US/osteocyte interaction

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Ultrasound and living tissues

UltraSounds (US) interact with living tissues : destroy (HIFU) and repair (LIPUS)

What is LIPUS ? **L**ow **I**ntensity **P**ulsed **U**ltrasound **S**timulation
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- Large literature (*Duarte 1983, Pilla et al. 1990, Heckman et al. 1994, Takikawa et al. 2000, Hemery et al. 2011, ...*)
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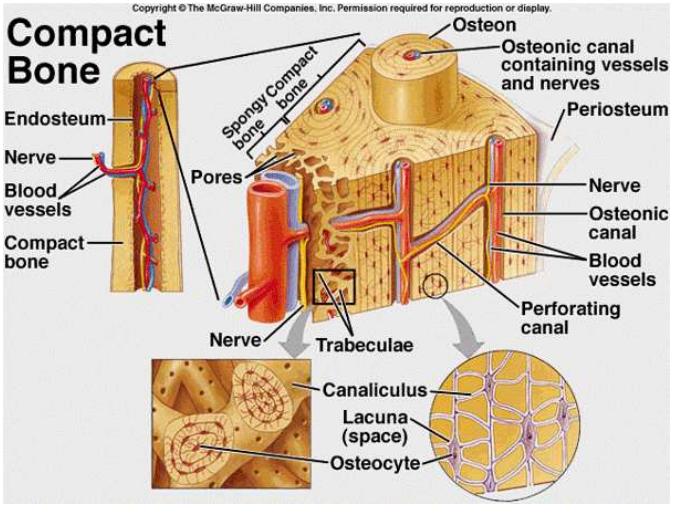
Bone Tissue

How is cortical bone tissue organized ?



- Multiscale and two-level porosity : Havers-Volkmann network (HV) and lacuno-canalicular network (LCN)
- Bone cells : osteocytes
- Multiphasic (solid bone matrix, interstitial fluid and water)

Mechanotransduction
Fluid shear stress on osteocyte
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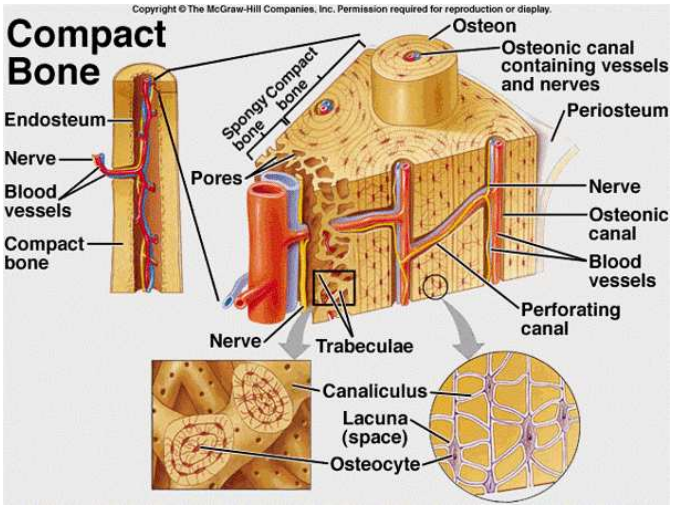

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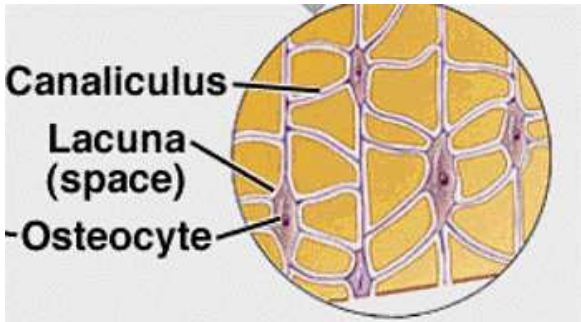
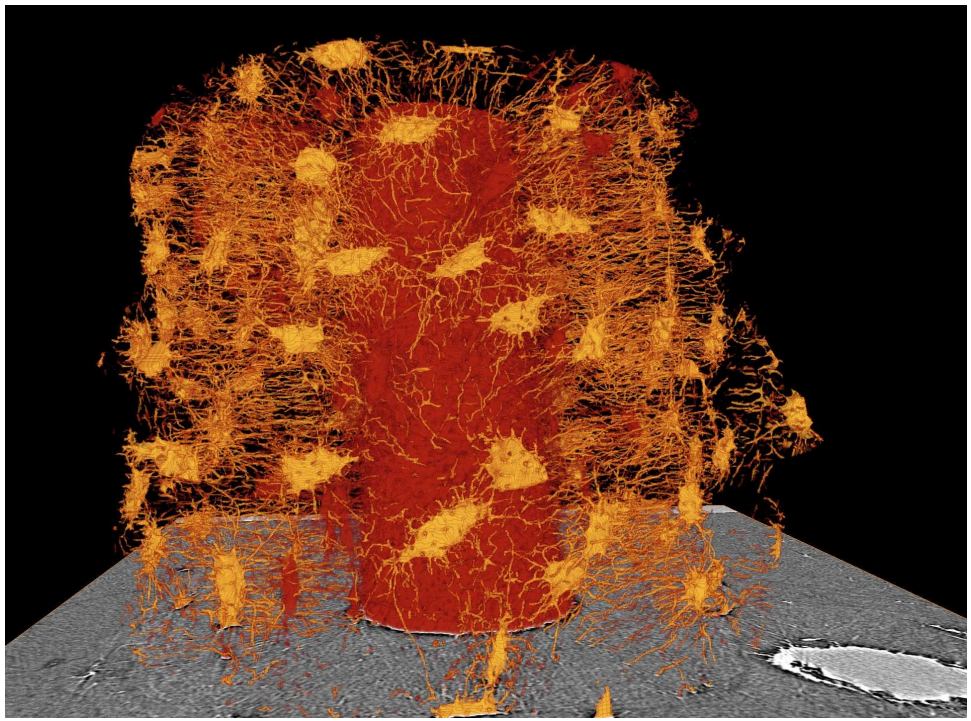
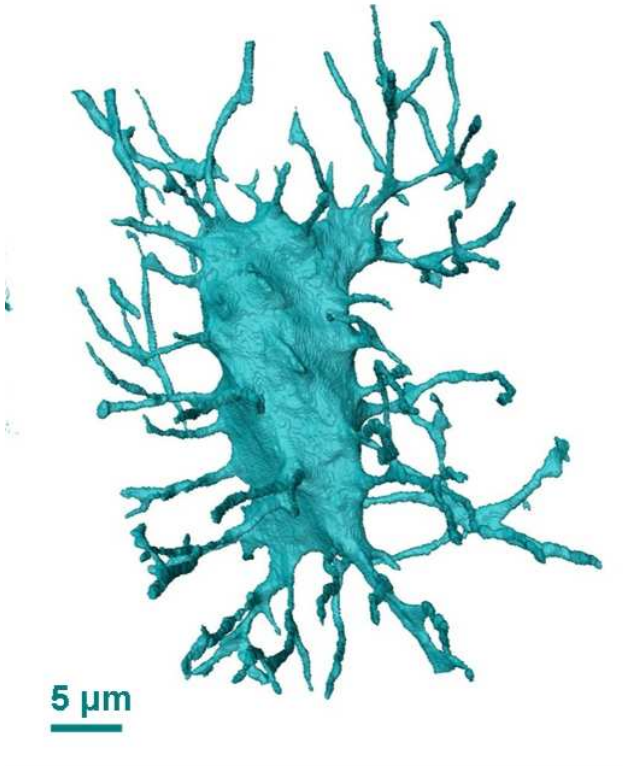


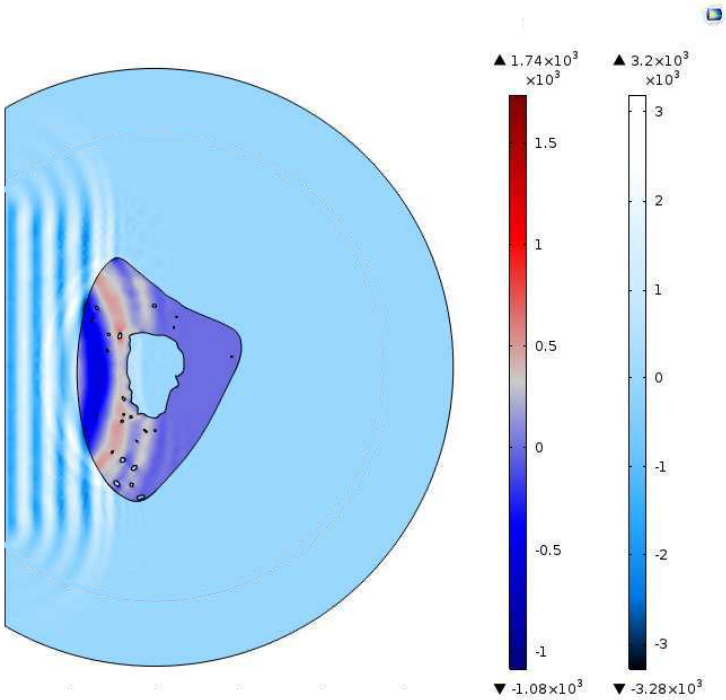
Lacuno-canalicular network and osteocyte ... (en vrai !)

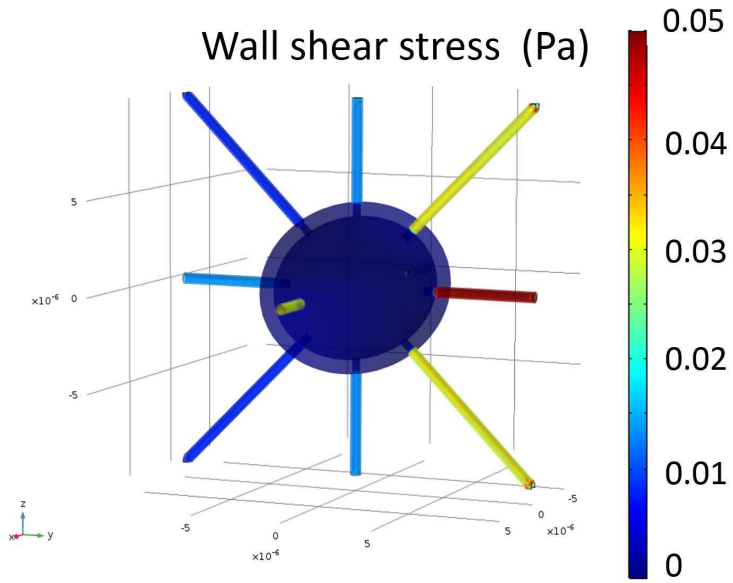




Images from Creatis, Lyon

ESB 2016 : Two-scale numerical model





US stimulation at tissue-scale ⟶ Fluid shear stress at micro-scale

Baron, Guivier Curien, Nguyen and Naili, ESB 2016

US/Osteocyte interaction

How does the osteocyte sense the US stimulation ?

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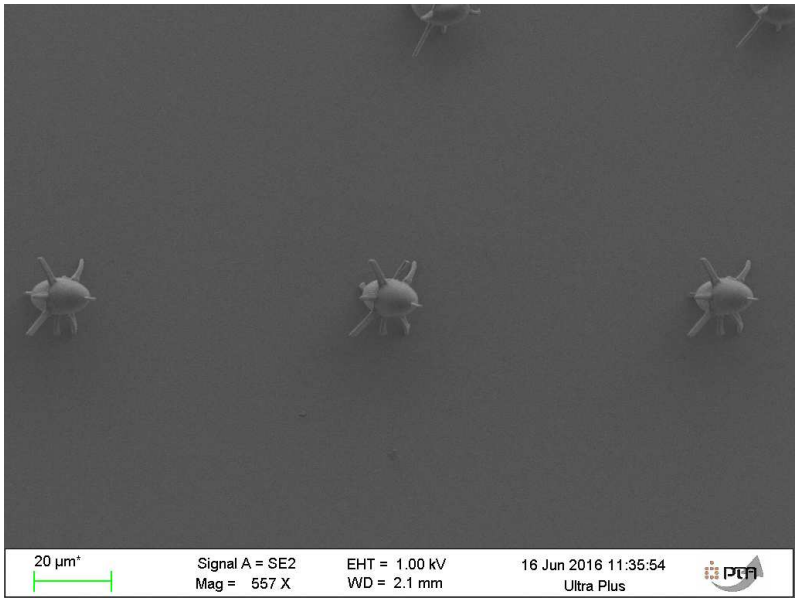
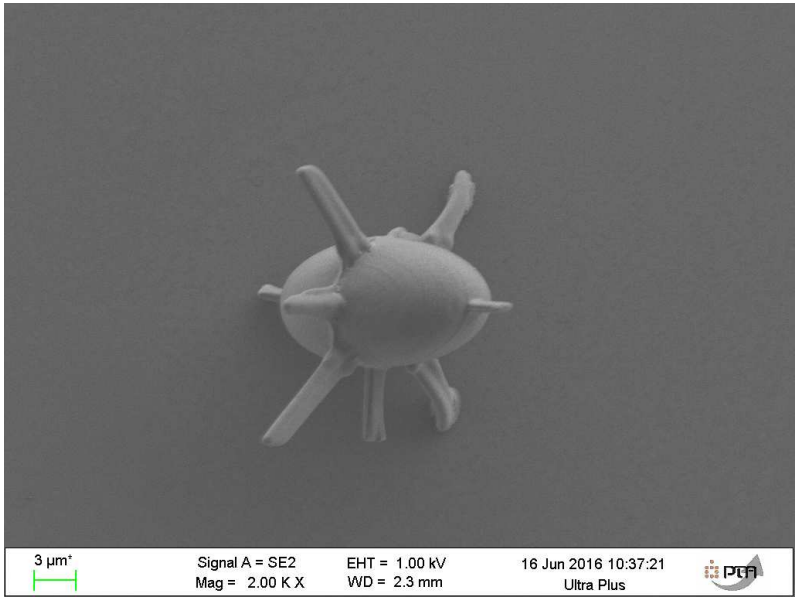
Some hints to mimic the LCN





Olivier Stephan, LiPhy, Grenoble

- Liphy (Grenoble) : High resolution (1-3 μm) but low Young's modulus (E<1 GPa)
- Mateis (Lyon) : Lower resolution (100 μm) but high Young's modulus (E>100 GPa)

How to couple both techniques ? Other techniques ? Sensors inside ?

Some hints

Which measurements ?

- Bone intrinsic properties : LCN permeability
- US stimuation effects
  - fluid flow velocity : 10 to 50 μm/s
  - fluid pressure in the LCN : 0.01 to 3 Pa (*Weinbaum 1994*)
  - pore fluid pressure relaxation time : 10 ms to 10 s (sensor response ?)
  - fluid shear stress on osteocyte processes membrane (pericellular annulus $\approx$ 0.1 μm) : 0.8 to 3 Pa under physiological loading (*Weinbaum 1994*)

but what about US stimulation ?

Perspectives

- 3D cell-culture in realistic environment :

  In addition, new micropatterning techniques have made it possible to seed bone cells in individual wells in a manner that allows them to form an interconnected network with narrow channels that simulate canaliculi in vivo (Guo et al. 2006, You et al. 2008). Such a network is clearly a more realistic model of the lacunar-canalicular system, and ***future studies analyzing the effects of FSS on osteocytes grown in these connected networks will help to identify the cellular pathways in mechanotransduction***'

  Fritton and Weinbaum, 2009

- US load vs physiological load (walk) : influence of the frequency