Hydrogels for 3D bioprinting

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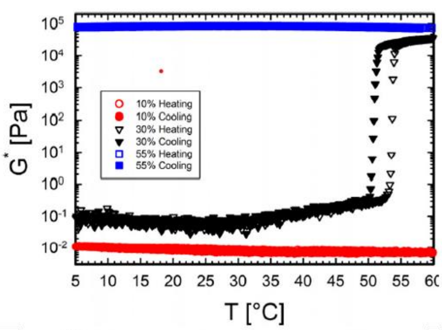
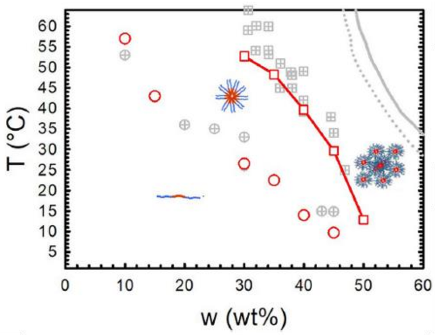
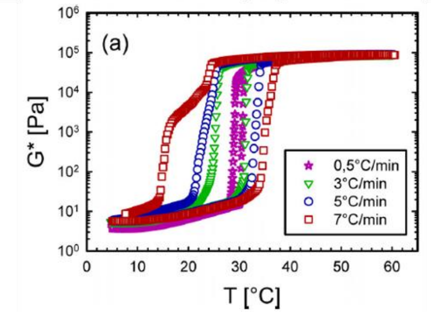
3D bioprinting is a manufacturing process of three-dimensional living tissues starting from biomaterials containing cell cultures. These tissues can be used in a wide range of biomedical applications, e.g. for transplants or to test new drugs. Although the potential of bioprinting is still under study, this technique has already proved effective in building human tissues such as skin, cartilage and bones.

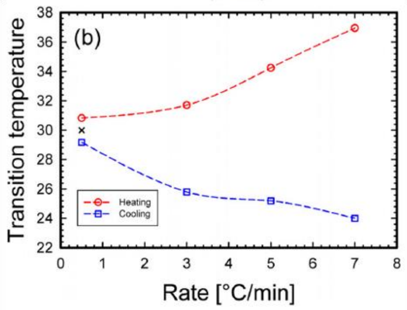
One of the most promising strategies for the fabrication of bio-tissues is that based on the extrusion of cell-loaded hydrogels. This approach consists in the deposition of a bio-ink filament layer by layer, to form a 3D construct on which cells, within the ink itself, proliferate. At the time of deposition, the filament must be in the liquid state (commonly called sol), and then gel to form the three-dimensional structure. To ensure a proper development of the biological construct with specific mechanical characteristics, it is necessary that the matrix with cells from liquid becomes gel in response to appropriate stimuli, and that the resulting gel has some specific viscoelastic properties. For example, the gelation of the bio-ink can be induced through temperature variation, reaction with a cross-linking agent, or ultraviolet radiation. The resulting gel must guarantee an optimal environment for cell proliferation, in terms of temperature, humidity and nutrient permeability. Furthermore, it must have mechanical stability to prevent the construct from collapsing during cell growth.

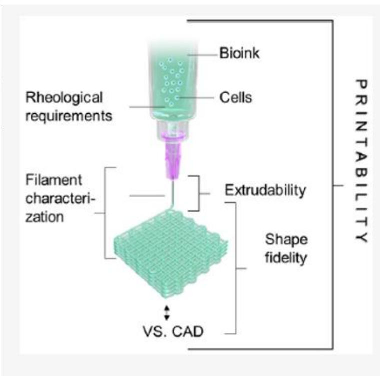
The matrices used for the manufacture of bio-inks are subject of growing interest for the scientific community. The commonly most hydrogels used are animal gelatin, collagen, chitosan, hyaluronic acid, cellulosic derivatives, and alginate. However, none of the listed materials are capable of forming optimal gels for bio-tissue fabrication. There is a lack of systematic studies that relate the viscoelasticity of bioinks during the sol-gel transition and their printing performance.











The aim of my PhD project is to study the viscoelastic properties related to the sol-gel transition of hydrogels for bioprinting with a dual objective:

1. Optimize the sol-gel transition process through the formulation of new hydrogels;
2. Correlate the viscoelastic properties of the resulting gel with the printing performance.

The project is based on the study of the rheology of the sol-gel transition of existing materials and formulation of biopolymers mixtures in order to optimize the transition process. Moreover, it is focused on the modification or construction of a bio-printer that allows to control the gelation process during printing through a correlation with the flow history during rheometric measurements. In addition, it wants to investigate the possibility of loading hydrogels with cells in order to build organic constructs.

References:

- Costanzo, S.; Di Sarno, A.; D'Apuzzo, M.; Avallone, P.R.; Raccone, E.; Bellissimo, A.; Auriemma, F.; Grizzuti, N.; Pasquino, R. Rheology and morphology of Pluronic F68 in water. *Phys. Fluids* **2021**, 33, 043113.
- Schwab, A.; Levato, R.; D'Este, M.; Piluso, S.; Eglin, D.; Malda, J. Printability and Shape Fidelity of Bioinks in 3D Bioprinting. *Chem. Rev.* **2020**, 120, 11028-11055.

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