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# Nanometric pores and cracks distribution in bioartificial pancreas using 3D X-ray phase nanotomography

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## Aims of the experiment and scientific background

The MAILPAN (MAcroencapsulation of PANcreatic Islets) is a bioartificial pancreas prototype dedicated to treating type 1 diabetes. Its development is a real challenge as it addresses an ever-increasing public health issue… This medical device is implantable: it encapsulates insulin-secreting cells in order to re-establish, physiologically and without immunosuppressant, a normal glycaemia in the patients. Today the prototype is functional and the next steps consist in bringing it to the clinical testing phase on human patients. The mechanical safety validation of MAILPAN has to meet very strict standards in order to eliminate any risk of rupture once it is implanted on a patient. It has to be sufficiently resistant so as to protect all through its life cycle not only the insulin-secreting cells from the recipient's immune system, but also the recipient from said insulin-secreting cells. In order to do that, it is composed of three inseparable PET membranes. The most important membrane is the internal one as it contains nanometric pores (30nm in diameter). This lets glucose and insulin go through but this 30nm critical size must not be exceeded to guarantee the immunoprotection These pores are obtained through ion bombardment followed by etching: if they are homogeneous in size, their distribution is more random, with either isolated pores or pores aggregated into clusters that can lead to local embrittlement.

The first objective is to focus on pore distribution in the membrane to check the real pore volume fraction, size and spatial distribution. Then, mechanical tests will be carried out on MAILPAN specimens in order to test their resistance to different loadings, which will enable to simulate moves of the human body once implanted and the possible contact with certain bones or organs. The objective is not to push the testing until failure, but to observe preloaded samples (after several cycles of loading and unloading representative of some human movements: tension, biaxial testing, bending...) to see if for a given cycle/stress value certain areas rich in pore clusters for instance have not locally embrittled the membrane and led to an increase of the pores diameter or to cracks superior to 30nm in size, thus compromising the functioning of MAILPAN.

A statistical study will then be carried out on those measurements so as to optimally qualify the porosity of the membrane, to verify that there are no pores superior to 30nm in the initial state, to check if there is a critical pore cluster size or a critical distance between pores not to overstep in order not to locally embrittle/crack the membrane during mechanical loading (tension and bending, in particular). The pore distribution is the key parameter. A finite elements model is developed in parallel (PhD work) to compare the results after loading with the nanotomography experiments in order to validate the MAILPAN and/or to propose some improvements.

## Experimental method

MAILPAN is a pure polyethylene terephthalate (PET polymer) structure composed of 3 layers/membranes the total thickness of which is about 200µm. The external and internal membranes contain pores around 1µm and 30nm, respectively. X-ray nanotomography with high resolution 3D imaging is therefore necessary to analyze these two membranes and to verify that the pore size is not superior to the critical 30nm, to check the absence of cracks larger than 30nm after mechanical testing and to see if some zones are more brittle due to possible clusters of pores.

17keV X-ray energy was used. Some specimens being several millimetres long, “local” measurements were made in selected regions to sample the whole.

## Results

Several specimens were analyzed considering different configurations; only a few of them are presented here. The three-layer membrane was first considered in order to determine the expected resolution for each layer; the 3D reconstruction is presented in figure 1a. It was possible to see all the details of two layers, but the nanometric pores of the internal one were very difficult to observe.

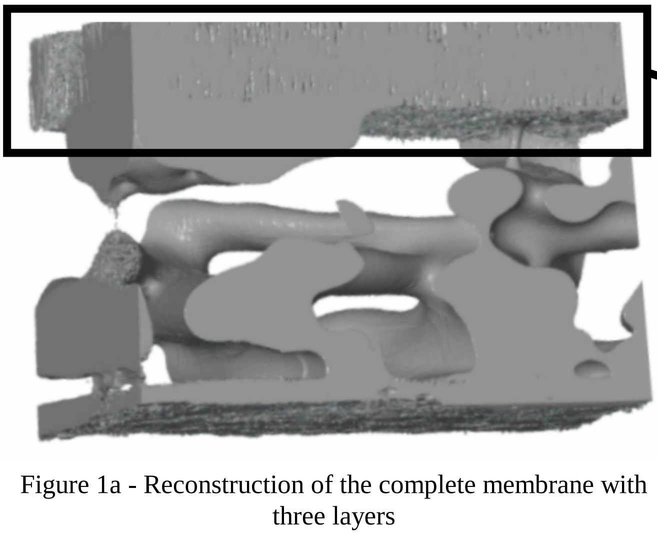

Figure 1a - Reconstruction of the complete membrane with three layers

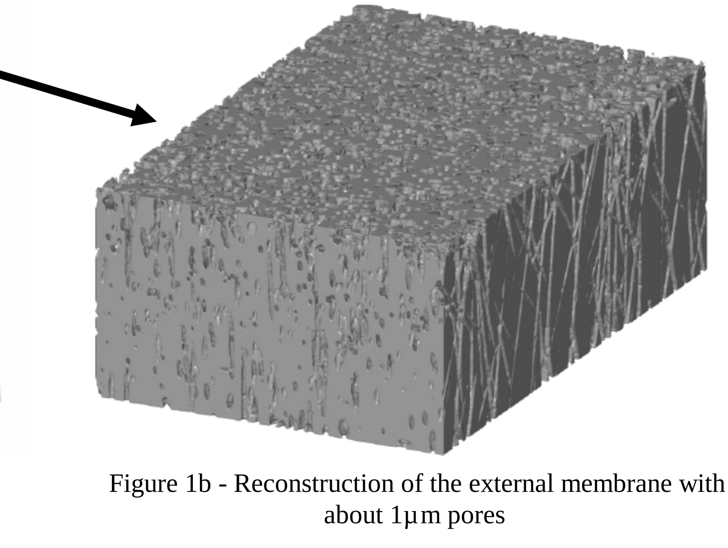

Figure 1b - Reconstruction of the external membrane with about 1µm pores

We decided to focus on the external membrane whose pores were obtained thanks to the same ion bombardment process (figure 1b). We can see the pore distribution with some clusters and the angle inclination in one direction. Some cavities are also observed corresponding to some "voids" in the material (figure 2). We will consider that the nanoporous internal membrane is similar.

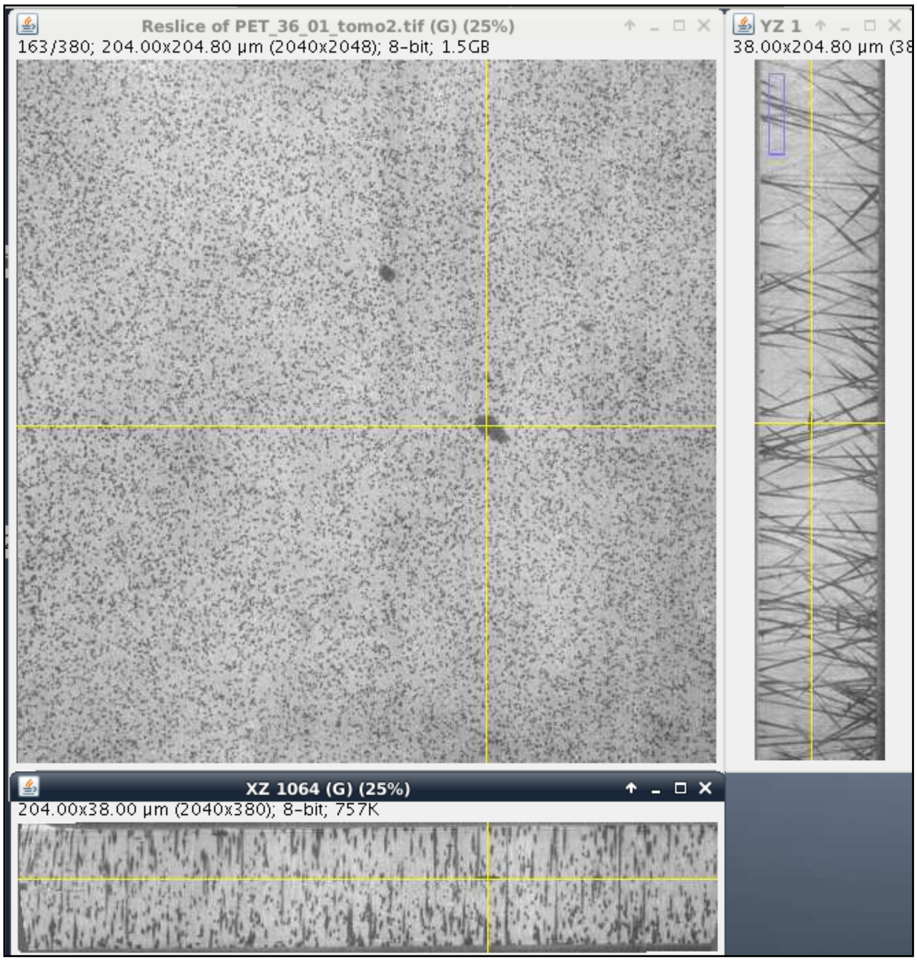

Figure 2 - External membrane pores and "voids"

It is now possible to develop 2D and 3D finite elements models to get the behavior of the MAILPAN under loading (simulation of different loading paths). All the results will be presented during international conferences and published in international scientific journals.