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# Ultrasound stimulation of bone cells: 3D finite-element model of acoustic streaming around osteocytes.

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## Abstract

### Introduction

Ultrasound (US) stimulation of bone remodeling remains an open question as the underlying mechanisms involved are still poorly understood. Among the possible hypotheses, the propagation of ultrasonic waves (US) in bone tissue could generate acoustic streaming (AS) resulting in fluid shear stress exerted on the wall of osteocytes known as the mechanosensitive conductors of bone remodeling. Osteocytes are dendritic cells surrounded by a viscous pericellular fluid (PCF), ubiquitous in the bone extra-cellular matrix (ECM) forming a complex micrometric 3D network called the lacuno-canalicular network (LCN).

This paper investigates the interaction of US with the osteocyte dendrite (OD) confined in a canaliculus, as it is considered as the most mechanosensitive part of the cell. The aim is to explore the relevance of taking into account the irregular 3D shapes of the canaliculus and dendrite in terms of mechanical solicitations induced by US stimulation.

### Material & Methods

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From images (FIB-SEM imaging "slice and view" in BSE mode (Gianuzzi 2004), FEI Helios NanoLab 660, pixel size  $16.78 \times 16.78 \times 20$  nm<sup>3</sup>), a realistic 3D geometry of a canaliculus of rabbit cortical bone is reconstructed and implemented in the Finite-Element software Comsol Multiphysics (v. 6.2). The geometry of the dendrite inside the canaliculus (not accessible by imaging) is deduced from the canaliculus wall geometry.

The acoustic properties of the cell dendrite and of the PCF are similar to those of water, except that the viscosity of the PCF is supposed to be 10 times higher than water dynamic viscosity ( $\mu_{\text{water}}=0.65 \cdot 10^{-3}$  Pa.s).

To mimic the US stimulation of bone cells inside the LCN, a first order oscillating velocity  $\mathbf{U1}$  is imposed along the ECM/PCF interface under the form of a harmonic acoustic wave at frequency  $f$  of 1 MHz with an amplitude of displacement  $d_0$  propagating in the US propagation direction:  $\mathbf{U1}(f) = i2\pi f d_0 \mathbf{e}_x$ .

The acoustic streaming is a second-order (non-linear) acoustic effect which results in a steady flow. In order to investigate the acoustic streaming induced by US stimulation inside the PCF, we need to solve the second-order Navier-Stokes equations obtained by the perturbation method.

In Comsol Multiphysics, the Thermoviscous Acoustics module (in frequency domain) is used to resolve the first order acoustic field which provides the source term for the second order equation implemented in the Laminar Flow module.

From the acoustic streaming velocity (time-averaged second-order term) thus obtained, the resulting wall shear stress (WSS) applied at the PCF/process interface is calculated.

## Results & Discussion

The WSS is plotted along the interface PCF/OD. The values are compared to those obtained for idealized 3D-geometries (annular tube) deduced from the realistic one and to the results obtained in 2D cross-sections as previously presented in (Baron 2023).

We investigate how canaliculus and dendrite geometries could have an influence on the US-induced PCF flow. Finally, the quantification of the WSS induced by acoustic streaming is questioned in regard of stress levels that can trigger a biological response (Weinbaum 1994).

**Keywords:** acoustic streaming; wall shear stress, osteocyte; mechanotransduction; FE model; FIB-SEM.

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