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Fabrication and biocompatibility properties of different soft intra-cortical implant designs.

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ANR Neuromeddle
Brain Micro Snooper ERC 640151

Introduction

Neuroengineering more efficient neural interfaces is crucial to develop better clinical rehabilitation solutions and for neural network exploration. Most of current intra-cortical implants are stiff and generate mechanical strain that results in complex cellular responses and instabilities in neural signal recording.

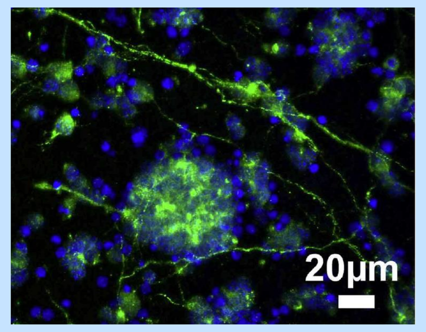
Designing soft intra-cortical neural implant with a high density microelectrode array has therefore become essential to faithfully record several neural units overtime and to facilitate for instance, brain computer interface performances and the study of memory and plasticity.

We developed a soft SU-8 polymer neural implant with 64 nanostructured gold 20µm electrodes and varied the design of the 2mm deep intra-cortical part of the implant. Leads were either 50µm, 20µm or 11µm wide with a straight or a wavy shape. In vivo biocompatibility tests in rodents were performed, astrocytes and microglia were first analyzed around a 12µm thick SU-8 implant.

1 - Goal

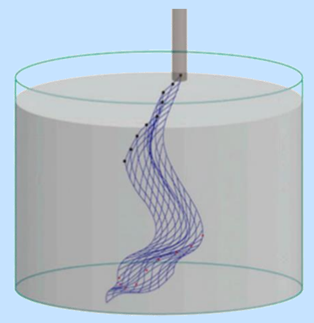
Our objective is to create a new implant answering to the following requirements:

1) Neuron-sized



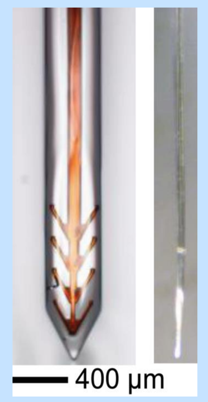
Piret et al, 2013

2) Flexible



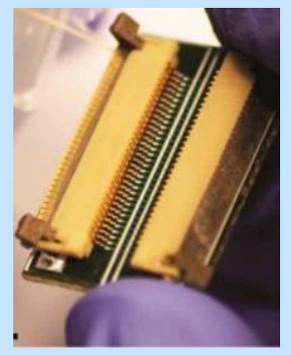
Zhou et al, 2017

3) Implantable



Tien et al, 2013

4) Easy to connect

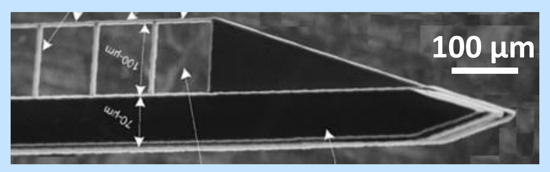


Schuhmann et al, 2017

2 - Design

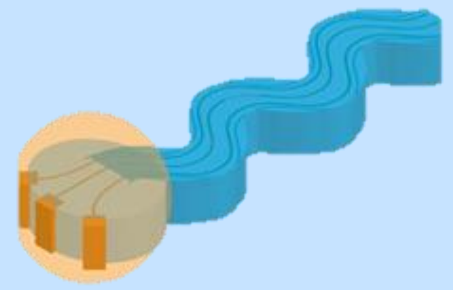
The implant design aims at combining the following characterisitics:

1) Low dimension for neuron repopulation



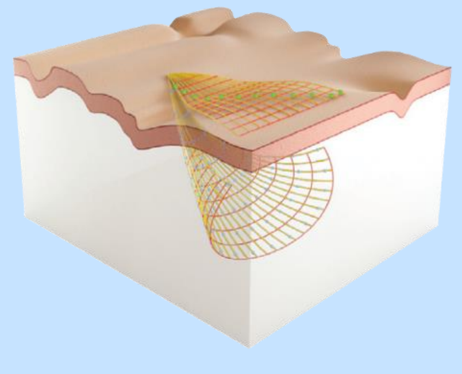
Seymour, J. P et al. 2007
Karumbaiah, L et al 2013

2) Wavy shape for brain movement absorption



Sohal et al. 2014

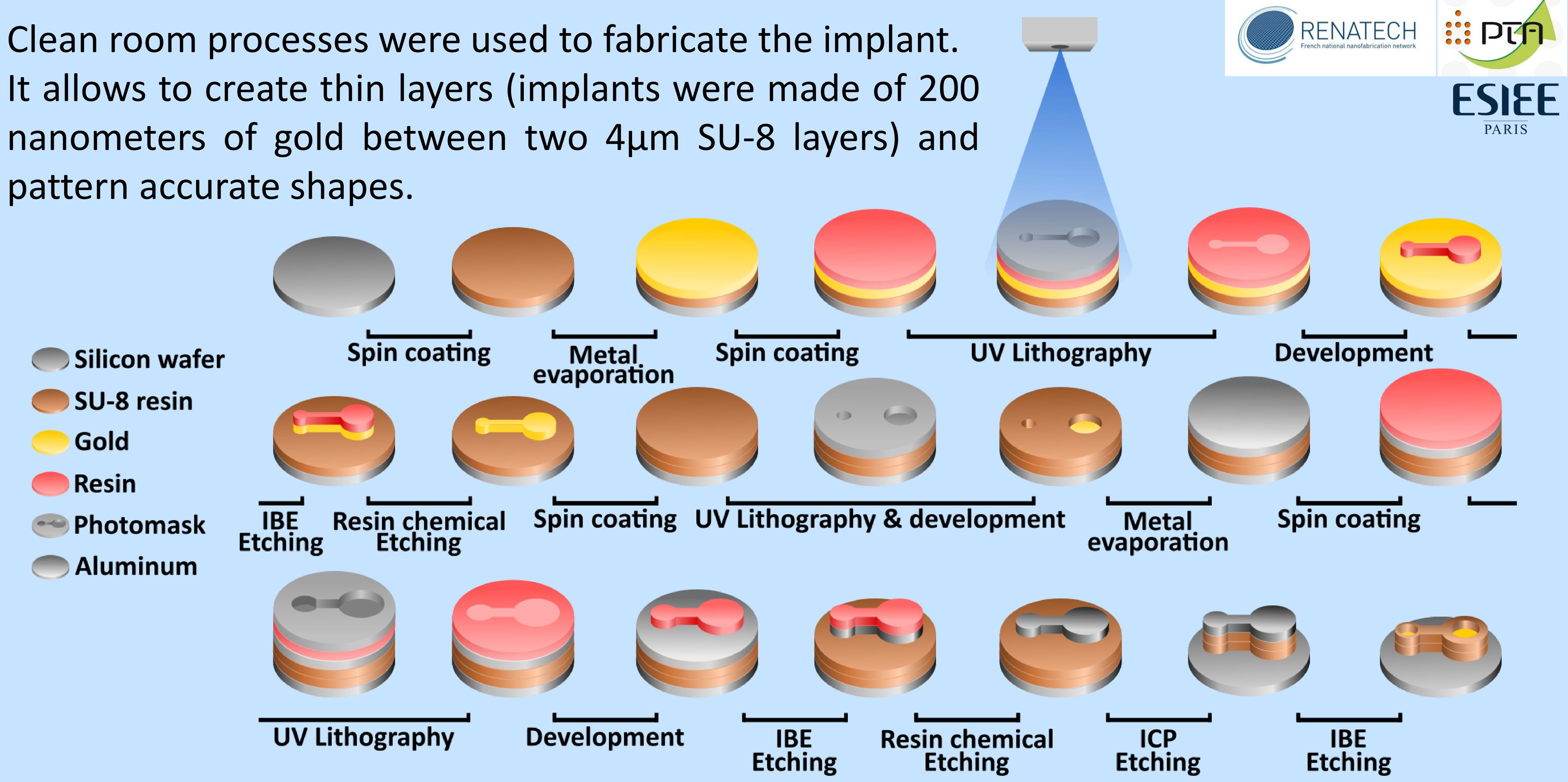
3) Wires to be free of mechanical strains



Liu et al. 2015

3 - Process

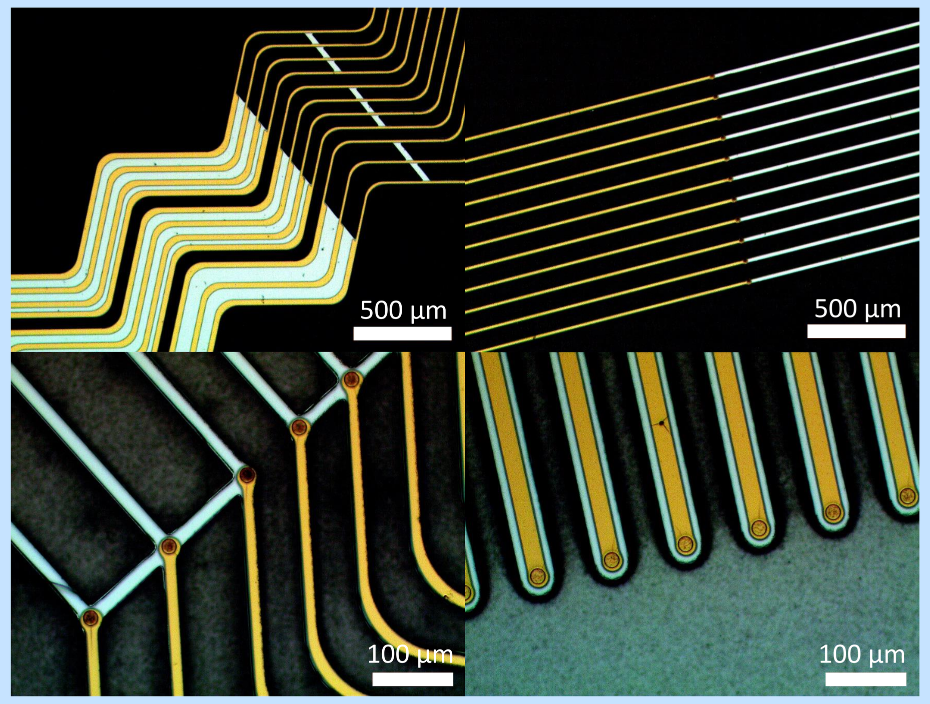
Clean room processes were used to fabricate the implant. It allows to create thin layers (implants were made of 200 nanometers of gold between two 4µm SU-8 layers) and pattern accurate shapes.



4 - Implant imaging

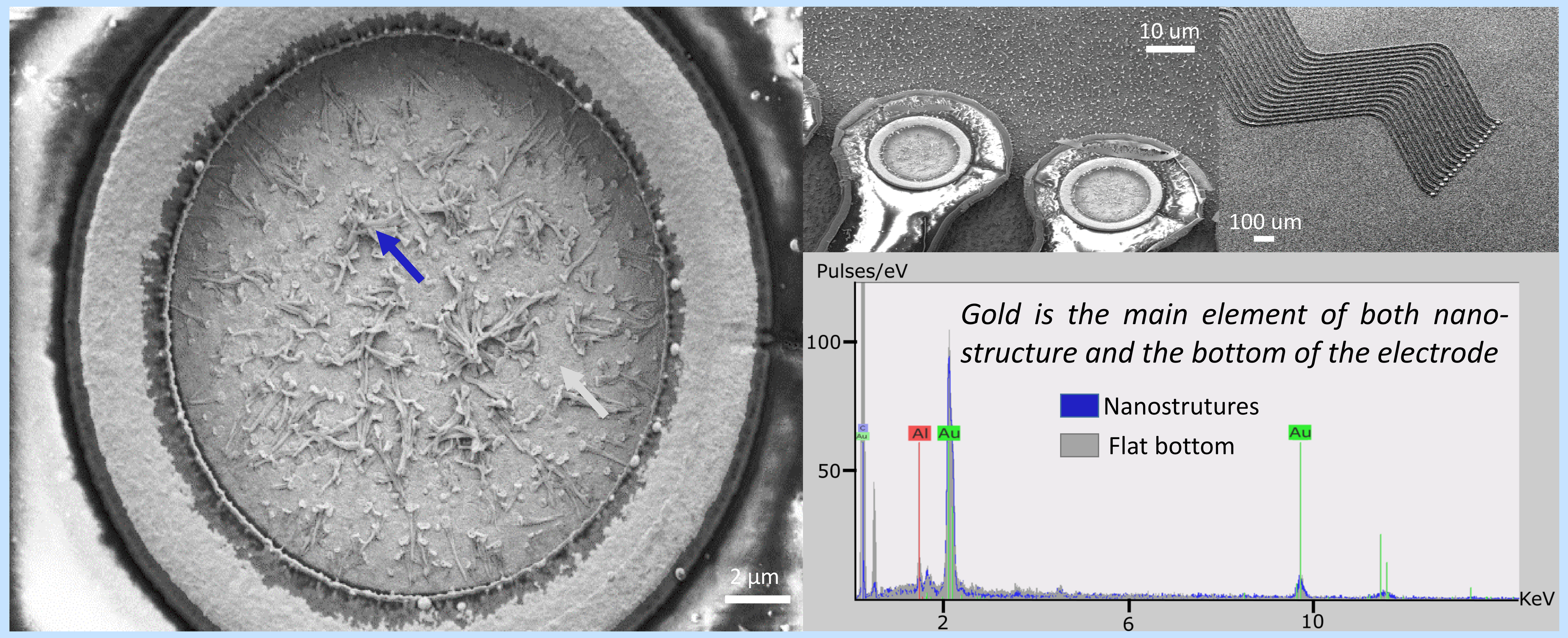
Microscope images

Different patterns compose the implant that is made of either wavy or straight wires of either 11 or 20 or 50 µm width. All electrodes have a 20 µm diameter. Similarly to a spring, wavy shapes should absorb movement from brain beating.

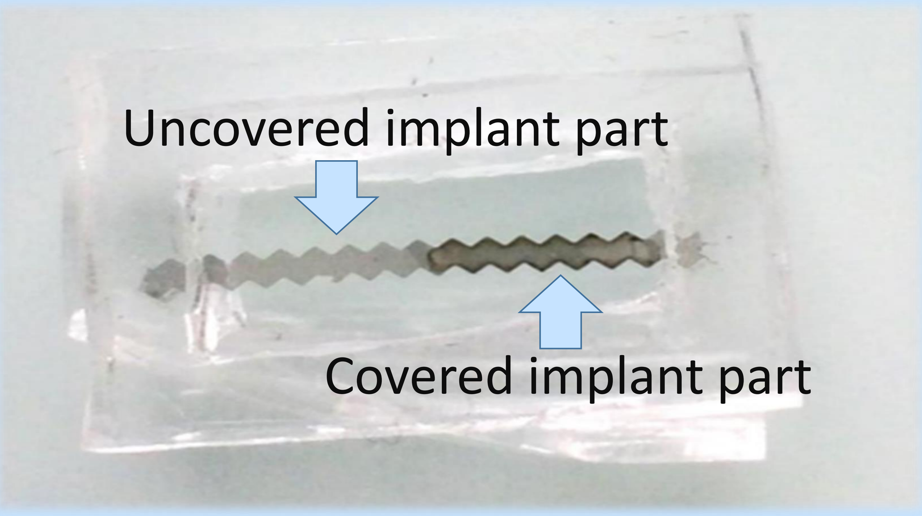


MEB images

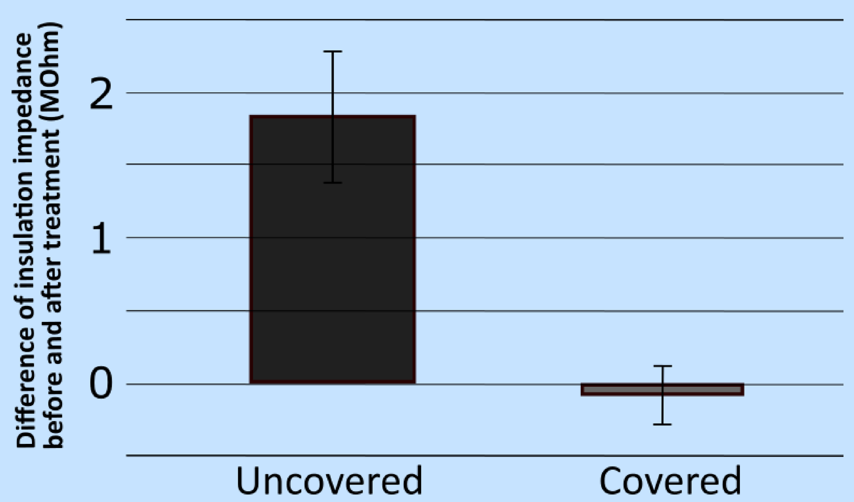
We could form nanostructured gold electrodes using ion beam etching (IBE), the last step of the clean room process. Nanostructures have been shown to improve neuron adhesion (Piret et al, 2013) and neural recording performances (Piret et al, 2015).



5 - Insulation resistance

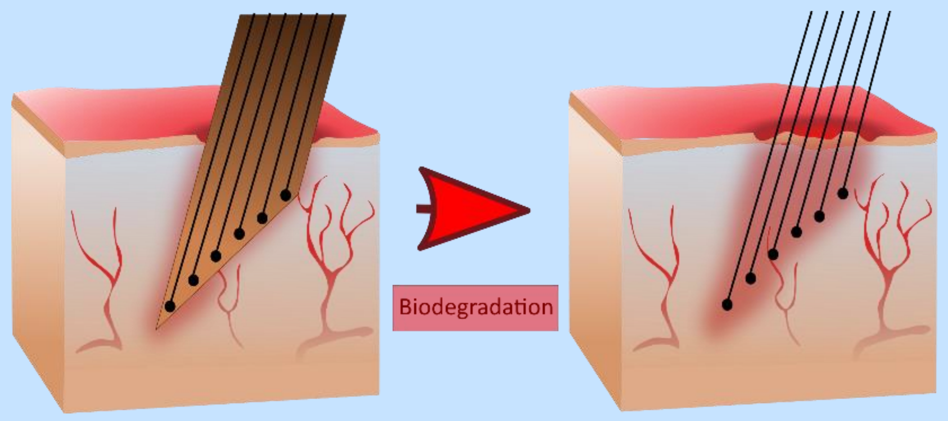


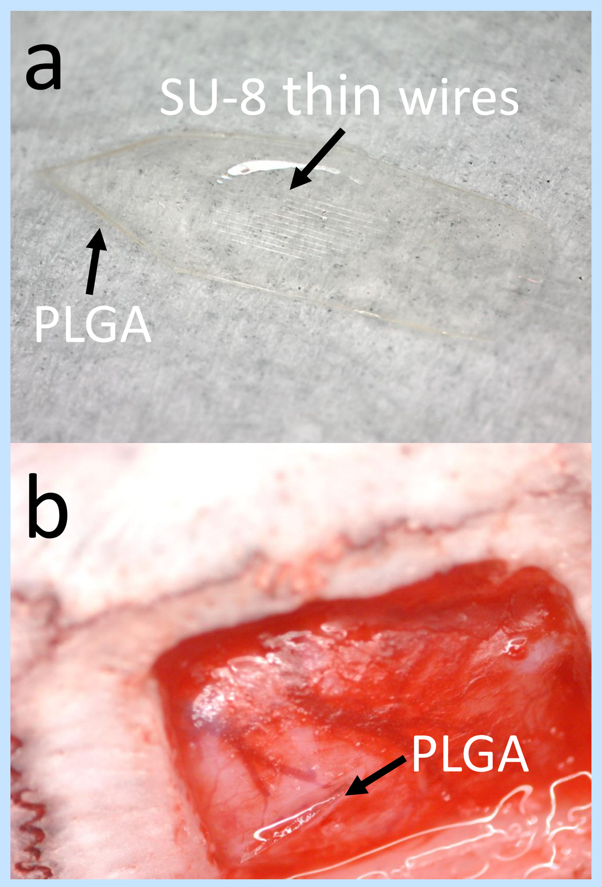
Covering implant with materials improves its resistance to corrosion



Corrosion after 2 weeks at 80 °C in PBS (2 years in brain)

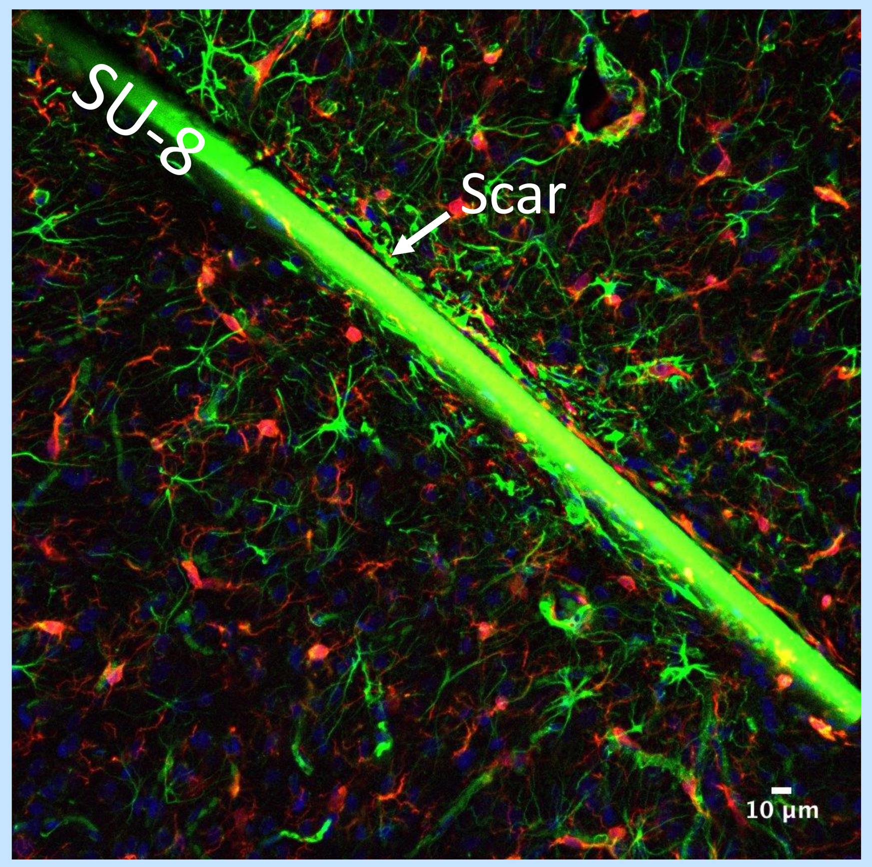
6 - Implant encapsulation





We successfully embedded the thin and flexible free wires of the implant with a Poly Lactic-co-Glycolic Acid (PLGA) biodegradable material (a) and that allowed its intra cortical penetration into the rat cortex (b).

7 - Biocompatibility



Immunology study was made after a 12 µm thick SU-8 piece, measuring 1 by 2 mm was implanted into rat brain. The immunostaining shows macrophages (in red) and an astrocyte glial scar around the SU-8 piece. The implant shown in box 4 that is 8 µm thick and has 50 µm, 20 µm and 11 µm leads may lower the immune response as compared to the present SU-8 piece.

IBA-1: microglia
GFAP: astrocytes
DAPI: cell nuclei

Conclusion and perspectives

The principal assets of this new implant that we fabricated are : 1) the small size 2) the thickness of the implant (thin enough to lower inflammation and thick enough to better resist to corrosion in time) 3) that each electrodes are not linked to each other and could intracortically inserted. 4) High microelectrode density. Next steps are to study the long term biocompatibility of the implant and to perform neural recording.