.

Overall, the study reads well, provides synergic solutions to a very remarkable challenge and demonstrates a path of continuous learning, through which the candidate has achieved research independence.

Accordingly, my review is **POSITIVE**. In my opinion, due to the already discussed excellence of results and complexity of the problem tackled with success, I would propose distinguishing the PhD thesis with **HONORABLE MENTION**, also according to the international standards of quality of PhD theses that I have directed and reviewed in different European countries.

May I be of any help, please do not hesitate to contact me. Meanwhile, please receive best wishes from Madrid.

Yours faithfully,

A handwritten signature in blue ink, appearing to read 'Andrés Díaz Lantada', with a stylized flourish at the end.

Firmado por DIAZ LANTADA ANDRES -
***2098** el día 22/06/2026 con un
certificado emitido por AC FNMT
Usuarios

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