Systèmes Biologiques et Concepts Physiques
Parcours Biophysique, IPB et PMB
Master 2 Research projects for 2022-2023

Proposition de stage de M2

Etude d'hydrogels de collagène poreux par Imagerie de Résonance Magnétique Nucléaire – Application à la mise au point de nouveaux modèles pour l'ingénierie tissulaire.

Study of porous collagen hydrogels by Nuclear Magnetic Resonance Imaging – Application to the setup of new models for tissue engineering.

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Project description :

1. The interest of 3D materials in cell culture and tissue engineering is now well established. Furthermore, various works in this field have shown the importance of porosity in these materials in order to facilitate, or even allow, on the one hand, colonization by pre-implantation or post-implantation cells and, on the other hand, for the transport of nutrients and oxygenation of the tissue [1]. The pore sizes generally sought are of the order of 100µm for cell colonization. The analysis of porosity in these biopolymer-based materials poses a major technical challenge due to their hydration and low elastic properties (which severely limits the use of conventional techniques such as nitrogen adsorption and/or mercury intrusion). Other three-dimensional characterization strategies, such as confocal or light sheet microscopy, only allow the analysis of a limited volume of samples, which makes it

impossible to describe the porous network of the materials. Other techniques, which are based on two-dimensional (2D) image analysis, are not satisfactory.

Nuclear Magnetic Resonance Imaging (MRI) is a non-invasive technique already widely used for in vivo imaging, including implant monitoring [2]. However, it is used very little - if at all - for the in vitro analysis of porous biomaterials for 3D cell culture and tissue engineering. It is therefore in this context that this project is placed.

Based on work done in recent months on alginate-based matrices, the objective of this internship will be to develop an MRI analysis protocol to probe the porosity of porous model materials based on dense collagen [3,4].

We will work on porosities decreasing in size and increasing in complexity, and using templates already manufactured in the laboratory. The study will continue with the observation of gels whose porosity has been obtained by the freeze-casting process. This technique, widely developed in the laboratory [5], consists in shaping the material by the controlled growth of an ice front within an aqueous solution or suspension, thanks to the control of the thermal gradient. In the case of collagen, freezing will take place in solution, then topotactic fibrillogenesis [5] will allow the material to pass to the fibrillar stage, an essential condition for mimicking the connective matrix of a tissue.

In a second phase, we will be able to calibrate the MRI signal in relation to the collagen concentration. This will allow us to determine the local collagen concentration in the walls of the freeze-casting samples. For this purpose, samples with a known collagen concentration, which can vary from 100 mg/mL to 900 mg/mL, will be made beforehand.

2. During this internship, we will mainly use Magnetic Resonance Imaging (MRI) [6] as a technique for structural characterization of the material. MRI is derived from Nuclear Magnetic Resonance (NMR), a technique also widely used in the laboratory, both in the liquid and solid state, thanks to the access to the NMR facility on the Pierre et Marie Curie campus. The trainee will become familiar with the use of the solid state NMR spectrometer "DYNAMAT" equipped with a micro-imaging probe in order to obtain images of the material under optimized contrast and resolution conditions. He/she will also be responsible for the synthesis of dense collagen-based model materials with a controlled physicochemical composition and perfectly calibrated porosity. He/she will then train in the freeze-casting technique to produce matrices of applicative interest. After this first experiment on model materials, the study of freeze-cast matrices colonized by cells will eventually be envisaged at the end of the course.

This study will be carried out in collaboration with Dr. Francisco M. Fernandes and Dr. Gervaise Mosser from LCMCP.

3. References

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[6] Mark A. BROWN and Richard C. SEMELKA, “MRI : Basic principles and applications”, Wiley & Sons, 3rd ed. (2003), ISBN 0-471-43310-1