

Mecanotransduction by Ultrasonic Stimulation in the context of Bone Regeneration

Mecanotransduction par Stimulation Ultrasonore dans le contexte de la Régénération Osseuse

- MecaSUROs -



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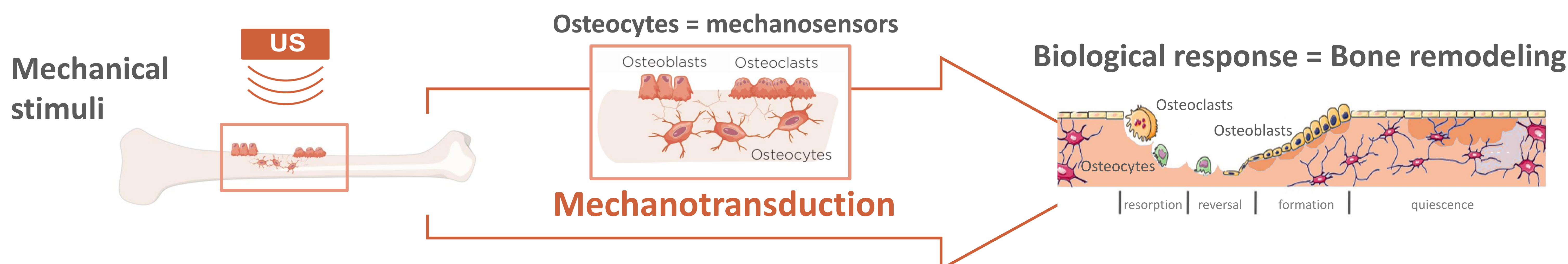
Background

Bone Living tissue able to adapt to mechanical environment.
Mechanosensors = **osteocytes** connected in the **complex 3D lacuna-canalicular network**, surrounded by fluid.

... But **HOW** can **US** heal bone? Still an open question → Focus on the **osteocyte** key role

Healing with Ultrasound (US) Stimulation ...

- **LIPUS**: Low Intensity Pulsed Ultrasound Stimulation.
- US stimulation known since 1950's.

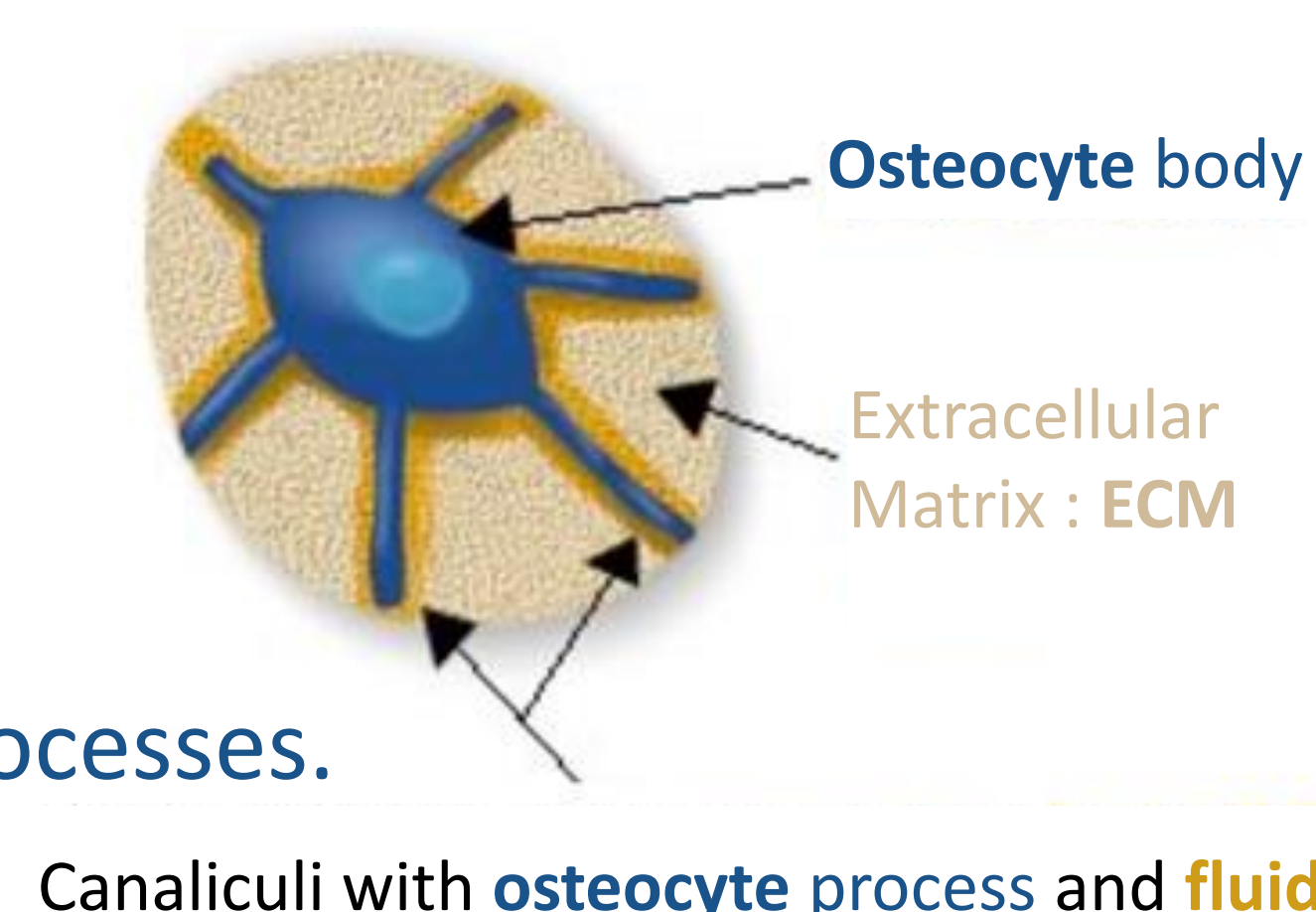


3D micro-environment of the osteocyte

Extracellular matrix (**ECM**) and lacuno-canalicular network (**LCN**): complex 3D porous **fluid-saturated** network.

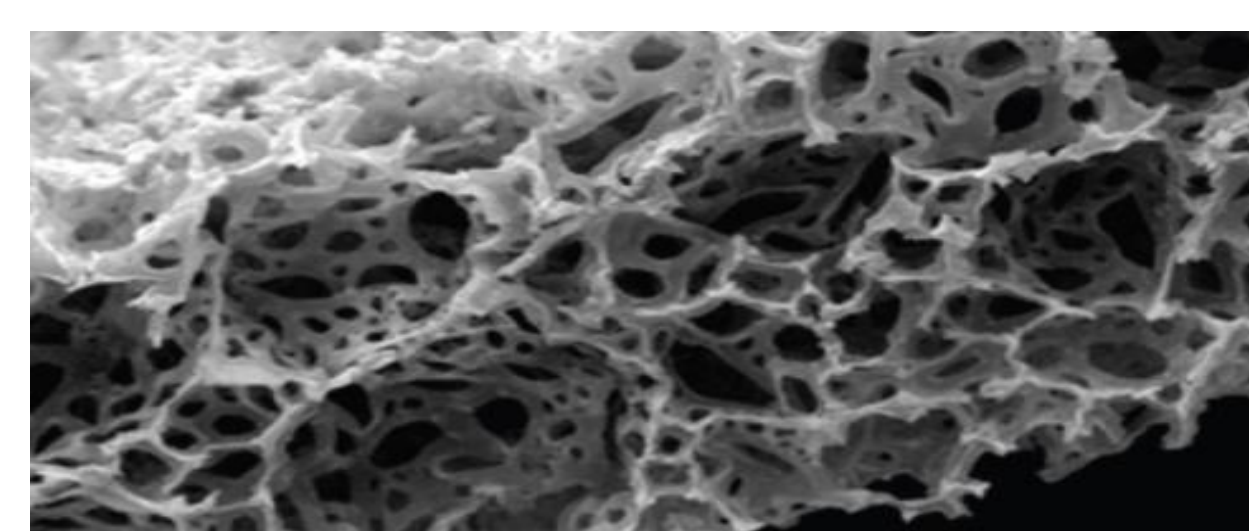
In lacuna: **osteocyte body**.

In canaliculi: **osteocyte dendritic processes**.



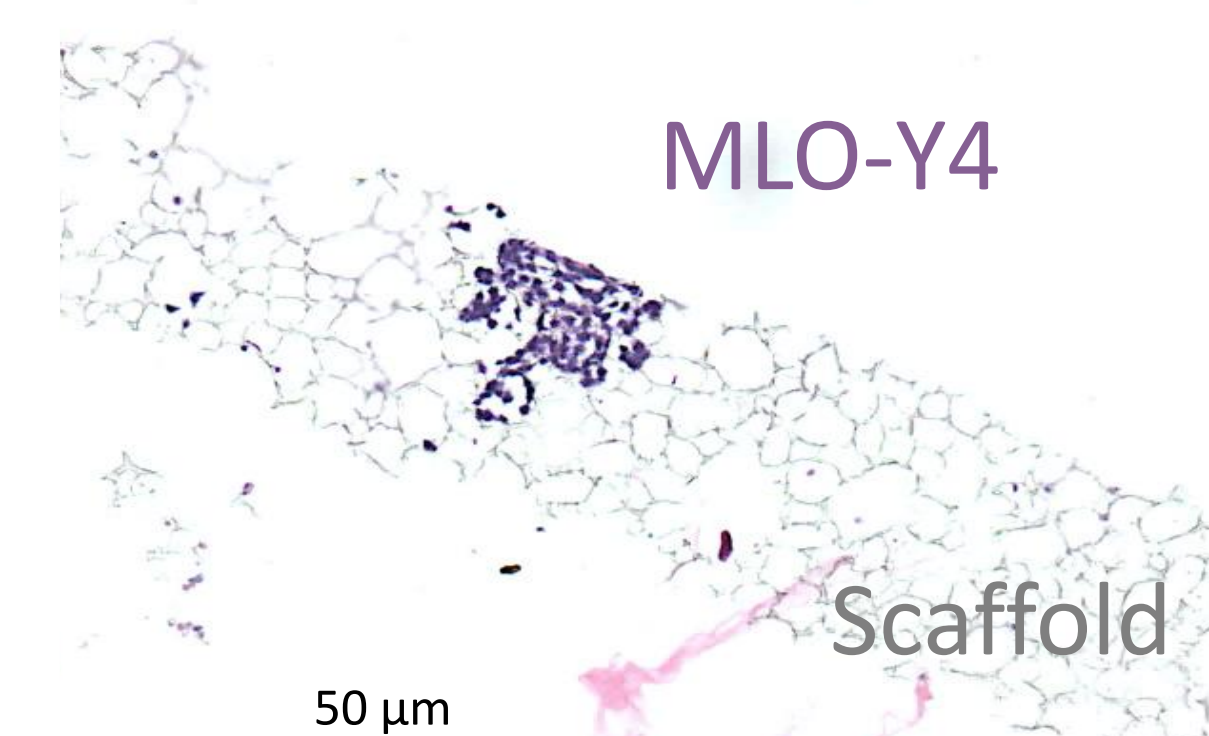
In Vitro Model

3D porous scaffold (Alvetex® 3D Cell Culture Technology)



Osteocytes (MLO-Y4) are seeded on the scaffold.

Histological (HE staining) and transcriptome (osteocyte markers) analysis show growing cells invading the scaffold



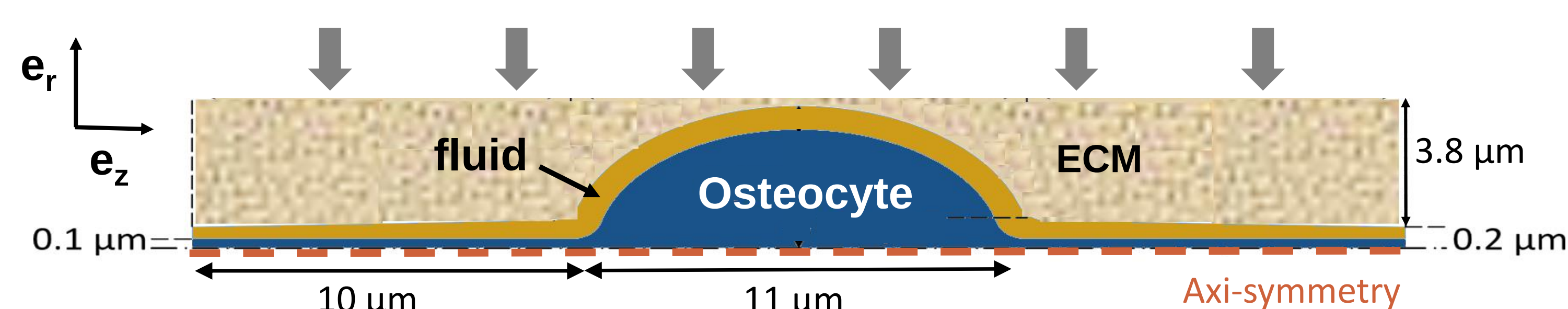
Scaffold adapted to go further ☒

Minimize human intervention and control of the US acoustic dose

In Silico Model

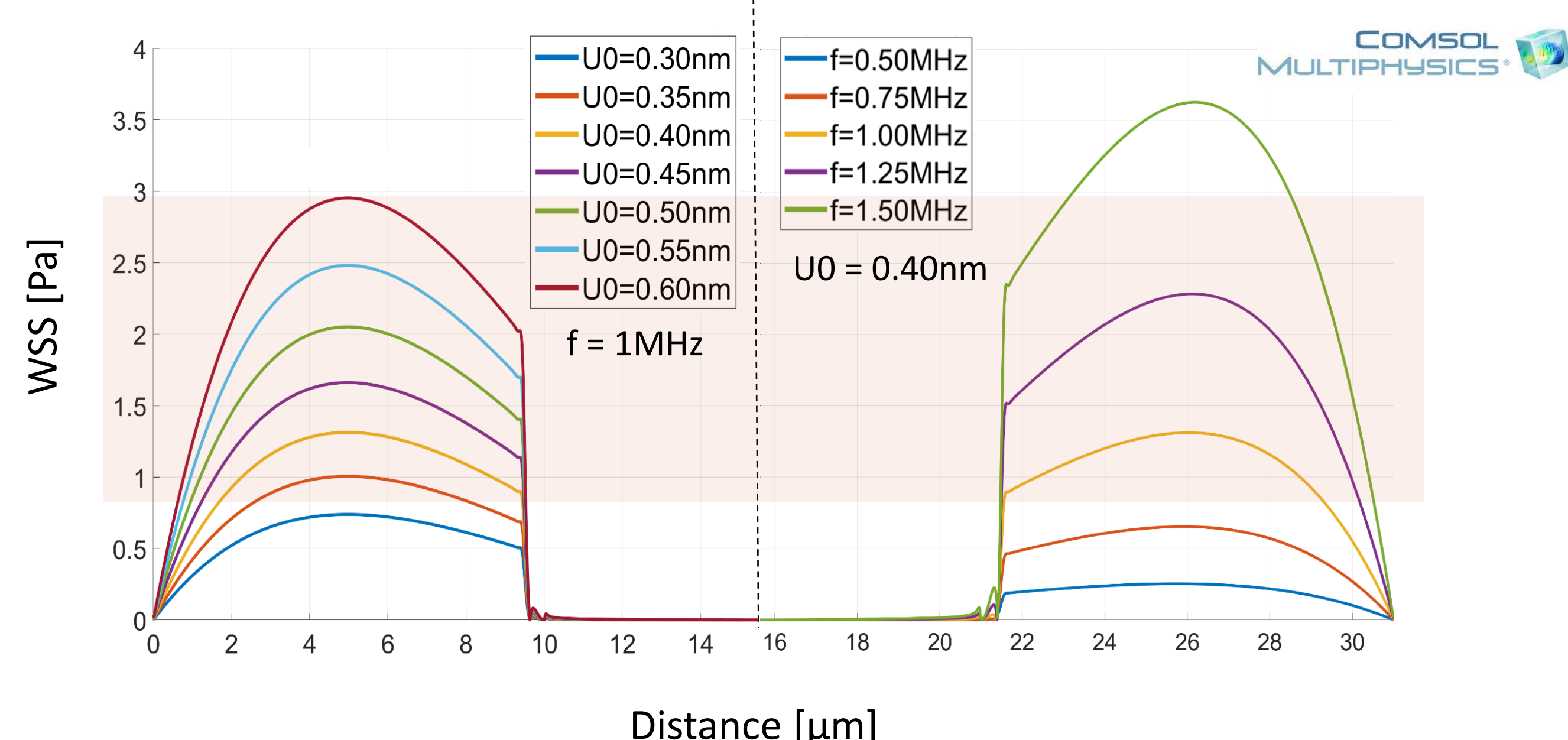
Hypothesis : acoustic pressure → ECM motion → fluid motion → Wall Shear Stress (WSS) on osteocytes.

Idealized 2D axisymmetrical model of one osteocyte in LCN.



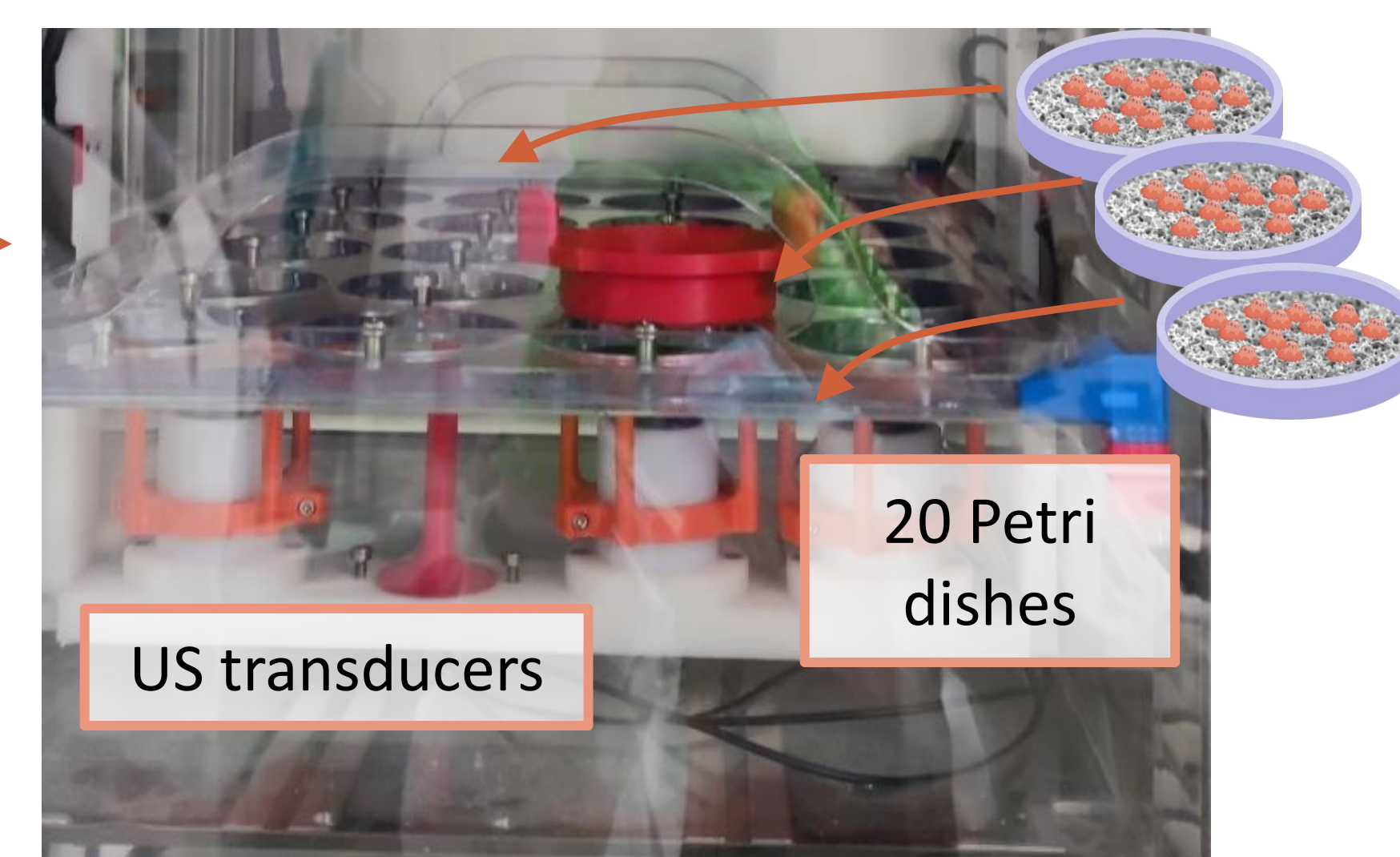
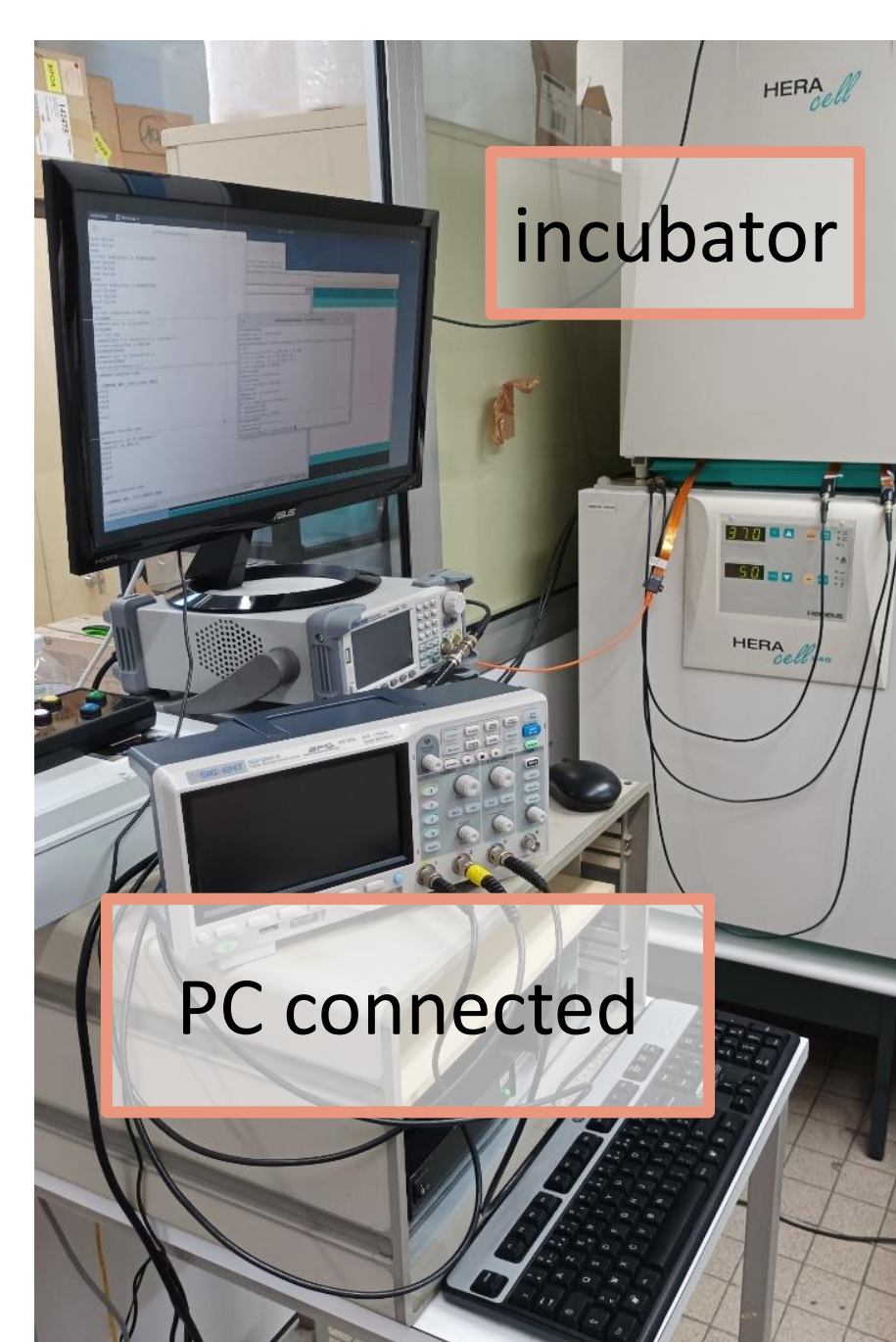
Parametric study:

Amplitude displacement (**U0**) of ECM and US frequency (**f**).



Range of values known to induce biological response under physiological loading ☒

Experimental set-up



Special transducers with integrated lens: Homogenize and enlarge stimulated zones.

Daily automatized motion of 20 Petri dish racks above US transducers for a selected stimulation duration

Experimental set-up ready for biological tests ☒

Next steps

- Validation of the mechanical hypothesis : Identification of other mechanical stimuli (acoustic streaming) ?
- Importing *in vitro* scaffold geometry into *in silico* models.
- Correlation of mechanical stimuli values and biological response.
- Definition of the activation threshold in US (same than physiological loading?) and optimization of acoustic parameters.

