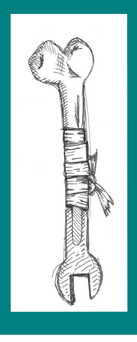
IN SILICO ULTRASOUND STIMULATION OF OSTEOCYTE IN BONE LACUNO-CANALICULAR NETWORK



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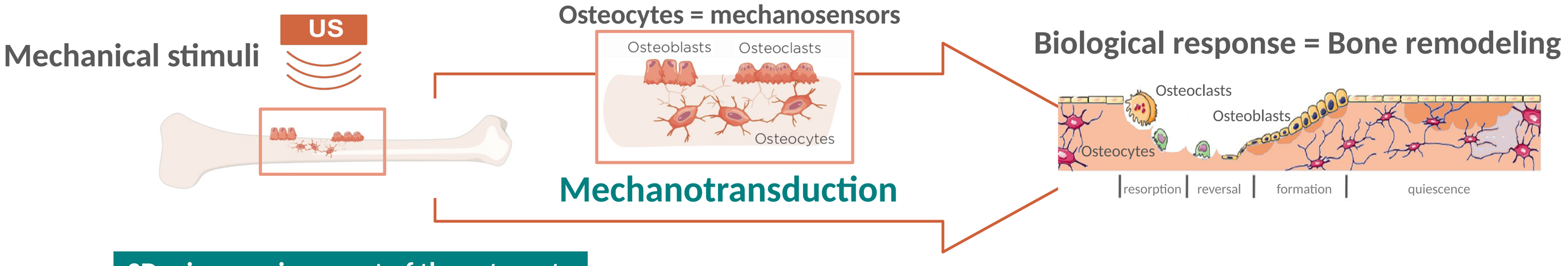
Background

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

Healing with Ultrasound (US) Stimulation ….

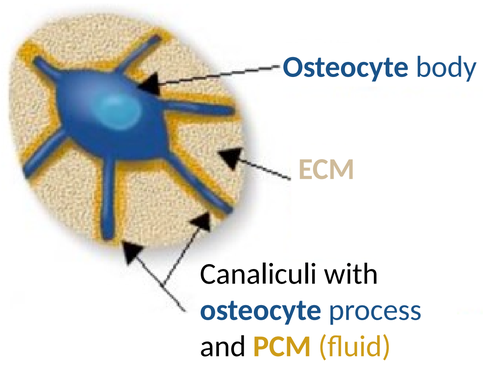
- LIPUS: Low Intensity Pulsed Ultrasound Stimulation.
- US stimulation known since 1950's.

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



3D micro-environment of the osteocyte

Osteocyte surrounded by the PeriCellular Matrix (**PCM**) considered as a fluid embedded in the ExtraCellular Matrix (ECM).



Acoustic streaming in PCM

US → ECM motion → Acoustic streaming → Wall Shear Stress (**WSS**) on osteocytes.

Theoretical background:

- compressible Newtonian fluid
- Eulerian framework
- Navier-Stokes equations
- Energy conservation
- No slip boundary condition

2nd order perturbation theory applied on fluid velocity field $\boldsymbol{v}$, pressure p and mass density ρ:

$$\begin{aligned} \boldsymbol{v} &= \mathbf{0} + \boldsymbol{v}_1 + \boldsymbol{v}_2 \\ p &= p_0 + p_1 + p_2 \\ \rho &= \rho_0 + \rho_1 + \rho_2 \end{aligned}$$

$$\eta\nabla^2\langle\boldsymbol{v}_2\rangle + \beta\eta\boldsymbol{\nabla}(\boldsymbol{\nabla}\cdot\langle\boldsymbol{v}_2\rangle) - \boldsymbol{\nabla}\langle p_2\rangle = \langle\rho_1\partial_t\boldsymbol{v}_1\rangle + \rho_0\langle(\boldsymbol{v}_1\cdot\boldsymbol{\nabla})\boldsymbol{v}_1\rangle,$$

$$\rho_0\boldsymbol{\nabla}\cdot\langle\boldsymbol{v}_2\rangle = -\boldsymbol{\nabla}\cdot\langle\rho_1\boldsymbol{v}_1\rangle.$$

$\langle\cdot\rangle$ time average
β viscosity ratio (β=1/3)
η dynamic viscosity

Finite-element model Comsol Multiphysics

- **PCM** fluid = water → incompressible ($\boldsymbol{\nabla}\cdot\boldsymbol{v} = \mathbf{0}$)
- Weak form PDE
- Thermoviscous acoustics – frequency domain p_1 $\boldsymbol{v}_1$
- Laminar flow module – steady state p_2 $\boldsymbol{v}_2$

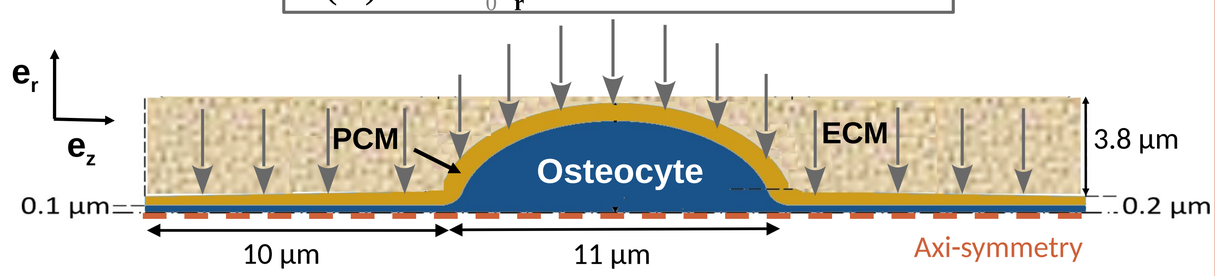
$\boldsymbol{v}_2$ **Streaming velocity → WSS =** η × **shear rate**

In Silico Model

Idealized 2D axisymmetrical model of one osteocyte in LCN.

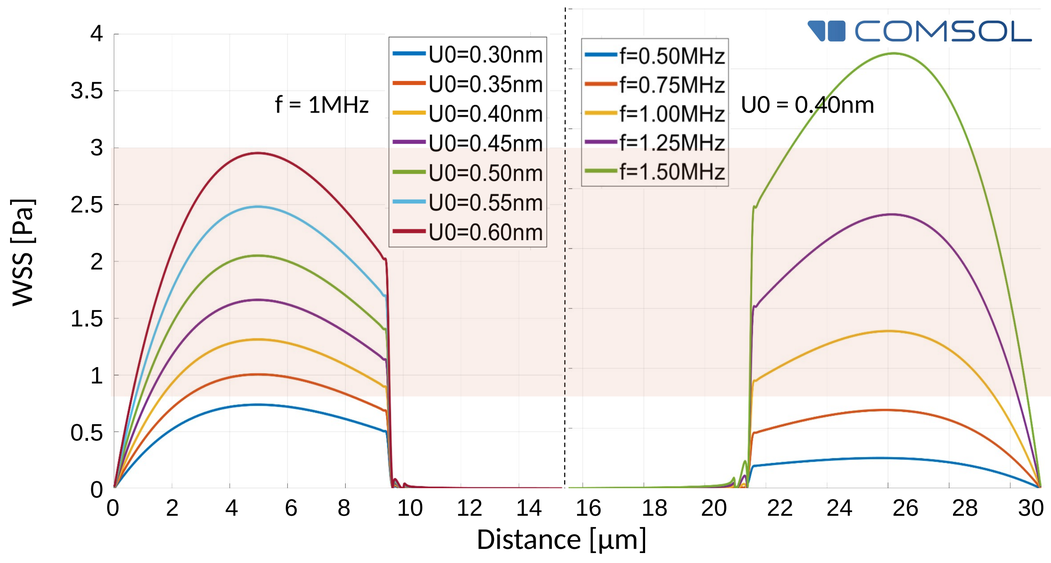
Harmonic displacement of ECM/PCM interface at frequency f

$$\mathbf{U}(\omega) = i\omega U_0 \mathbf{e}_r \quad \text{with } i^2 = -1 \text{ and } \omega = 2\pi f$$



Parametric study:

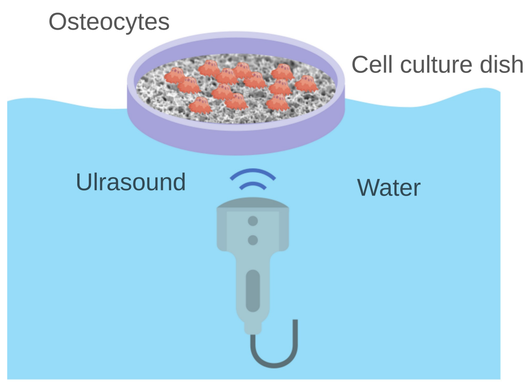
- Amplitude displacement of ECM/PCM interface (U_0);
- US frequency (f).



WSS range of values → biological response under physiological loading

(Weinbaum, J. Biomechanics, 1994)

In Vitro Model

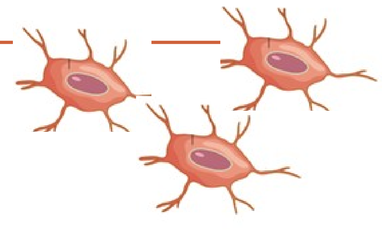


Osteocytes (MLO-Y4) seeded on a 3D porous scaffold (Alvetex® 3D Cell Culture Technology)

Acoustic streaming inside the scaffold?

In progress…

- Acoustic streaming in PCM → WSS liable to trigger biological response;
- Acoustic boundary conditions at PCM/osteocyte interface to be improved;
- Realistic osteocyte geometry;
- Osteocytes network in an osteonal unit.



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